

OXIDATION OF SULFAMIDES
AND
TRIAZINONES

By

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at the University of Leicester

September, 1970

Department of Chemistry,
University of Leicester.

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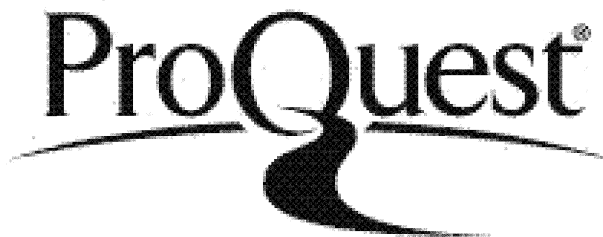
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STATEMENT

The work described in this thesis was carried out by the author in the Department of Chemistry of the University of Leicester under the supervision of Professor C. W. Rees and Dr. T. L. Gilchrist. No part of it is concurrently being submitted for any other degree.

Signed.....*Douglas L. Forster*.....

Douglas L. Forster

September 1970

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Abstract

Part I.

The Favorskii and Ramburg-Bäcklund reactions are reviewed, together with the thermolysis and photolysis of ketones and sulfones.

In contrast with NN'-dialkyl sulfamides the hypochlorite oxidation of diaryl sulfamides is not found to be a general route to aromatic azo compounds; instead the major products are usually quinoneanils, formed in a new aromatic rearrangement. Photolysis of the aryl sulfamides and thermolysis of their NN'-dichloro derivatives do give azo compounds, however. The photochemical reaction appears to be intramolecular, possibly involving extrusion of sulfur dioxide as the first step.

Part II.

Oxidation of 3-aminobenzotriazin-4-ones with lead tetra-acetate proceeds by two independent routes, involving the loss of one mole of nitrogen to form indazolones and of two moles of nitrogen to form benzocyclopropenones. The indazolones, which can be intercepted by dienes, react

with nucleophiles without rearrangement of the carbonyl group. Benzocyclopropenones react with nucleophiles with rearrangement of the carbonyl group to give isomeric pairs of benzoic acid derivatives. Concerted fragmentations of intermediate amino-nitrenes are proposed to explain these results. The mechanisms suggested are supported by a ^{15}N -labelling experiment and by extended Hückel molecular orbital calculations.

A method is described for the gas phase thermal fragmentation of cyclic α -carbonyl azo compounds. By this method 3-indazolone gave biphenylene and phthalaz-1,4-dione gave benzocyclobutene-1,2-dione.

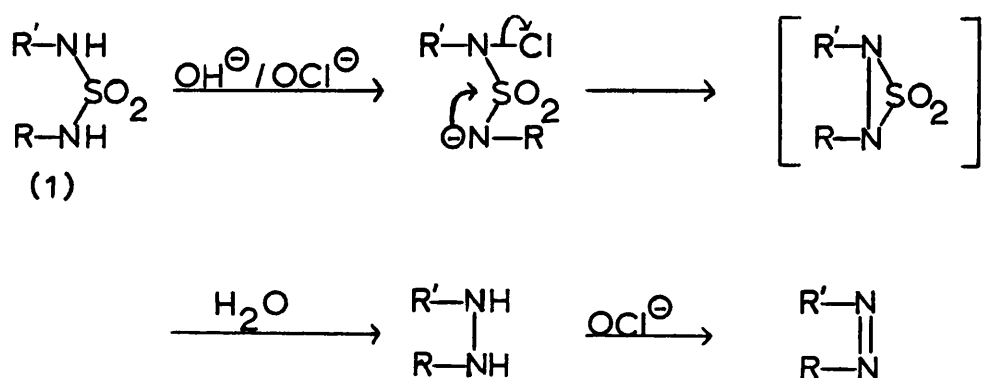
PART I

OXIDATION OF SULFAMIDES

INTRODUCTION

Introduction

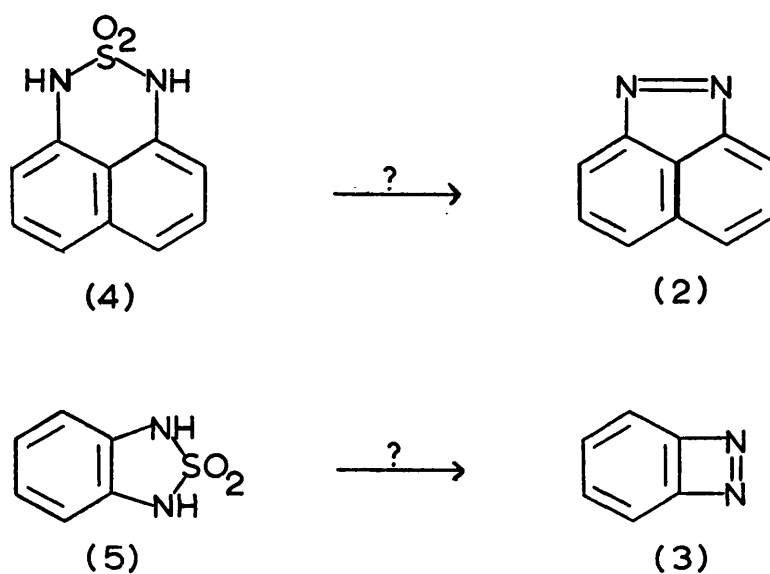
A report by Ohme and Schmitz that dialkyl sulfamides (1) gave azoalkanes in good yield via an intramolecular mechanism involving 1,3-dehydrohalogenation¹ (Scheme 1), led us to consider the formation of the elusive benz[c,d]indazole² (2) or of benzo[c]1,2-diazete (3) by oxidation of the



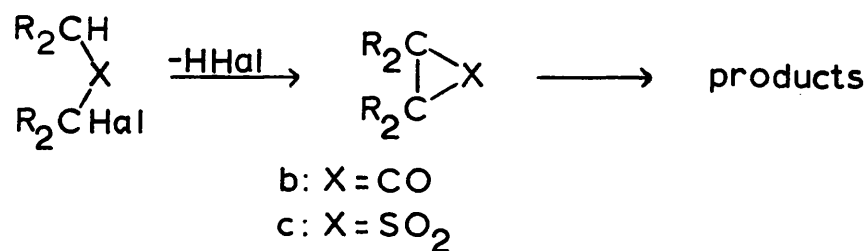
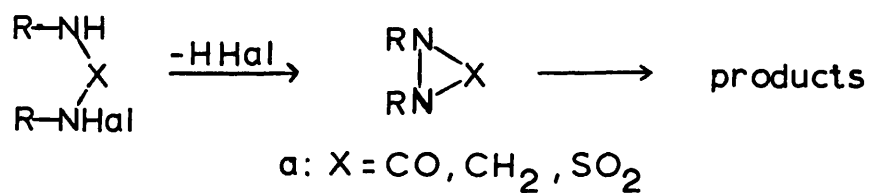
(Scheme 1)

corresponding sulfamides (4) and (5). Presumably (3) would be unstable and might be expected to fragment to nitrogen and benzyne, or to form cis,cis-muconodinitrile via o-phenylenedinitrene.³

Displacement reactions of the form shown in Scheme 2a have been studied preparatively, but not mechanistically.

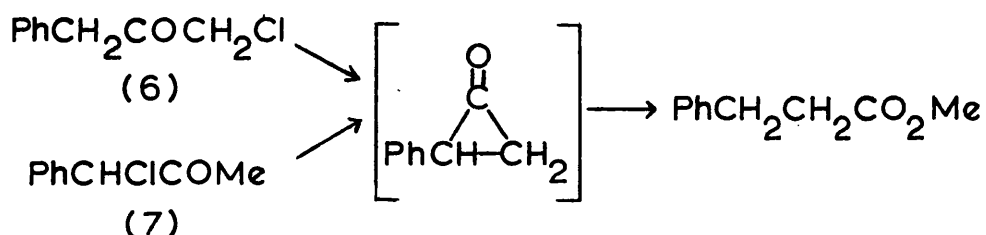


Detailed mechanisms have, however, been proposed for the better known carbon analogues, the Favorskii (Scheme 2b) and Ramberg-Bäcklund (Scheme 2c) reactions.

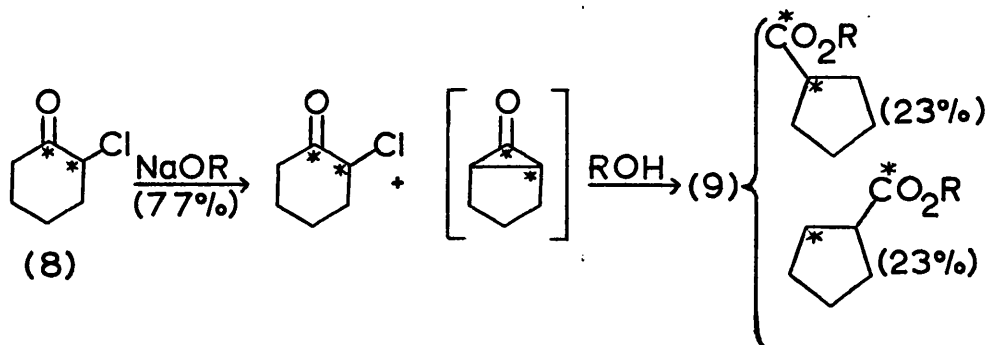


(Scheme 2)

The base induced rearrangement of α -haloketones to give carboxylic acid derivatives, the Favorskii rearrangement⁴, is the most familiar member of this series of 1,3 rearrangements. Evidence for a symmetrical intermediate was given by the observation that the isomeric chlorophenylacetones (6) and (7) both gave methyl hydrocinnamate in methanolic sodium methoxide,⁵ and

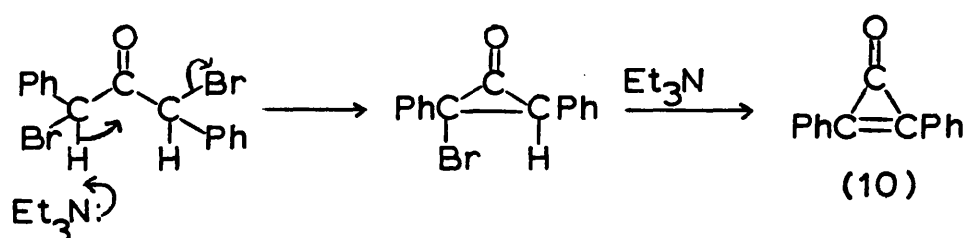


that 2-chlorocyclohexanone-1,2-¹⁴C (8) on interrupted treatment with sodium 1-methylbutoxide gave 1-methylbutyl cyclopentanecarboxylate (9) and recovered starting material with the labels as shown.⁶



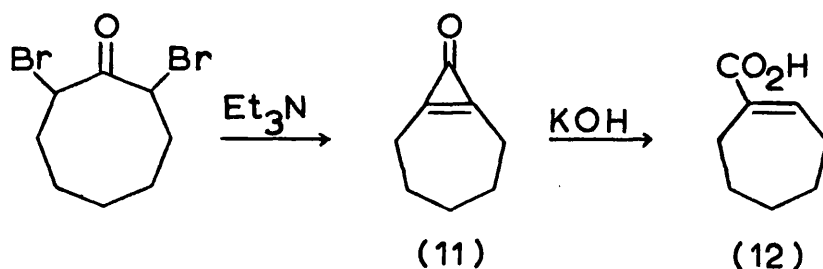
Further evidence was firstly given by Breslow's synthesis of diphenylcyclopropenone (10) from α, α' -dibromodibenzyl

ketone and of cycloheptenocyclopropanone (11) from 2,8-dibromocyclooctanone by the action of triethylamine in an inert solvent.⁷



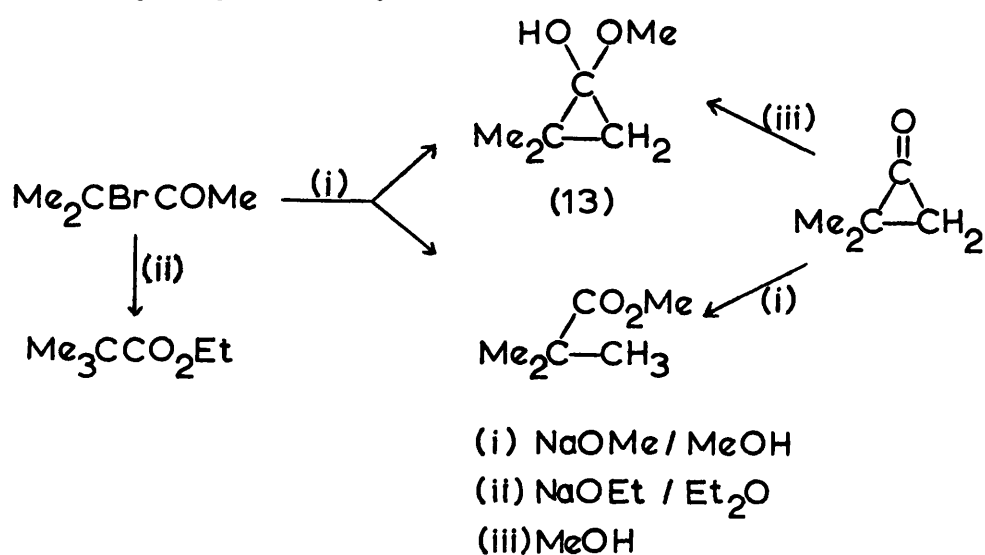
Treatment of (11) with aqueous potassium hydroxide gave the expected cycloheptene-1-carboxylic acid (12).⁷

Secondly, Hammond and Turro observed that 2,2-dimethylcyclopropanone gave a hemiketal (13) with methanol, and only

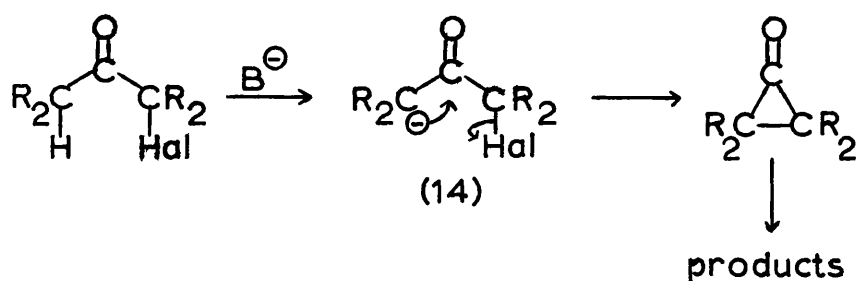


methyl trimethylacetate on treatment with methanolic sodium methoxide.⁸ These products were identified from the rearrangement of 3-bromo-3-methyl-2-butanone in methanolic sodium methoxide, while the action of sodium ethoxide in ether

gave only ethyl trimethylacetate.⁹



These results are best satisfied by a carbanionic mechanism (Scheme 3) with a general base B^- and nucleophilic attack on the intermediate cyclopropanone to give the observed products. Recent work has been designed to find the rate



(Scheme 3)

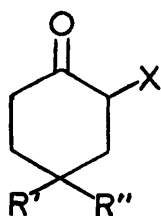
determining step of the reaction, and whether a discrete

carbanion (14) is involved in an internal S_N2 displacement of halide as shown.

The rearrangements of 2-chloro-, 2-bromo- and 2-iodocholestan-3-one had a primary deuterium isotope effect and an order of reactivity $I > Br > Cl$, showing that both α' -proton loss and elimination of halide occur in rate determining steps. Interruption experiments showed the expected fast pre-arrangement α -proton exchange with all three haloketones, with a superimposed 40% α' -proton exchange in the 2-chlorocholestan-3-one.¹⁰ This latter is consistent with initial formation of the carbanion at C_4 , followed at a comparable rate by the ring closing elimination of chloride. No α' -proton exchange was observed for the bromo- or iodoketones, leaving the question of a concerted or consecutive breaking of the C-H and C-Hal bonds undecided.

Bordwell and co-workers, however, studied the Favorskii rearrangement of the substituted cyclohexanones (15)¹¹. For steric reasons epoxy ether formation, a principal side reaction for bromoketones, was inhibited in (15b). Under these circumstances they found a small α' -deuterium isotope effect for (15b) with partial pre-rearrangement α' -proton exchange; but no isotope effect and complete pre-equilibrium exchange

for (15a). The large halogen effect $k_{\text{Br}}:k_{\text{Cl}}$ of 116 for (15a) and (15b) was consistent with a carbanionic mechanism, especially as this value was a minimum, k_{Br} being still limited by the initial α' -ionisation. In other bromoketones e.g. (15c) and the bromocholestanone reported above, the rate determining step was usually the initial proton abstraction, and this effect became noticeable in the corresponding chloroketones. The variable leaving group effects were better



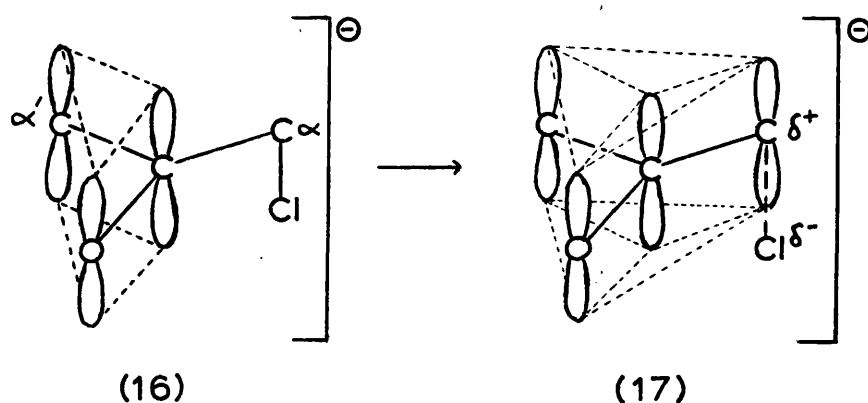
(15)

- a: $R' = R'' = \text{Ph}$; $X = \text{Cl}$
 b: $R' = R'' = \text{Ph}$; $X = \text{Br}$
 c: $R' = \text{Ph}$; $R'' = \text{Me}$; $X = \text{Br}$

explained by a stepwise rather than a concerted elimination mechanism, for which $k_{\text{Br}}:k_{\text{Cl}}$ should be almost constant.

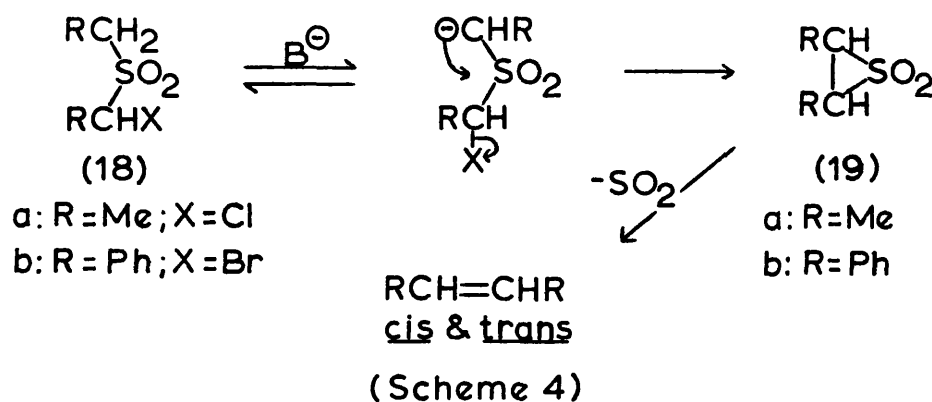
Bordwell and Scamehorn then studied the effect of electronic and structural variations on the rate of rearrangement of ring substituted α -chlorobenzyl methyl ketones, which they showed lost halide in the rate determining step. Their

observations¹² that electron donating substituents favoured the Favorskii path while electron withdrawing substituents decreased the yield of rearranged ester, that a plot of $\log k_{\text{Favorskii}}$ vs. Hammett σ^+ values gave an excellent straight line with negative ρ constant, coupled with the large $k_{\text{Br}}:k_{\text{Cl}}$ ratio found previously, favoured an extensive heterolysis of the C-Cl bond in the transition state; coupled with strong carbanionic character and thus incomplete formation of the C-C bond of the cyclopropanone. It was suggested that ionisation of the halide was assisted by overlap of the developing p orbital at C_α with the parallel π orbitals of the enolate ion (16).

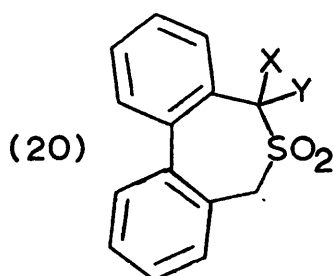


This transition state (17) for displacement of halide is inherently more likely than the alternative internal S_N2 displacement involving rotation of the $C\alpha'$ -carbanion out of conjugation with the carbonyl π system. The stability of (17) should be enhanced by conjugated aryl substituents. It has been postulated as an intermediate to explain the increased reactivity of α -chlorodibenzyl ketone compared with chloroacetone towards methanolysis in the presence of 2,6-lutidine as a weak non-nucleophilic base.¹³

The related Ramberg-Bäcklund base-induced rearrangement of α -halosulfones to give olefins (Scheme 4) has also been mechanistically studied.¹⁴



The existence of rapid, reversible carbanion formation has been established by finding that in deuterated base α -chloroethyl sulfone (18a) rearranged to give 2-butene,¹⁵ 2-chloro-2,7-dihydro-3,4:5,6-dibenzothiepin 1,1-dioxide (20; X=H, Y=Cl) gave phenanthrene,¹⁶ and α -bromobenzyl benzyl



sulfone (18b) gave stilbene,¹⁷ all with essentially complete di-deuteration at the new double bond. The possibility of the deuterium incorporation occurring in the episulfone (19) was eliminated since, under similar conditions to those of the rearrangement of (18a), (19a) gave 2-butene with only 5% deuterium incorporated,¹⁵ and interruption experiments on (18b) gave recovered sulfone with complete α,α' -tri-deuteration.¹⁷

From similar experiments to those described for the Favorskii reaction, the α -sulfonyl carbanion has been found to lie on the rearrangement path. For example, the

leaving group effect $k_{Br}:k_{Cl}$ for benzyl α -halobenzyl and benzyl α -halomethyl sulfones is large (120-620),¹⁷ more in accord with known carbanionic mechanisms than the smaller (ca. 50) value observed in concerted 1,2 eliminations. The alternative intermediacy of an α -sulfonyl carbene was ruled out by the observation that α,α -dichlorodibenzyl sulfone underwent a ready rearrangement to give tolan and 1,2-diphenylethylene-1-sulfonic acid, and that (20; X=Y=Cl) gave 9-chlorophenanthrene and phenanthrene-9-sulfonic acid¹⁸; while phenyl α -chlorobenzyl sulfone and tert-butyl chloromethyl sulfone (both without α' -hydrogen) did not eliminate chloride ion.¹⁷

These results showed that the transition state is formed via a carbanion and has an extensively heterolysed C-Hal bond; but, in direct contrast to the Favorskii reaction, the observation of a positive ρ slope for the series $ArCH_2XSO_2Me$ ¹⁹ showed that the carbanion must have largely completed the C-C bond of the episulfone.

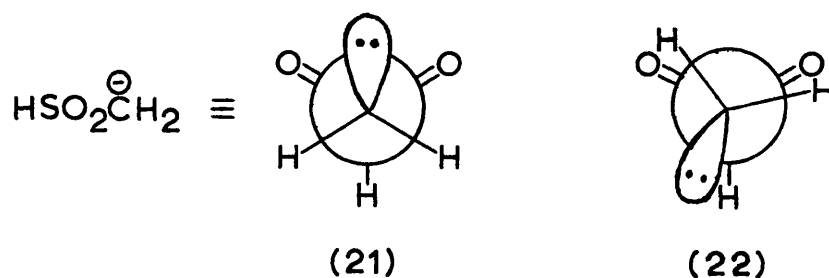
The stereochemical aspects of the rearrangement have been studied, particularly in view of the strong preference for formation of the thermodynamically less favourable cis-olefin. The rearrangement of (18a) in a variety of bases

gave 3:1 cis:trans-2-butene, while decomposition of the episulfone cis-(19a) under similar conditions was stereospecific, giving only cis-2-butene (>99%). With the strong base tert-butoxide, cis-(19a) exchanged α -protons and epimerised faster than it decomposed, and predominantly trans-2-butene was isolated. The olefin did not isomerise under the reaction conditions.¹⁵ In methanolic sodium methoxide, however, both cis- and trans-(19b) decomposed to give trans-stilbene at identical rates,²⁰ although the thermal extrusion of SO₂ was stereospecific.^{20,21}

Epimerisation of (19b) cis to trans was clearly occurring in the base; but exchange experiments showed that cis-(19b) exchanged protons with retention of configuration faster than it epimerised.²⁰

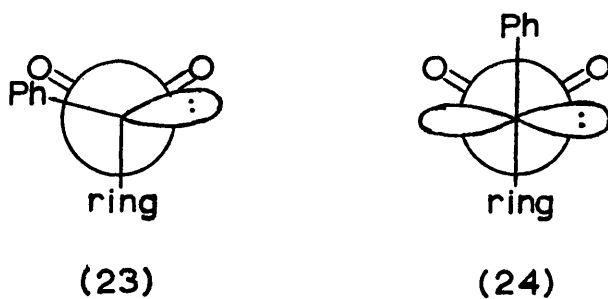
An explanation for this can be given. Various workers have assumed either a pyramidal carbanion with hindered inversion²², or a planar carbanion with hindered rotation²³ to explain the observed retention of configuration in α -sulfonyl carbanions. A total energy contour diagram has been calculated for the hydrogen methyl sulfonyl carbanion.²⁴ This shows a marked energy minimum in a pyramidal conformation (21) with

the carbanion electron pair directed along the bisector of the acute OSO angle. The rotational conformer (22) is an



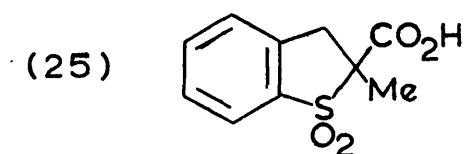
energy maximum for the pyramidal geometry.

Due to the configurational requirements of the ring, (19b) must ionise to an eclipsed pyramidal carbanion (23) which epimerises via the planar carbanion (24). From the energy



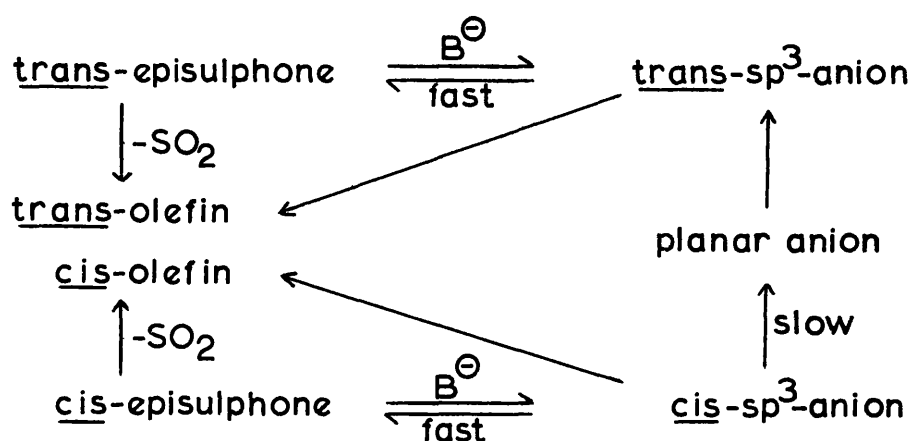
surface of (21), a conformation such as (23) would be more

stable than one such as (24) by ca. 1.1 k.cal:mole. Qualitatively, despite the bulk of the phenyl group, the small S-C-C angle of the ring would be expected to stabilise (23) in favour of (24). Such stabilisation would explain the stereospecific proton exchange of cis-(19b) via (23) while allowing slower epimerisation via (24). A similar argument can explain the racemisation during decarboxylation of the optically active substituted dihydrobenzo[b]thiophene (25),²⁵ which is also constrained to an eclipsed carbanion.



The conformation of the α -sulfonyl carbanion was considered by Corey and Lowry, whose stated requirements²⁶ are fulfilled by (21).

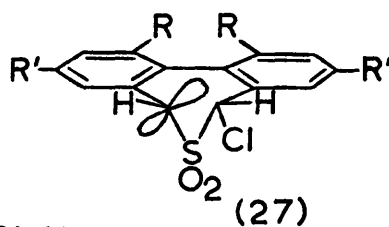
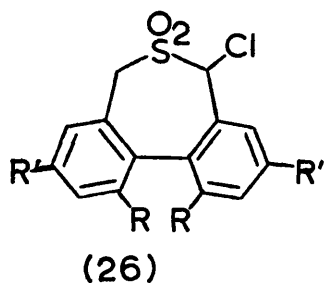
The observed epimerisation of the cis-episulfone in strong base can thus be explained by a path such as (Scheme 5). The proportion of trans isomer is dependent on the lifetime



(Scheme 5)

of the episulfonyl carbanion, and hence on the acidity of the α -proton in the reaction medium.

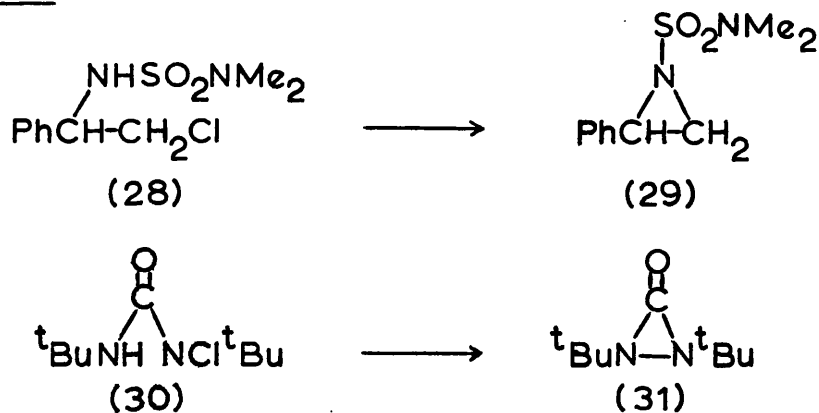
An explanation has been given by Paquette for the isomeric ratio of olefins under conditions where the episulfone does not epimerise. The observed rearrangements of (26,a and b) and the inertness of (26c) were rationalised¹⁶ in terms of a semi-W-transition state²⁷ via the quasi-stable conformation (27), sterically disallowed for (26c).



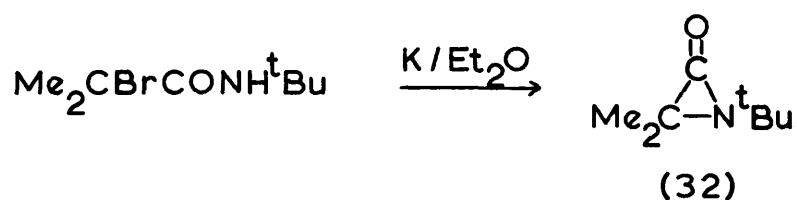
- a: R = R' = H
 b: R = H; R' = Me
 c: R = Me; R' = H

In general the Ramberg-Bäcklund displacement requires a carbanion anti to the sulfonyl oxygens, and from ref. 21 such an anion would be expected to be of lowest energy when planar. On this basis a conformational analysis²⁸ showed smaller non-bonding interactions in the equilibrium steps to the cis-semi-W-transition state than to the trans, thus leading preferentially to the cis-episulphone, and hence to the cis-olefin.

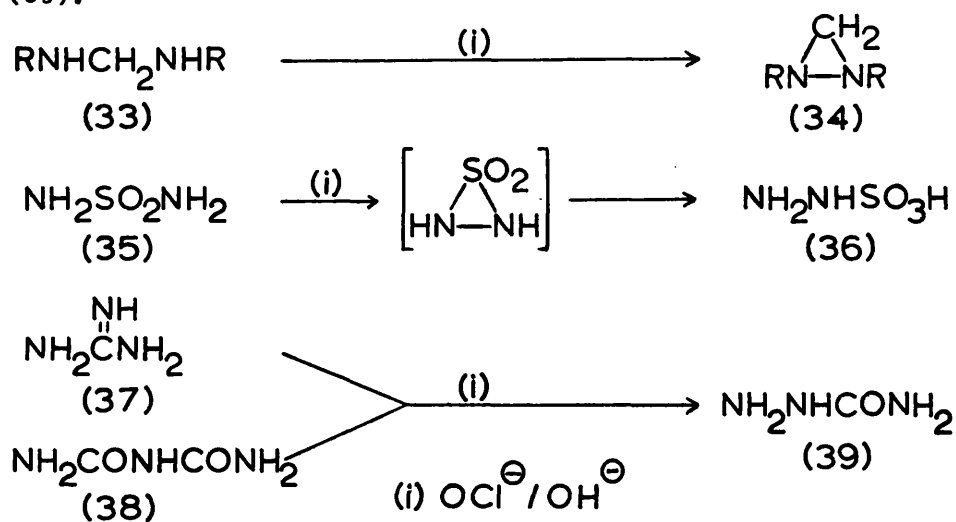
Besides the work of Ohme referred to on page 1, there have been extensions of these reactions to systems containing nitrogen heterocyclic intermediates. The aziridine (29) was prepared²⁹ by base cyclisation of the substituted sulfamide (28) and Green and Stowell³⁰ obtained di-tert-butyldiaziridinone (31) from N,N'-di-tert-butyl-N-chloroureia (30) and potassium in pentane or tert-butoxide in tert-butanol.



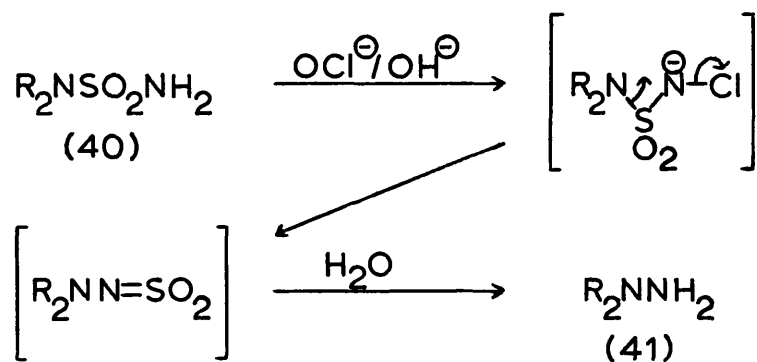
The marked stability of (31) towards thermolysis and nucleophilic attack was reminiscent of cyclopropenones, and was in contrast to the lability of the similarly prepared α -lactam, 1-tert-butyl-3,3-dimethylaziridinone³¹ (32).



N-Halogeno intermediates were also postulated in the cyclisation of the dialkyl amins (33) to the diaziridines (34)^{32,33} of sulfamide (35) to hydrazinosulfonic acid^{32,34} (36), and of guanidine (37) and biuret (38) to semicarbazide (39).³²

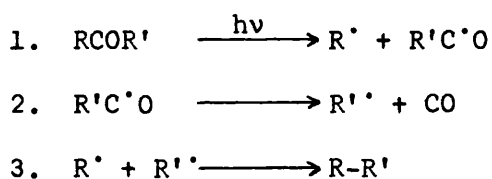


During the course of the work described in this thesis, Ohme³⁴ extended the original N,N'-dialkylsulfamide oxidation to include N-alkyl and N-acylsulfamides which gave the corresponding hydrazine or hydrazide respectively. He also observed the oxidation of N,N-dialkylsulfamides (40) to the hydrazines (41) and proposed the mechanism shown.



During the course of work on the generation of aryl azo compounds, we observed their formation via the intramolecular photolytic desulfonation of diaryl sulfamides. As acyclic sulfones are in general stable to photolysis and thermolysis, it seemed valuable to survey cases of intramolecular extrusion of sulfur dioxide from sulfones, and the related decarbonylations of ketones or amides.

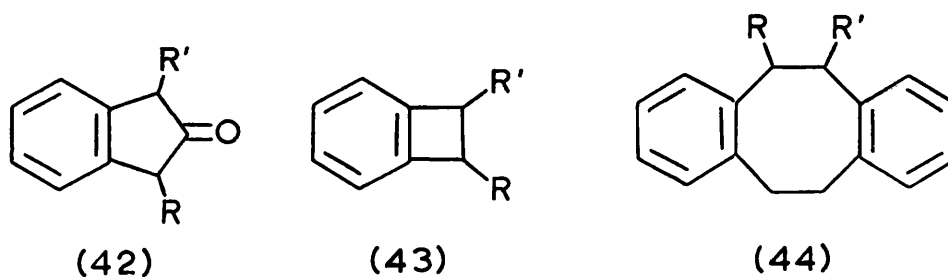
Photolytic decarbonylation is a general gas phase reaction of cyclic and acyclic ketones. The mechanism - the "Norrish Type I Process" - involves decarbonylation of an intermediate acyl radical and subsequent radical recombination (Scheme 6).³⁵



Scheme 6

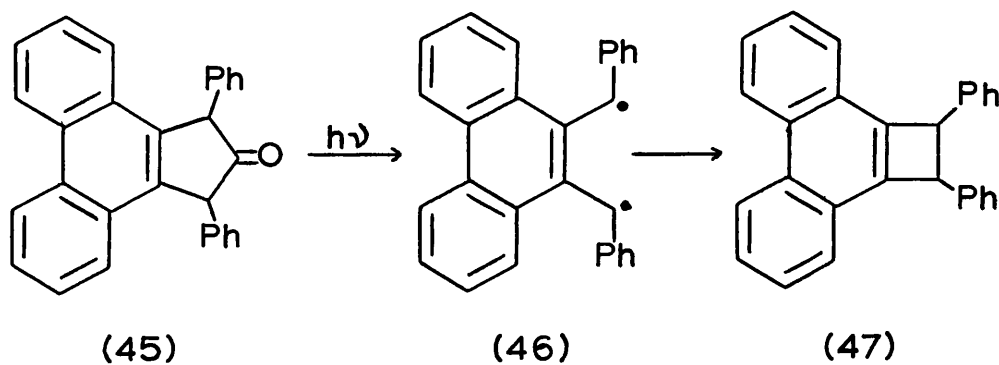
In solution, the scope of the intramolecular decarbonylation is severely limited to small and medium ring cyclic ketones, and is only of preparative importance when the intermediate diradical is structurally stabilised. Thus ketones (42b) and (42c) on irradiation in benzene gave the dimeric dibenzooctadienes

(44a) and (44c) respectively; only ketone (42a) gave any benzocyclobutene (43a - 80% yield)³⁶

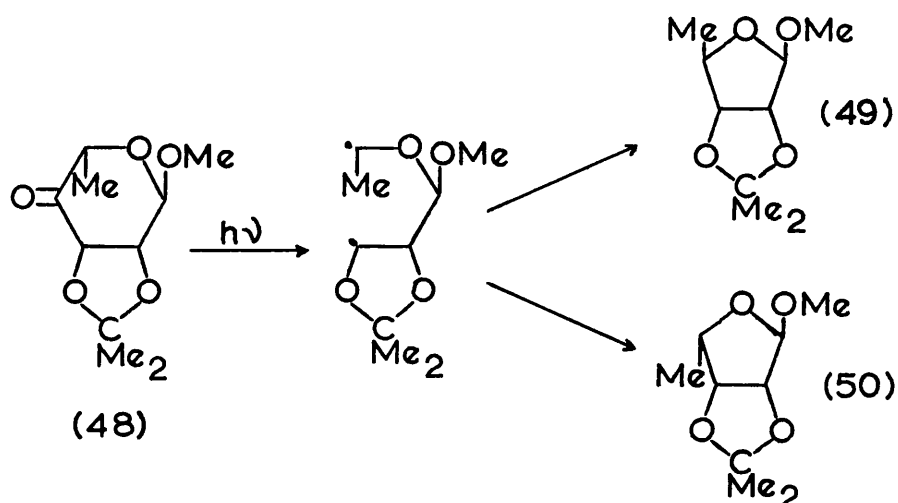


a: $R = R' = \text{Ph}$
 b: $R = \text{Ph}; R' = \text{H}$
 c: $R = R' = \text{H}$

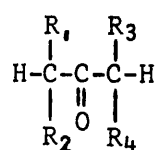
Cava and Mangold similarly prepared the phenanthro[1]-cyclobutene (47) from dihydrophenyclone (45) in benzene via the highly stabilised diradical (46);³⁷ and stabilisation,



this time by α,α' -alkoxy groups was invoked in the ring contraction in pentane of the pyranosidulose (48) to the furanosides (49) and (50).³⁸



Decarbonylation has been observed for the phenyl acetones (51). The intermolecularity of this reaction was established by isolating the same ratio of phenylated ethanes from the photolysis in benzene of ketone (51c) and of an equimolar mixture of tetraphenylacetone (51a) and dibenzyl ketone (51b).³⁶



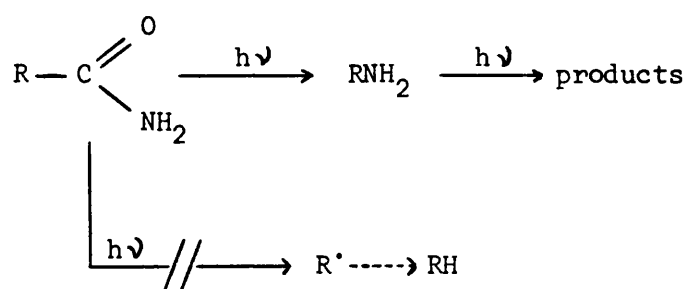
a; $R_1 = R_2 = R_3 = R_4 = \text{Ph}$

b; $R_1 = R_3 = \text{H}; R_2 = R_4 = \text{Ph}$

c; $R_1 = \text{H}; R_2 = R_3 = R_4 = \text{Ph}$

(51)

Intramolecular decarbonylation, however, was claimed by Norrish and Booth to occur during the photolysis in dioxan of primary alkyl amides.³⁹ Their observations indicated the formation and subsequent photolytic decomposition of a primary amine (Scheme 7). The absence of methane from

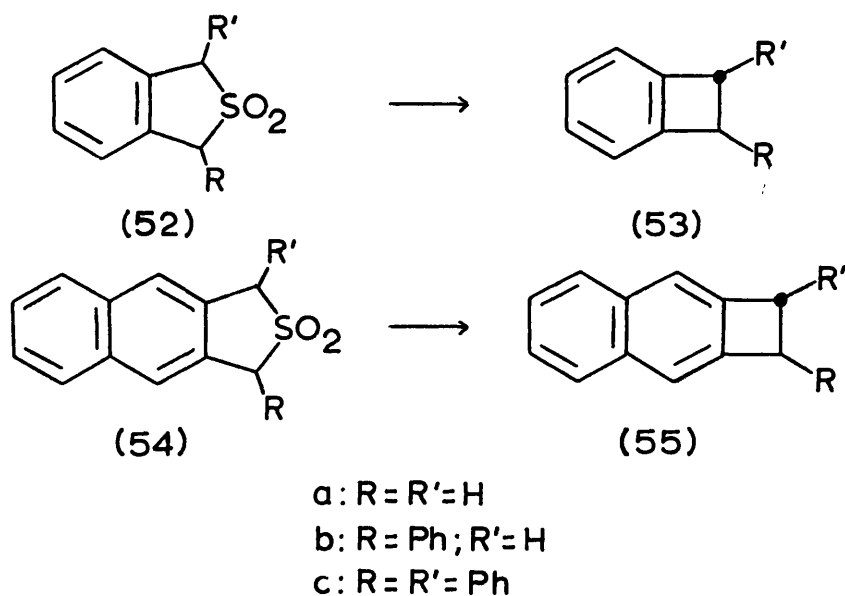


Scheme 7

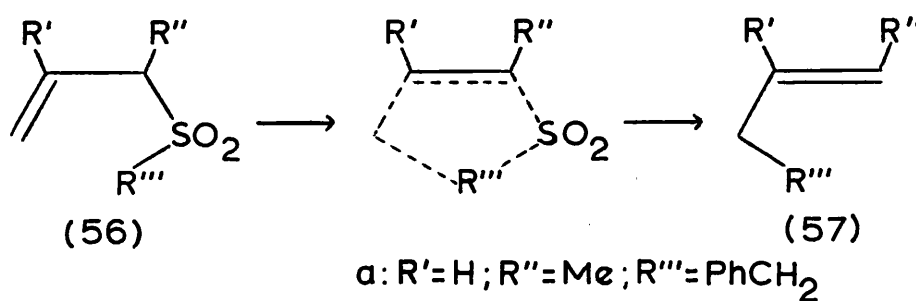
the photolytic products of acetamide ruled out the intermediacy of free methyl radicals, which would be expected to abstract hydrogen from the solvent.

A similar rationale can be put on the pyrolytic and photolytic desulfonylation of sulfones.⁴⁰ Thus liquid phase pyrolysis of sulfone (52a) gave benzocyclobutene (53a) in low yield (improved in gas phase pyrolysis)⁴¹, while liquid phase pyrolysis of sulfone (54a) gave the cyclobutene (55a) in over

60% yield.⁴² Photolysis of sulfones (52c) and (54c) in solution gave the corresponding trans-cyclobutenes (53c) and (55c) while sulfones (52a) and (54a) failed to react.⁴³

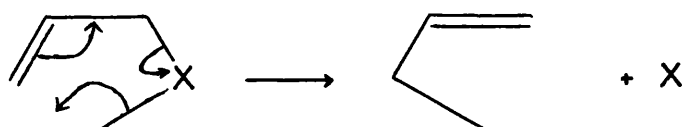


The only examples of intramolecular desulfonylation in the liquid phase of acyclic sulfones are the thermal decompositions of the allylic sulfones (56) to the olefins (57)⁴⁴.



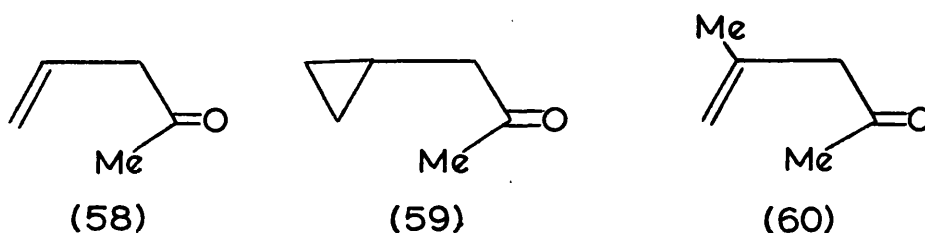
The absence of crossed products from the unsymmetrical sulfone and the production of 5-phenyl-2-pentene (57a) from benzyl α -methylallyl sulfone (56a) was rationalised by the five-centred mechanism shown; but it has been pointed out^{40b} that cross-termination is frequent in radical reactions and that the authors made no reference to the formation or otherwise of the isomeric 4-phenyl-3-methyl-1-butene.

The general reaction (Scheme 8) has components



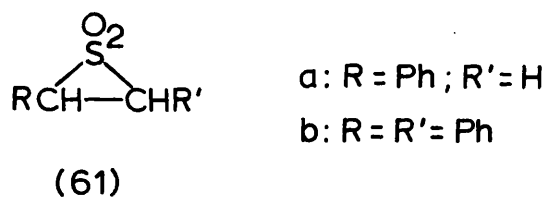
Scheme 8

$\sigma^2_s + \sigma^2_s + \pi^2_s$, i.e. an odd total of $(4n + 2)$ suprafacial and $(4n)$ antarafacial components, and is thus thermally allowed on orbital symmetry considerations.⁴⁵ The corresponding photochemical extrusion should be disallowed, and although photolysis of sulfone (56) has not been reported, photolytic decarbonylation of the related ketones (58), (59)⁴⁶ and (60)⁴⁷ gave intermolecular decarbonylated products.



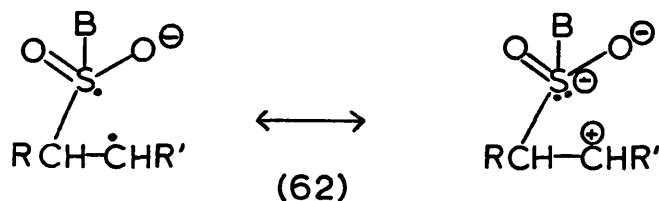
Thermal extrusion of SO_2 from episulfones to give olefins is also disallowed on orbital symmetry grounds, having components $\sigma_s^2 + \sigma_s^2$. The extrusion, however, is stereospecific.^{15,20,21}

Bordwell²⁰ found that the thermal decomposition in good ionising solvents of the episulfones (61a) and trans-(61b) proceeded at identical rates, suggesting that only one phenyl group in trans-(61b) was stabilising the transition state. This, together with the marked base-catalysis of the decomposition

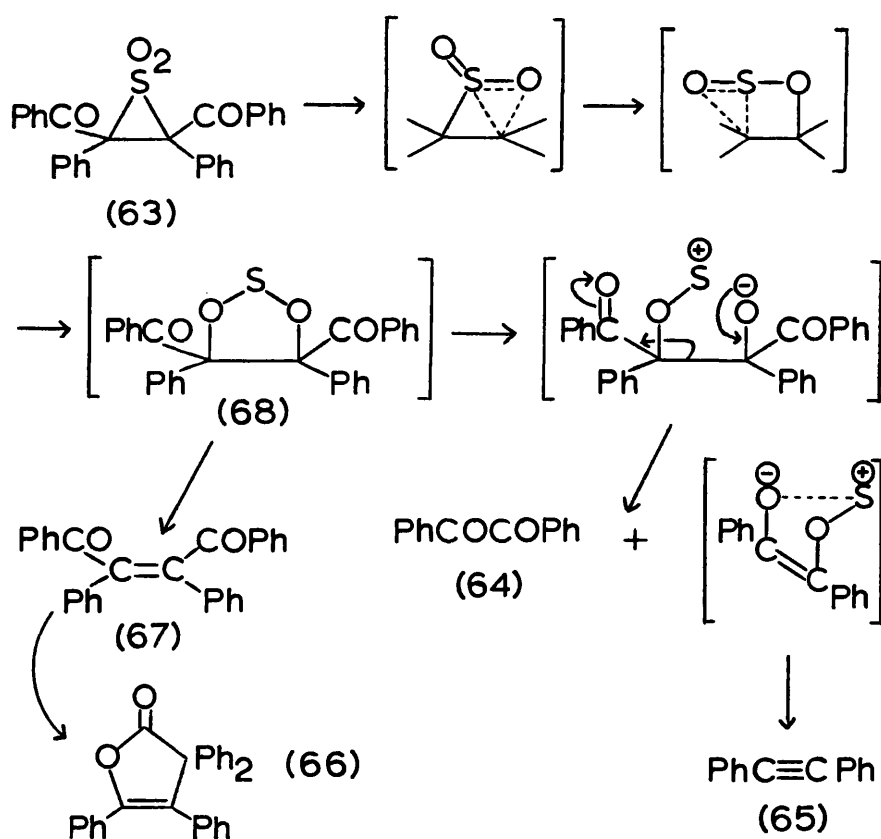


suggested a non-concerted mechanism via a diradical anion.

The observed stereospecificity was attributed to a barrier to rotation in the transition state (62).



An alternative mechanism was given by Dittman.⁴⁸ Pyrolysis of the episulfone of cis-dibenzoylstilbene (63) gave benzil (64), tolan (65), and a lactone (66) derived from cis-dibenzoylstilbene (67). The products were explained by a mechanism involving preliminary ring expansions to the five membered cyclic 1,3,2-dioxathiolane (68).



The thermal extrusion of SO₂ from intermediate (68) would be an allowed reaction, and the suggestion was advanced that this

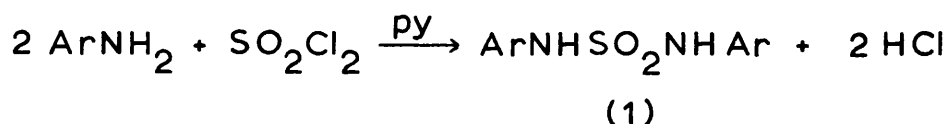
preliminary ring expansion was general for the thermal loss of SO_2 from episulfones.

The photolytic extrusion of SO_2 from episulfones is allowed, however, and was observed²⁰ during low temperature photolysis of the episulfones (61 a and b). The stereochemistry of the products was not rigorously clarified.

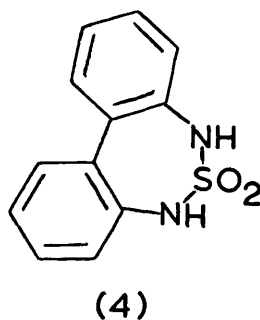
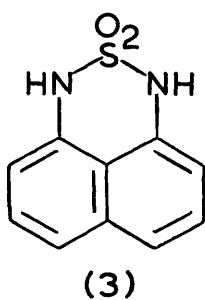
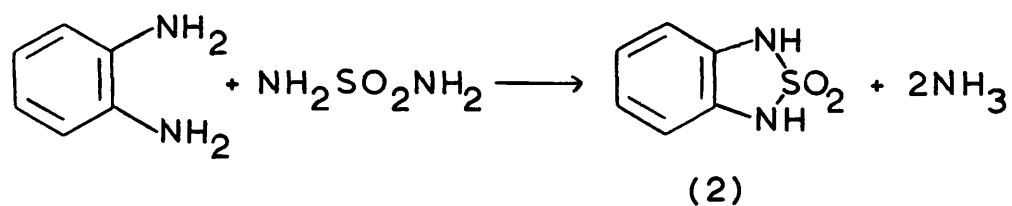
DISCUSSION

Preparation of Symmetrical Diaryl Sulfamides

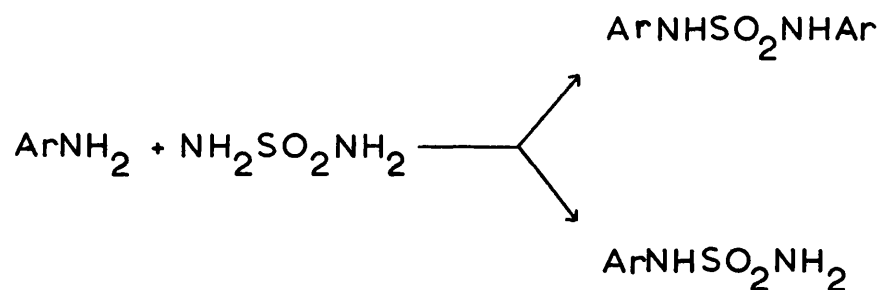
The first synthesis of sulfanilide in good yield (59%), reported by Wohl and Koch,⁴⁹ was from the reaction of aniline with sulfuryl chloride. Attempts to repeat this synthesis gave sulfanilide in low yield (3%), so the required symmetrical sulfamides (1) were prepared by the reaction of the appropriate arylamine with sulfuryl chloride in the presence of pyridine. This method⁵⁰ gave good yields (40%) even with weakly basic amines.



The obvious extension of this synthesis to the aromatic diamines, o-phenylenediamine and 1,8-diaminonaphthalene, failed to give cyclised products, despite claims to the contrary.⁵¹ Oxidation and polymerisation of the amines were observed. The required 1H, 3H[2,1,3]benzothiadiazoline 2,2-dioxide (2) was prepared by the condensation of sulfamide with o-phenylene_diamine in anhydrous diglyme.⁵¹

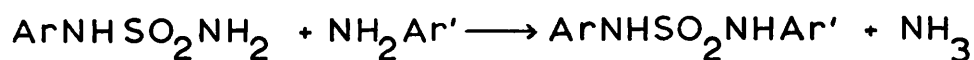


An exactly analogous procedure was used to prepare the related 1H, 3H, naphtho[1,8-cd][1,2,6]thiadiazine 2,2-dioxide (3) and 1H, 3H, dibenzo[d,f][2,1,3]thiadiazepine 2,2-dioxide (4). A similar reaction at lower temperature between m-toluidine and sulfamide gave both the N-aryl and N,N'-diaryl sulfamides.⁵²



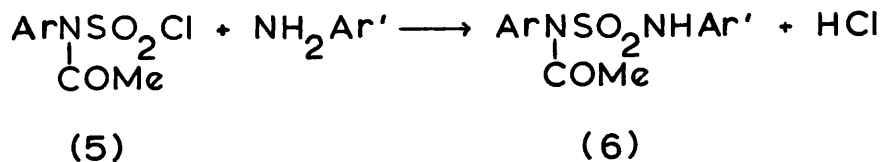
Preparation of Unsymmetrical Diaryl Sulfamides

The simplest synthesis of an unsymmetrical N,N'-diaryl sulfamide would be the condensation of an amine with an N-aryl sulfamide;



It was found, however, that even at 75°, amide exchange competed effectively with the condensation giving a statistically random mixture of products. This exchange had previously been noted at much higher temperature (refluxing aniline).⁵³

The required sulfanilides were prepared by the reaction of an aromatic amide N-sulfochloride (5) with the requisite arylamine. The use of excess of arylamine is reported⁵⁴ to aminolyse the N-acylsulfani-



lide (6) to the sulfanilide and this was observed for the acylsulfanilide (6; Ar=Ph); but (6; Ar=p-ClC₆H₄)

was obtained in good yield from 4-chloroacetanilide-N-sulfochloride and excess of arylamine. The N-acyl group was removed by aqueous alkaline hydrolysis to give the required sulfanilides.

Preparation of N-Chloro Aryl Sulfamides

N-Chloro, or N,N'-dichlorosulfanilides have not hitherto been reported; but treatment of sulfanilides with excess of chlorine in aqueous sodium hydroxide, a method for chlorinating dialkyl sulfamides,⁵⁵ gave the required N,N'-dichlorosulfanilides quantitatively. Some ring chlorination was observed when the sulfanilides lacked deactivating substituents. Attempts to mono-N-chlorinate sulfanilide specifically failed. The action of one equivalent of tert-butyl hypochlorite in benzene gave both mono and di-chlorinated products, as did the use of chlorine in aqueous sodium bicarbonate buffers.^{56 57} Sulfanilide was inert to reagents such as N-chlorosuccinimide and N-bromosuccinimide.

The ring chlorination of the N-chlorosulfanilides was as expected, by analogy with the Orton rearrangement of N-haloanilides. The observed inertness of the cyclic sulfamides(2), (3) and (4) to N-chlorination

was surprising. In aqueous solution the sulfanilides could be recovered from conditions that readily chlorinated the acyclic sulfamides.

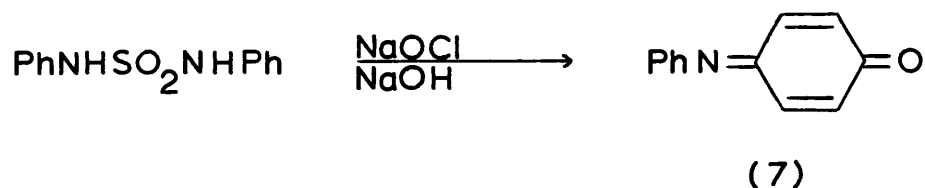
N,N'-Dichlorination was effected with an excess of tert-butyl hypochlorite in benzene; but was accompanied by ring chlorination. The use of one equivalent of hypochlorite gave mixtures of chlorinated products together with recovered starting material. The action of excess of chlorine in inert solvents caused complete oxidation of the sulfamides.

As the cyclic sulfamides are more acidic than the acyclic compounds, an explanation of the relative inertness to chlorination may involve the amido nitrogen being insufficiently nucleophilic to attack the halogen molecule.

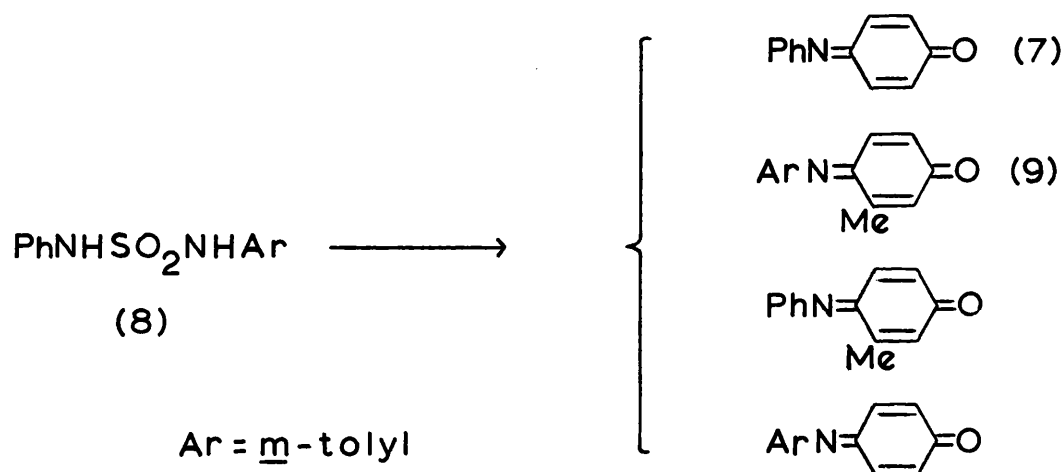
Aqueous Oxidation of Diaryl Sulfamides

As stated in the Introduction, there are reports of azo-alkane production by intramolecular 1,3-displacement of chloride from N-chlorinated dialkyl sulfamides. It was decided to investigate the scope of this displacement in diaryl sulfamides, where the resultant azo compounds would be known and stable, preparatory to attempting the synthesis of the benz[c d]indazole system.

Oxidation of sulfanilide with aqueous sodium hypochlorite or hypobromite in sodium hydroxide gave benzoquinoneanil (7) in good yield. No azobenzene was obtained and none was produced by variations in reagent concentrations or temperature.



The intermolecularity of the reaction was established by studying the oxidation of the unsymmetrical 3-methylsulfanilide (8).



The mixed benzoquinoneanils were obtained in the correct ratio of 1:2:1; the analysis was performed by mass spectroscopy of the mixture since the products were not readily separated by chromatography. Sensitivity corrections are difficult to make for thermally unstable solids, so it was assumed that the spectrometer sensitivity would be identical for all four products. If, as is almost certain, initial ionisation is from nitrogen or oxygen,⁶⁰ and the parent ion is a major peak in the spectrum (and hence has a long lifetime), the assumption should be a reasonable one. The spectrum of authentic anil (9) did not exhibit any M-14 or M-28 peaks. This formation of anils (7) and (9), when the unsymmetrical sulfanilide (8) had less than 1% of symmetrical impurities as measured from the mass spectrum, renders a completely intramolecular mechanism impossible. The ratio of quinoneanils observed makes a completely intermolecular mechanism probable.

The effect of para blocking groups was considered. Oxidation of 4,4'-dichlorosulfanilide gave a small (2%) yield of 4,4'-dichloroazobenzene. The major product isolated was 4-chloro-p-benzoquinoneanil (20%). Oxidation of 4,4'-dimethylsulfanilide gave no characterisable products.

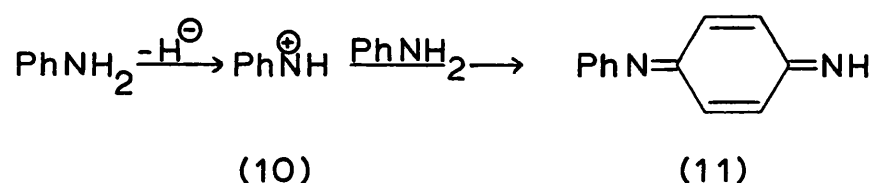
Thus, even with para substituents present, azobenzene formation was minimal, attack on the aromatic ring together with expulsion of a readily displaced blocking substituent being the preferred reaction pathway.

The only report³⁴ of formation of an azobenzene from a diaryl sulfamide under these conditions involves aqueous alkaline hypochlorite oxidation at 90° of 4,4'-dinitrosulfanilide to 4,4'-dinitroazobenzene (31%). These conditions, coupled with the reported ease of hydrolysis of this particular sulfanilide,^{50 58 59} render it likely that the dinitroazobenzene was obtained by hydrolysis of dinitrosulfanilide and intermolecular oxidation of the resulting p-nitroaniline.

In our hands, in separate experiments, hydrolysis of 4,4'-dinitrosulfanilide in dilute aqueous sodium hydroxide gave p-nitroaniline, and oxidation of the nitroaniline under conditions similar to those used for dinitrosulfanilide³⁴ gave 4,4'-dinitroazobenzene as sole

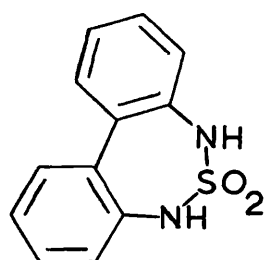
product.

An obvious mechanism for the formation of the quinoneanil (7) from sulfanilide would involve this initial hydrolysis of the sulfanilide and subsequent oxidation of the resulting amine; alkaline oxidation of aniline is known to give products derivable from the ion (10) and N-phenylquinonediimine (11)⁶¹.

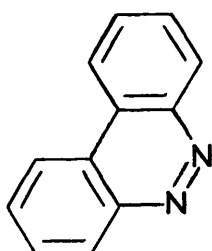


Evidence against such a mechanism was provided by our failure to isolate any quinoneanil (7) from the oxidation of aniline in alkaline hypochlorite, even under very mild conditions. Oxidation of sulfanilide with alkaline potassium permanganate gave only 3.5% quinone anil, although the reaction conditions were equally as capable of generating the anilinium ion (10) from aniline.⁶¹ Furthermore, sulfanilide did not undergo alkaline hydrolysis under conditions much more vigorous than those of the hypochlorite oxidation. This resistance to dilute alkaline hydrolysis parallels that of N-phenylsulfamide⁵⁹ and of sulfamide⁵⁸ itself.

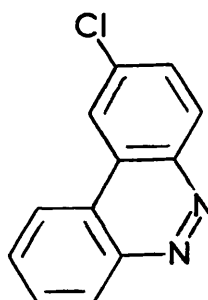
Oxidation of the cyclic sulfamide (4) with sodium hypochlorite in aqueous sodium hydroxide gave up to 9% of benzo[c]cinnoline (12) and 2-chlorobenzo[c]cinnoline (13) presumably by a genuine intramolecular 1,3 elimination of hydrogen chloride. The low yield obtained, however, showed that this route is energetically unfavourable for this molecule. The major product was an acidic polymer. A similar yield of benzo[c]cinnolines was isolated after prolonged hypochlorite oxidation using sodium carbonate, in which sulfamide (4) is ionised, as



(4)



(12)



(13)

base.

Electrophilic substitution of benzo[c]cinnoline, e.g., nitration^{90 91} and bromination^{92 93} has been shown to occur in the 1- and 4- positions. The molecule is inert to bromination by molecular bromine under radical

or ionic conditions⁹². These observations suggest that in our cyclic sulfamide oxidation the production of 2-chlorobenzo[c]cinnoline occurs via chlorine migration to the aromatic ring, presumably via an Orton type rearrangement, prior to the oxidation.

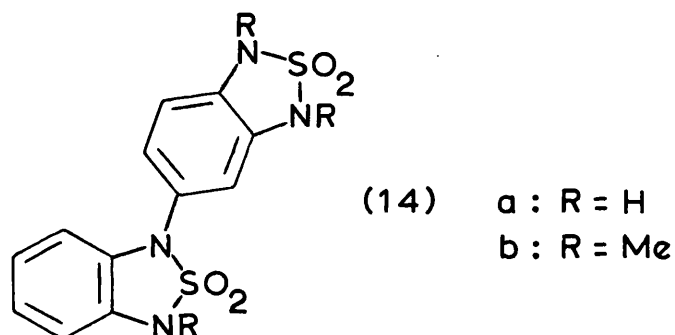
The cyclic sulfamides, naphthothiadiazone dioxide (3) and benzothiadiazone dioxide (2) were oxidised under the conditions outlined above. With sodium hypochlorite in aqueous sodium carbonate, or sodium hydroxide, both gave quantitative amounts of polymerised acidic material. No neutral or basic products could be isolated. The sulfamide (3) when oxidised in the presence of tetracyclone, which might be expected to form a Diels-Alder adduct with any benz[c d]indazole formed, gave the same material as above. Tetracyclone was recovered quantitatively.

The product from benzothiadiazone dioxide was studied further. The broad peaks observed in the i.r. and p.m.r. spectra together with the elemental analysis and the similarity of the u.v. spectrum ($\lambda_{\text{max.}}$ 288 n m.

$E_{1\text{ cm.}}^{1\%}$ 2.1×10^6) to that of the starting material

($\lambda_{\text{max.}}$ 285 n m. $E_{1\text{ cm.}}^{1\%}$ 1.6×10^6 , $\epsilon = 2680$) supported

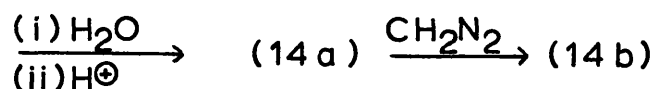
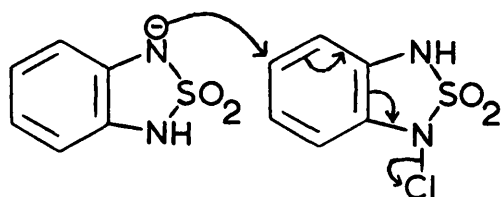
a structure based on simple polymerisation with no extension of conjugation. The mass spectrum showed only a peak for m/e 64. Methylation of the polymer with diazomethane failed to give a more volatile product for mass spectrometry. The use of a deficiency of hypochlorite in the oxidation and methylation of the products gave both N,N'-dimethylbenzothiadiazoline dioxide and the methylated dimer (14b).



A continuation of this polymerisation would give a polymer whose structure agreed with the observed properties.

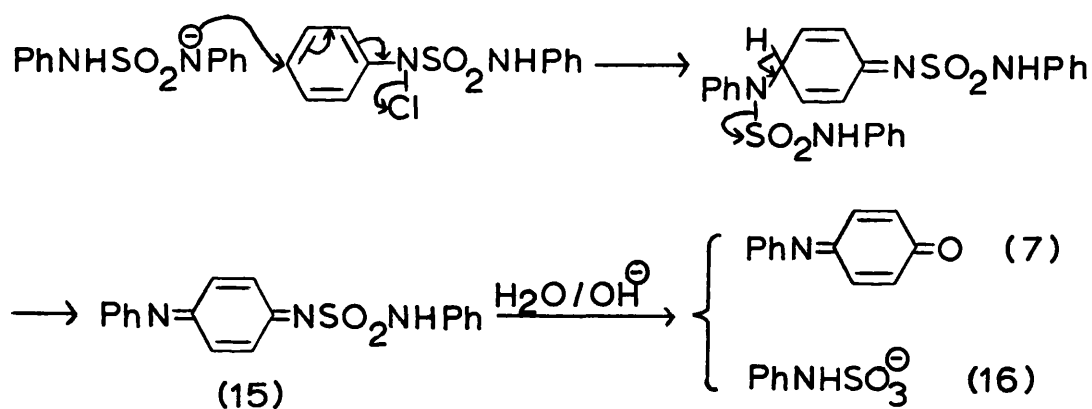
As the oxidation requires both base and hypohalite, the mechanism presumably involves nucleophilic attack by a benzothiadiazolinium dioxide anion upon an N-chlorinated sulfamide, the attack being assisted by the ready displacement of chloride anion. The position of coupling; i.e. ortho or meta to the heterocyclic

ring could not be unambiguously assigned from the available i.r., u.v., or p.m.r. spectral data. It is shown as meta in Scheme 1, as this mode would involve less steric hindrance in the transition state.



(Scheme 1)

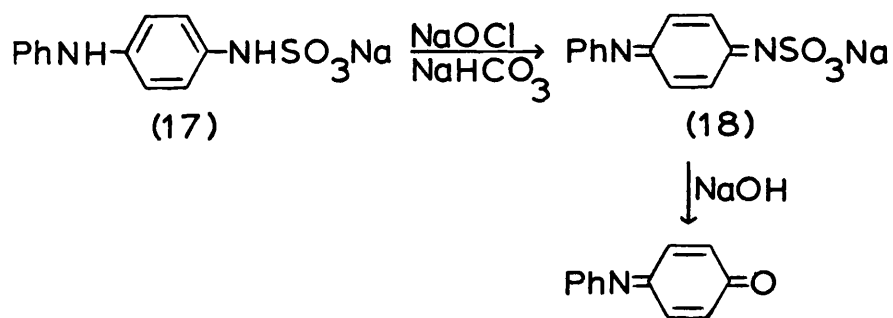
An analogous mechanism (Scheme 2) can explain the products obtained from oxidation of the acyclic sulfanilides. Initial nucleophilic attack upon the N-chlorosulfanilide would be assisted by the departing chloride anion.



(Scheme 2)

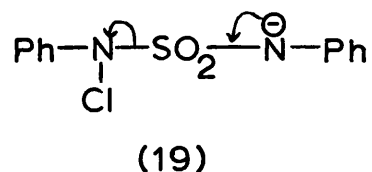
The hydrolysis of the sulfanilide amide bond was supported by the detection of an aryl sulfamate in the reaction mixture after completion of the oxidation.

The hydrolysis of the quinonediimine (15) in aqueous sodium hydroxide would accord with the known formation of benzoquinoneanil from sodium p-amino-diphenylamine sulfamate (17); this reaction has been shown to proceed (Scheme 3) via the N-phenylbenzo-1,4-quinonediimine-N'-sulfonate (18).⁶²

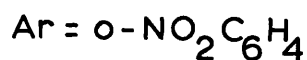
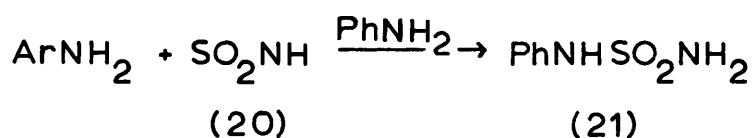
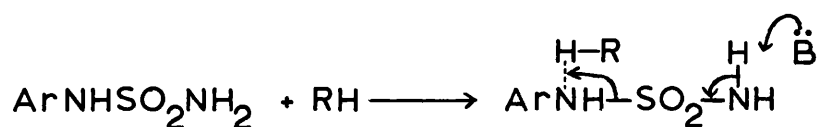


(Scheme 3)

A second mechanistic possibility involves initial S - N bond cleavage in the N-chlorosulfanilide anion (19) which will also be formed under the reaction conditions.



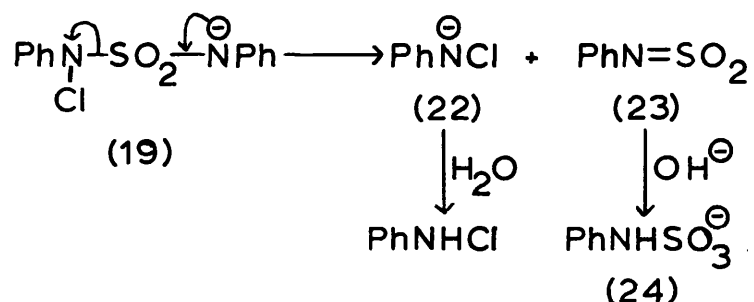
An analogy for this S_N1 attack at sulfur can be found in the hydrolysis or aminolysis of ortho- and para- nitrophenylsulfamides.⁵⁹ The mechanism (Scheme 4) postulated as best fitting the kinetic data involved free sulfimide (20) as an intermediate and general base catalysis. This reaction was not observed in aqueous base due to the ionisation of the acidic anilino proton and consequent inhibition of the nucleophilic displacement at sulfur. The necessity for an ionisable proton



(Scheme 4)

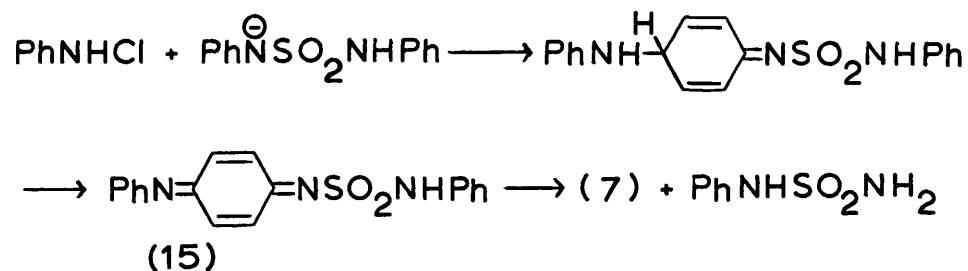
at the second nitrogen was established by the inertness of N,N-diethyl-2-nitrophenylsulfamide to the reaction conditions. The free sulfimide (20) could be trapped as phenylsulfamide (21) when aniline was used as base⁵⁹.

Cleavage of sulfanilide in alkaline hypochlorite in this manner would give N-phenylsulfimide (23) and the N-chloroaniline anion (22). Nucleophilic attack by base on the sulfimide (23) at sulfur would rapidly give the N-phenylsulfamate ion (24) as in Scheme 5. In aqueous solution the N-chloroaniline anion would exist largely as the conjugate acid, N-chloroaniline.



(Scheme 5)

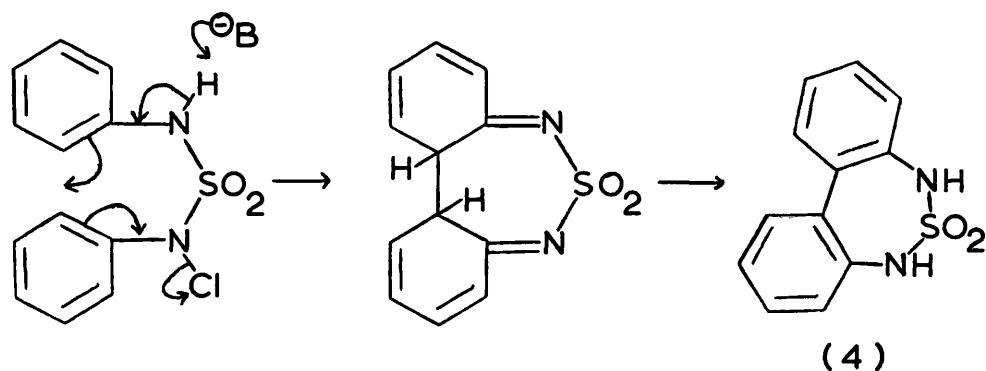
The formation of p-benzoquinoneanil would then proceed via nucleophilic attack upon N-chloroaniline by a sulfanilide anion (Scheme 6) to give the quinonediimine (15) again as an intermediate.



(Scheme 6)

In an attempt to isolate an intermediate such as (15) sulfanilide was oxidised in aqueous sodium carbonate. (No reaction was observed on attempted oxidation in aqueous sodium bicarbonate). A small yield of quinoneanil (7) was obtained together with a mixture of acidic products. The minor product gave a mass spectrum with parent $m/e = 337$, correct for the quinonediimine (15). The principal breakdown pattern of (P-91) and (P-64)⁸¹ supported by metastable peaks is similar to that observed for sulfanilide. However, the product could not be separated completely from material of higher molecular weight. This isolation of a compound with m/e similar to the quinonediimine (15) tends to rule out a mechanism involving prior cleavage of sulfanilide and subsequent recombination of fragments.

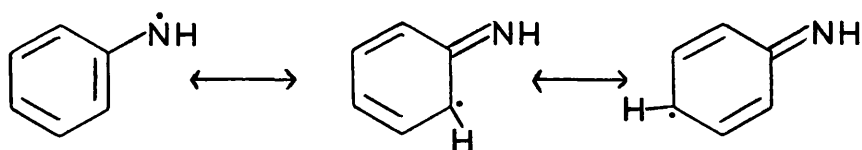
The major acidic product, probably formed via a mechanism such as given in Scheme 7, was the intramolecularly cyclised sulfamide dibenzothiadiazepine dioxide (4). The failure to isolate this product or its degradation product benzo[c]cinnoline, vide infra,



(Scheme 7)

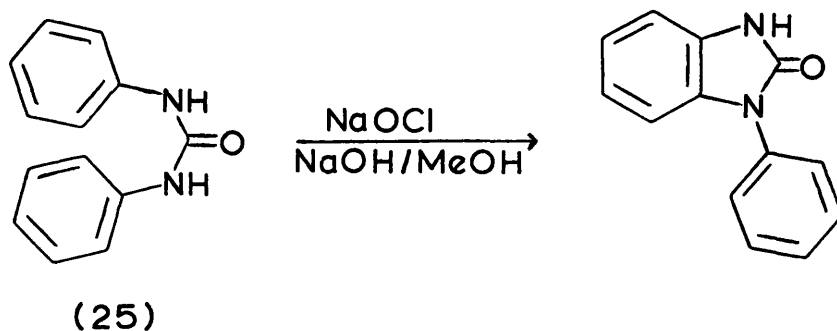
from oxidation of sulfanilide in aqueous sodium hydroxide suggested its formation from unionised sulfanilide. Support for this lack of ionisation was given by our recovery, by ether extraction, of sulfanilide from aqueous sodium carbonate, but not from aqueous sodium hydroxide.

Generally, oxidation coupling of aromatic compounds is a radical reaction.⁶³ Initiation is normally by one-electron oxidation of an amino or phenolic substituent such that the resulting radical possesses structural stability. For example, aromatic amines couple via the mesomeric radical shown:⁶⁴



Only N,N'-dichlorosulfanilide was isolated, however, from the action of excess of chlorine upon sulfanilide in aqueous sodium bicarbonate, showing the necessity during the cyclisation for a reaction medium of higher pH. This observation rendered a radical pathway initiated by homolysis of the N-Cl bond unlikely, as did the failure of N,N'-dichlorosulfanilide to cyclise during pyrolysis or photolysis in benzene or carbon tetrachloride, i.e. under typical homolytic conditions.

The absence of azobenzene from the reaction products, together with the readiness with which the sulfanilide cyclisation proceeds, despite the necessity for destroying the aromaticity of both phenyl rings in the intermediate, indicates that the base-induced direct 1,3 elimination of hydrogen halide from nitrogen is highly unfavourable in these molecules. This interpretation is supported by the known cyclisation of carbanilide (25) under similar conditions.⁶⁵ No azobenzene was formed, the cyclisation occurring exclusively on nitrogen as shown. Ring chlorination, which was observed with excess of hypochlorite, was assumed to occur from chlorine formed in the acidic work-up.

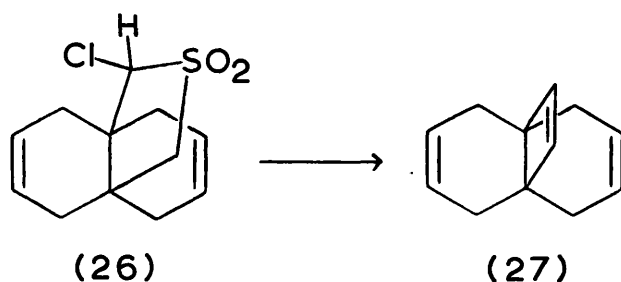


As the reaction was inhibited by alkylation of one nitrogen, a displacement similar to the sulfanilide cyclisation, requiring both an N-Cl and an ionisable amide proton was suggested.

The formation of sulfamide (4) from sulfanilide is potentially an entry into the 2,2'-diaminobiphenyl system. The cyclic sulfamide, however, was recovered from attempted hydrolysis in strong aqueous base - conditions known to hydrolyse sulfamide itself.⁵⁸

Non-Aqueous Oxidation of Diaryl Sulfamides

The oxidising system tert-butyl hypochlorite, potassium tert-butoxide in benzene was studied as a strongly basic, weakly nucleophilic system in the hope of reducing the final nucleophilic attack at the quinonediimine (15). Paquette had observed the production of the derived cyclobutene (27) from the chlorosulfone (26) and potassium tert-butoxide in T.H.F., although no elimination occurred in aqueous sodium hydroxide.



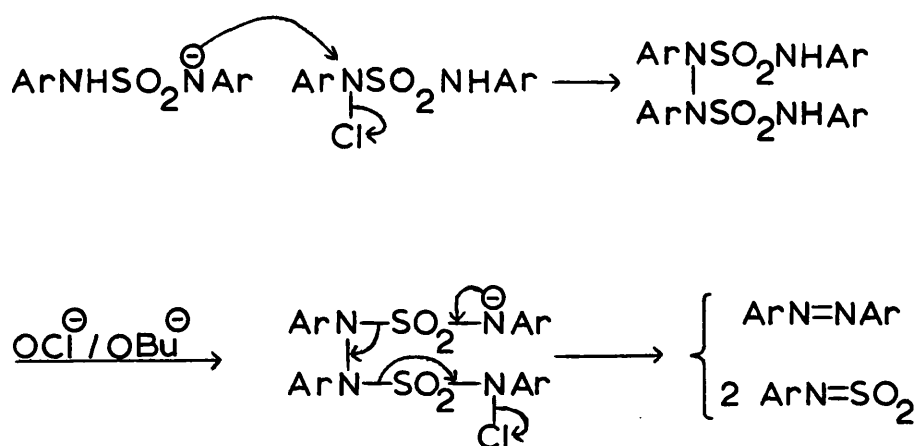
Solvation of the anion in water, and consequent inability to attain the required semi-W-transition state for elimination, was proposed in this case.⁶⁶ A similar effect could have been operative in our sulfanilide anions.

Oxidation of 4,4'-dichlorosulfanilide with tert-butyl hypochlorite and tert-butoxide gave the corresponding

4,4'-dichloroazobenzene (20%). The intermolecularity of the reaction was established, however, by observing crossed azobenzenes from the oxidation of the unsymmetrical sulfanilides, 4-bromo-4'-chlorosulfanilide and 3-methylsulfanilide. In both cases the products were obtained in a 1:2:1 ratio showing that there was no detectable superimposed intramolecular displacement.

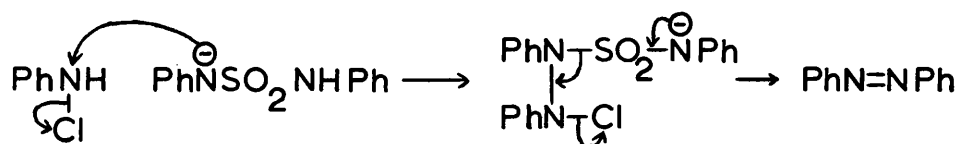
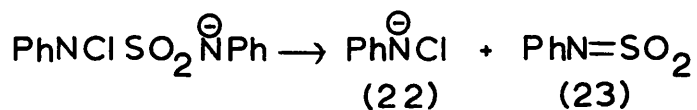
The possibility that random exchange had occurred prior to or after the oxidation was discounted after recovering 4-bromo-4'-chlorosulfanilide and 4-bromo-4'-chloroazobenzene unchanged from solution in potassium tert-butoxide, tert-butanol.

The sulfanilide cleavage again appears to require the N-Cl group together with an anionic amide centre. The failure to isolate any quinoneanils on aqueous work-up and the production of azobenzenes from sulfanilides with or without blocking para substituents suggests that attack upon the phenyl ring is unimportant. A possible mechanism (Scheme 8) would again involve initial S_N2 attack by a sulfanilide anion, this time at nitrogen with elimination of chloride. Subsequent oxidation and fragmentation would by analogy with the fragmentation shown previously in Scheme 4,⁵⁹ give the azobenzene;



(Scheme 8)

The alternative intermediacy of N-chloroaniline, generated as in Scheme 5, can be postulated. Nucleophilic substitution at nitrogen by the sulfanilide anion followed again by oxidation and elimination would give the required product:

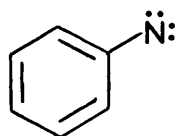


N-chloroaniline or the anion (22) is similar to chloramine or the chloramide anion NHCl^- , an intermediate in the base catalysed Raschig hydrazine synthesis.

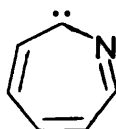
Yagil and Anbar⁶⁷ have shown that both these species can undergo nucleophilic attack by amines, presumably via transition states with a polarised $\text{N}^{\delta+} - \text{Cl}^{\delta-}$ bond. Hence it is reasonable to postulate nucleophilic attack upon nitrogen activated by a chlorine atom.

Complete elimination of chlorine ion from anion (22) to give the aryl nitrene with subsequent dimerisation or attack upon sulfimide (23) is unlikely. Although certain aryl nitrenes, notably those with electron releasing substituents, dimerise to azobenzenes in good yield when generated from the azides in inert solvents,⁶⁸ generally hydrogen abstraction from solvent to give anilines and hydrazobenzenes is also observed.^{69 70}

The alternative ring expansion to azepines is only observed in solution in the presence of strong nucleophiles (amines⁷¹ or phosphites⁷²) as traps. Crow and Wentrup⁷³ have elegantly demonstrated the preference, in the absence of nucleophilic stabilisation, for the nitrene (28) to exist as such, rather than as the ring expanded carbene (29).



(28)



(29)

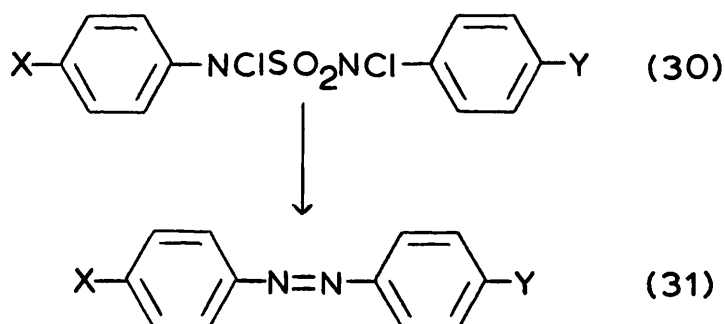
However, the absence of basic products from the sulfanilide oxidation, coupled with the documented^{68a} failure to obtain dichloroazobenzene from photolysis of p-chlorophenyl azide although para-halonitrenes or nitrenoids are generated by this means,⁷⁰ renders it improbable that a discrete aryl nitrene is an intermediate in this reaction.

Oxidation of the cyclic sulfamide (4) under these condition did not give any neutral or basic components; in particular no benzo[c]cinnoline was obtained. A low recovery of starting material was effected, the remainder forming highly coloured material. Similar observations were made for the sulfamides (2) and (3).

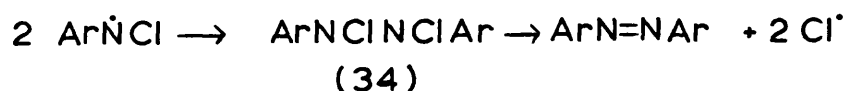
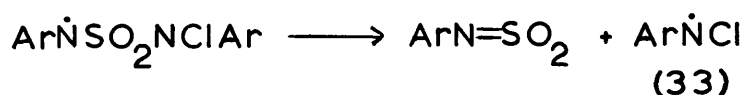
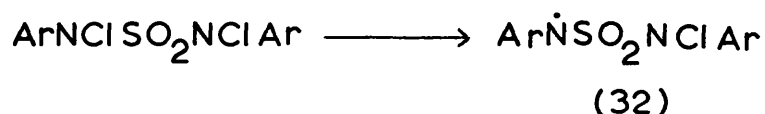
Thermolysis of N-Chlorinated Sulfamides

It was noted that N,N'-dichlorosulfanilide decomposed at room temperature to a tar containing traces of azobenzene. Controlled pyrolysis under reflux in dry benzene or carbon tetrachloride gave azobenzene and traces of chlorinated azobenzenes. The N,N',4,4'-tetrahalosulfanilides were selected for further study, firstly because the substituted aryl ring was deactivated to attack by free halogen, and secondly because the halogenated products were readily identified from their mass spectra.

Pyrolysis of the tetrachlorosulfamide (30; X=Y=Cl) in dry carbon tetrachloride gave dichloroazobenzene (31; X=Y=Cl) in moderate yield (36%).

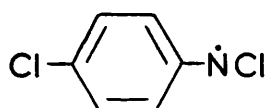


Chlorine was evolved during the pyrolysis, and this together with the isolation of 4,4'-dichlorosulfanilide and only a trace of dichloroazobenzene from pyrolysis in dry ether where hydrogen abstraction can occur, suggested initial homolysis of the N-Cl bond rather than the N-S bond, (Scheme 9).

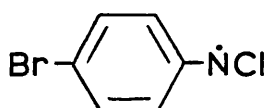


(Scheme 9)

The pyrolysis of 4-bromo-N,N',4'-trichlorosulfanilide (30; X=Cl, Y=Br) gave a mixture of the dihaloazobenzenes (31; X=Y=Br), (31; X=Br, Y=Cl) and (31; X=Y=Cl), showing that the reaction is intermolecular. The observed ratio, 1:2:1, suggested equal reactivity for the radicals (33a) and (33b).



(33a)



(33b)

Thus when radical abstraction from solvent is energetically unfavourable (benzene) or mechanistically degenerate (carbon tetrachloride), the intermediate sulfanilide radical (32) must fragment. Homolysis such as in Scheme 9 with an obvious analogy to the base-induced cleavage discussed previously would be a possible path.

The N-chloroanilino radical (33) may dimerise and eliminate chlorine, or homolyse to chlorine and an aryl nitrene; but the previously mentioned apparent reluctance of para-halophenylnitrenes to dimerise made it more likely that 1,2 elimination of chlorine was occurring from an intermediate N,N'-dichloro-N,N'-diaryl hydrazine (34). The failure to identify sulfur dioxide from the reaction argued against mechanisms involving fragmentation of N-arylsulfimide after attack by radicals such as (33).

Photolysis of the tetrachlorosulfanilide (30; X=Y=Cl) also gave dichloroazobenzene (8%). A mechanism similar to that outlined above seemed possible.

Attempts at synthesising N,N'-dichlorinated cyclic sulfamides, under conditions known to chlorinate the acyclic diaryl sulfamides, failed. A polychlorinated product with no amide absorption in the infrared was obtained from prolonged chlorination with tert-butyl hypochlorite of the dibenzothiadiazepine dioxide (4). On pyrolysis highly coloured products were formed; but no benzo[c]cinnoline or chlorinated benzo[c]cinnolines were isolated.

Both the cyclic sulfamides (2) and (3) formed polychlorinated products with tert-butyl hypochlorite in benzene. It proved impossible to N,N'-dichlorinate the sulfamides before at least one chlorine had substituted the aromatic ring. Pyrolysis of the resulting polychlorinated sulfamides in all cases gave intractable mixtures of highly coloured tarry products.

Photolysis of Diaryl Sulfamides

It was noted during the above work, that the cyclic sulfamides (2) and (3) were sensitive to daylight. This observation, together with the formation of azobenzene by photolysis of N,N'-dichlorosulfanilide, led to an investigation of the photolytic reactions of the aryl sulfamides.

Photolysis of sulfanilide in methanol solution with a Hanovia medium pressure lamp and a quartz filter, gave azobenzene, hydrazobenzene and aniline. The detection of hydrazobenzene was qualitative; but analysis of the reaction solution by t.l.c. in several different solvent systems indicated its presence. Quantitative analysis for azobenzene and aniline showed them to be present in close to a 1:2 molar ratio respectively. This observation suggested their formation from the known intramolecular photolytic disproportionation of hydrazobenzene.^{74 75} Hashimoto, Sunamoto and Nishitani found⁷⁵ the disproportionation best followed a mechanism such as given in Scheme 10.



(Scheme 10)

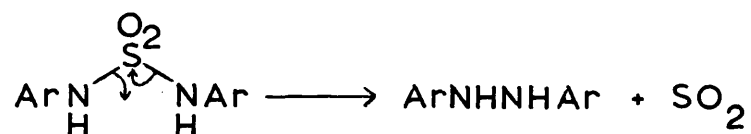
The observation of the Japanese workers that the aniline: azobenzene ratio was slightly less than 2, was also found in the sulfanilide photolysis. However, we cannot rule out the possibility in our work of some azobenzene being formed by autoxidation of the hydrazobenzene by dissolved oxygen, despite careful deoxygenation of the initial reaction solutions. The combined yield of aniline and azobenzene in the sulfanilide photolysis was 35% based on recovered sulfanilide, in the 3-methylsulfanilide case it was 41%. These figures are minima for the initial conversions to hydrazobenzenes, as some hydrazobenzenes remained after the photolyses.

Photolysis of 3-methylsulfanilide under similar conditions gave 3-methylazobenzene. No azobenzene or 3,3'-dimethylazobenzene could be detected; demonstrating the probable intramolecularity of the reaction. A

basic oil formed in the reaction could not be resolved by t.l.c., or g.l.c., but had an i.r. spectrum identical to that of an authentic equimolar mixture of aniline and m-toluidine.

Thus sulfanilide on photolysis appears initially to extrude sulfur dioxide, forming hydrazobenzene which undergoes further reaction.

A possible mechanism involves a synchronous migration of σ bonds in a cheletropic reaction (Scheme 11).



(Scheme 11)

The reaction involves both bonds migrating with retention of configuration at both ends i.e. two σ_s^2 components and hence is allowed by orbital symmetry^{4,5} for a photochemical reaction.

The corresponding thermal extrusion should be symmetry forbidden, and in fact no azobenzene or hydrazobenzene was obtained from the thermal decomposition of sulfanilide.

The application of orbital symmetry correlations to

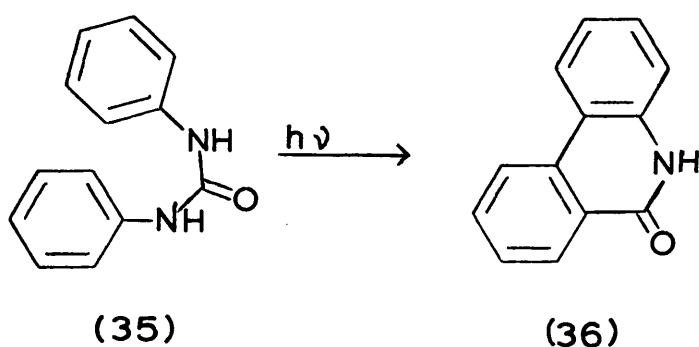
extrusions without an initial sigma bond joining the residual portion is unusual but the observation of the exclusively intramolecular reaction under photolytic conditions and not on pyrolysis strongly suggests orbital symmetry control.

An alternative mechanism of S-N bond homolysis and subsequent radical dimerisation occurring within a solvent cage cannot be eliminated, but is unlikely, as exclusively intramolecular desulfonation was observed in solvents of widely differing polarity (methanol, methylene chloride and benzene).

The yield of azobenzene decreased with decreasing solvent polarity and trouble was experienced with polymer precipitation on the lamp and the walls of the reaction vessel.

As discussed in the Introduction, liquid phase intramolecular desulfonation of acyclic sulfones is rare. To our knowledge the only analogous reaction is the photolytic decarbonylation of acetamide³⁹ demonstrated by Norrish and Booth. An obvious systematic extension would be the photolytic decarbonylation of N,N'-diphenyl-urea (35). Swenton has reported⁹⁴ the formation of phenanthridone (36) in low yield from this photolysis

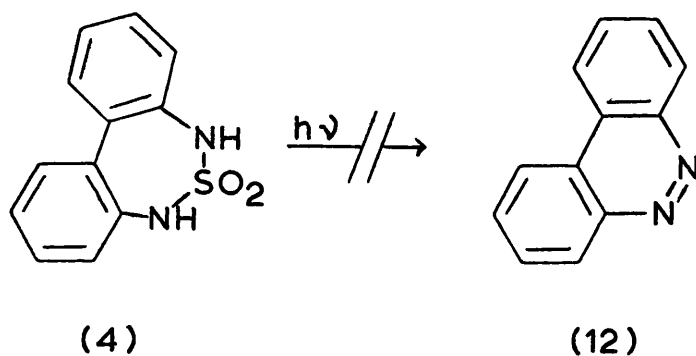
with no mention of further products.



Photolysis of N,N'-diphenylurea under similar conditions to those used for sulfanilide gave no indication of hydrazobenzene, azobenzene or aniline formation. The intramolecularity of our reaction also contrasts with the exclusively intermolecular photolytic desulfonation of diphenyl sulfone reported by Kharasch,⁷⁶ where the products were explained by the subsequent reactions of initially formed phenyl radicals.

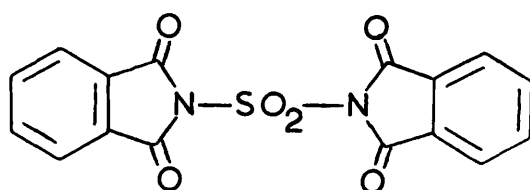
The cyclic sulfamides (2), (3) and (4), on irradiation in methanol solution with either quartz or pyrex filters, reacted rapidly to give complex mixtures of products. Complete characterisation of the products was not attempted; but a careful search, by t.l.c. and column chromatography failed to identify benzo[c]cinnoline (12) in the photolysis products from cyclic

sulfamide (4).



The expected initial product, 5,6-dihydrobenzo[c]-cinnoline would be rapidly autoxidised⁹⁵ to benzo[c]-cinnoline, which blank experiments proved stable to the reaction conditions.

The scope of the photolytic extrusion thus seems limited to acyclic aryl sulfamides. In an effort to find a system where the initial product would be stable to further photolysis, the synthesis of the biphthalimidosulfone (37) was attempted. The stability to photolysis of the expected extrusion product, N-phthalimidophthalimide, has been demonstrated.⁷⁷



(37)

No tetraacylsulfamides are reported, however, despite the availability and stability of phthalimido-N-sulfonyl chloride,⁷⁸ and both potassium phthalimide and sulfuryl chloride, and potassium phthalimide and phthalimido-N-sulfuryl chloride, failed to give the desired compound.

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

Instrumentation and Experimental Techniques

1. Infra red (i.r.) spectra were recorded in the range 4000-650 cm^{-1} by Perkin Elmer 237 and 257 grating spectrophotometers. Spectra of solids were taken as Nujol mulls and liquids as thin films between sodium chloride plates. Polystyrene was used as a reference with the Perkin Elmer 237 spectrophotometer.
2. Ultra violet and visible spectra were recorded in the range 200-700 n.m. using a Unicam S.P. 800 recording spectrophotometer. Spectra were taken as solutions in absolute ethanol.
3. Proton magnetic resonance (p.m.r.) spectra were recorded on Varian Associates type A60 and T60 spectrometers. Spectra were taken on approx. 7% solutions in CDCl_3 or CCl_4 .
4. Mass spectra (m/e) were recorded on a G.E.C./A.E.I. mass spectrometer type M.S.9, fitted with a direct insertion probe. Unless otherwise stated, spectra were run at 70eV with the ionisation chamber temperature below the sample melting point.
5. Melting points (m.p.) were taken on a Kofler Micro Heating Stage and were corrected.
6. Column chromatography was carried out using Hopkin and Williams silica gel M.F.C. and Camag neutral alumina

grade II as stationary phases. Reagent grade solvents were used as eluants without preliminary drying.

7. Solvents:

- a. Petrol refers to petroleum spirit b.p. 40-60°
- b. Ether was dried by standing over sodium wire.
- c. Benzene was dried by refluxing under a Dean and Stark apparatus, then distilling onto, and standing over, sodium wire.
- d. A. R. Carbon tetrachloride was dried by refluxing over and distilling onto molecular sieve type 4A.
- e. A. R. Chloroform was washed with water, initially dried with anhydrous magnesium sulfate, then dried as for carbon tetrachloride. It was stored in the dark and used soon after drying.

8. Photochemical reactors:

- a. Rayonet photochemical reactor containing sixteen 21 watt lamps, giving a broad emission spectrum between 250-360 n.m. with a maximum at 300 n.m.
- b. Hanovia photochemical reactor containing a 100 watt medium pressure mercury lamp, with maxima at 254, 265, 297, 313 and 336 n.m.

N,N'-Diphenylsulfamide, Sulfanilide⁵⁰

Redistilled sulfuryl chloride (40 ml., 0.49 mole) was added over 2 hr. to a vigorously stirred solution of aniline (96 g., 1 mole) and pyridine (66 ml., 0.8 mole) in ethanol-free chloroform (500 ml.) under anhydrous conditions at -10° . The resulting dark solution was allowed to stand at room temperature overnight, then poured with stirring into acetic acid (2N, 1200 ml.). The chloroform layer was removed, extracted with cold aqueous sodium hydroxide (1N, 3 x 200 ml.) and the extract acidified with cold 2N hydrochloric acid. The resulting precipitate was washed with water, dried at the pump, and recrystallised from chloroform to give sulfanilide (59 g., 47%) as prisms, m.p. $111-112^{\circ}$ (lit.⁴⁹ m.p. $111-112^{\circ}$).

ν_{\max} . 3260, 1490 (NH), 1600 (C=C), 1340, 1155, 1145 (SO_2), 745, 695 cm^{-1}

λ_{\max} . (EtOH) 207 (ϵ 10,800), 232 (15,200), 273 nm, (1420).

The following were prepared by a similar procedure:

4,4'-Dimethylsulfanilide (10%) m.p. 95° from petrol (lit.⁴⁹ m.p. $96-97^{\circ}$).

ν_{\max} . 3260 (NH str.), 1610 (aromatic C=C str.), 1505 (NH bend), 1320, 1160 (SO_2), 800, 695 cm^{-1} (p-disubst. benzene)

4,4'-Dichlorosulfanilide (25%) m.p. $119-120^{\circ}$ from petrol (lit.⁵⁰ m.p. $120-121^{\circ}$)

$\nu_{\text{max.}}$ 3240 (NH str.), 1490 (NH bend), 1330, 1160 (SO₂), 810 cm.⁻¹
(p-disubst. benzene).

4,4'-Dinitrosulfanilide (45%) m.p. 185-190° (decomp. m.p. variable with rate of heating) (lit. m.p. 195-197°, ⁵⁰ 204-205°⁷⁹).

$\nu_{\text{max.}}$ 3240, 1600, 1520, 1420, 1350, 1300, 1240, 1115, 940, 850, 750, 695 cm.⁻¹

m/e 338 base, 303, 372, 201, 138.

1H,3H,[2,1,3]Benzothiadiazoline 2,2-dioxide⁵¹

A solution of o-phenylenediamine (10.8 g., 0.1 mole.) and sulfamide (9.6 g., 0.1 mole) in dried diglyme (100 ml.) was added over 30 min. to dried diglyme (200 ml.) heated under reflux. The heating was continued for a further 15 min., while ammonia was evolved, and the reaction then stopped by cooling the flask and its contents rapidly in an ice bath. The reaction mixture was filtered to remove a white precipitate and the solvent removed by distillation under reduced pressure (55°, 15 mm.). A solution of the residue in warm ether (200 ml.) was washed successively with hydrochloric acid (2N, 3 x 50 ml.) and saturated brine (50 ml.) and dried over CaSO₄. The addition of benzylamine (10 ml.) precipitated the sulfamide salt which was isolated by filtration, washed with ether, and decomposed by shaking with hydrochloric acid (2N, 200 ml.). Extraction of the acidic solution with

ether (4 x 100 ml.), drying the extract (CaSO₄) and evaporating to dryness gave 1H,3H,[2,1,3]benzothiadiazoline 2,2-dioxide (14.2 g., 83%), m.p. 175-177°, m.p. 180-182° from benzene (lit.⁵¹ m.p. 181-183°),
 $\nu_{\text{max.}}$ 3280, 1485 (NH), 1600 (aromatic C=C), 1330, 1320, 1160, 1150 (SO₂), 740, 730 cm.⁻¹ (o-disubst. benzene).

Diglyme was dried by heating to reflux over, and distilling from, calcium hydride, and storing over molecular sieves (type 5A). Failure to use rigorously dried diglyme reduced the yield, e.g. to 3.6%.

1H,3H,Naphtho[1,8-cd][1,2,6]thiadiazine 2,2-dioxide

From 1,8-diaminonaphthalene (15.9 g., 0.1 mole) and sulfamide (9.6 g., 0.1 mole) was prepared similarly 1H,3H,naphtho-[1,8-cd][1,2,6]thiadiazine 2,2-dioxide (13.8 g., 63%) as needles m.p. 219-222° from benzene-ether (Found: C, 54.5; H, 3.6; N, 12.7; S, 14.2. C₁₀H₈N₂O₂S requires C, 54.55; H, 3.7; N, 12.7; S, 15.5%)
 $\nu_{\text{max.}}$ 3210, 3180, (NH), 1600 (C=C), 1310, 1300, 1150 (SO₂), 810, 750 cm.⁻¹
 m/e 220 (C₁₀H₈N₂O₂S, base), 186, 156, 155, 128, 78, 64.

1H,3H,Dibenzo[df][2,1,3]thiadiazepine 2,2-dioxide

A solution of 2,2'-diaminobiphenyl (9.1 g., 0.049 mole) and sulfamide (4.7 g., 0.049 mole) in dry diglyme (50 ml.) was added dropwise over 25 min. to dry diglyme (100 ml.) heated under reflux. The heating was continued for a further 20 min. while ammonia was evolved, and the flask and its contents were then cooled rapidly in an ice bath. After the solvent had been removed by distillation under reduced pressure (55°, 15 mm.), the residue was dissolved in warm ether (150 ml.) and the solution extracted with aqueous sodium hydroxide (2N, 2 x 50 ml.). Acidification of the extract with acetic acid (2N, 350 ml.) and recrystallisation of the resulting precipitate from chloroform gave 1H,3H,dibenzo[df][2,1,3]thiadiazepine 2,2-dioxide (63%), m.p. 209-212° (decomp.) (Found: C, 58.2; H, 4.1; N, 11.0; S, 12.7. $C_{12}H_{10}N_2O_2S$ requires C, 58.5; H, 4.1; N, 11.3; S, 13.0%.

ν_{\max} . 3250, 1490 (NH), 1290, 1150 (SO₂), 970, 760, 720 cm.⁻¹ (o-disubst. benzene).

λ_{\max} . 220 (ϵ 15,600), 250 nm. (7,800).

m/e 246 ($C_{12}H_{10}N_2O_2S$, base), 182, 181, 180, 167, 154, 152, 127, 91, 77, 76.

3,3'-Dimethylsulfanilide and N-m-tolylsulfamide

m-Toluidine (1 mole) and sulfamide (0.2 mole) were allowed to react at 100° as described in the literature⁵² to give 3,3'-dimethylsulfanilide (8%), m.p. 132-133° from chloroform (Found: C, 60.6; H, 5.7; N, 9.2; S, 11.6. $C_{14}H_{16}N_2O_2S$ requires C, 60.9; H, 5.8; N, 10.1; S, 11.6%)

ν_{\max} . 3250, 1490 (NH), 1610, 1590 (C=C), 1320, 1170, 1150 (SO₂), 780, 690 cm^{-1} (m-disubst. benzene).

p.m.r. (CDCl₃) 2.9-3.5 τ (10H, m); 7.78 τ (6H, s).

and N-m-tolylsulfamide (31%), m.p. 83-85°, from chloroform (lit.⁵² m.p. 76-78°) (Found: C, 44.9; H, 5.4; N, 15.2. Calc. for $C_7H_{10}N_2O_2S$: C, 45.2; H, 5.4; N, 15.0%)

ν_{\max} . 3400, 3280 (NH, NH₂), 1610 (C=C), 1330, 1150 (SO₂), 780, 690 cm^{-1} (m-disubst. benzene).

m/e 186 ($C_7H_{10}N_2O_2S$) base, 169, 107, 106, 105.

3-Methylsulfanilide

a) N-m-tolylsulfamide (3.7 g., 0.02 mole) and aniline (9.3 g., 0.1 mole) were heated together at 75° for 20 hr. The dark reaction mixture was cooled, dissolved in ether (100 ml.) and shaken with cold aqueous sodium hydroxide (2N, 150 ml.). Acidification of the aqueous extract with cold 2N hydrochloric acid precipitated an oily product (1.0 g.), m.p. 82-87°.

Recrystallisation from chloroform gave needles, m.p. 95-98° which were analysed by p.m.r. 2.5-3.2 τ (45H,m); 7.75 τ (3H,s); i.e. 3:1 ratio of sulfanilide:3-methylsulfanilide. m/e of mixture: 276, 262, 248 in ratio 1:12:40 ion currents. The mixture proved inseparable on column chromatography.

b) Acetanilide (25.3 g., 0.185 mole) was converted to acetanilide-N-sulfochloride, without isolation from the final benzene solution, by the method of Battegay,⁸⁰ and m-toluidine (64 g., 0.6 mole) in dry benzene (150 ml.) added dropwise at 3-5°. The reaction mixture was filtered to remove a precipitate of the amine hydrochloride, then washed successively with hydrochloric acid (2N, 3 x 150 ml.) and aqueous sodium hydroxide (2N, 3 x 100 ml.). The alkaline extract on acidification precipitated a colourless solid (6.1 g.), m.p. 98-100°. Chromatography of this on a silica column (3 x 20 cm.) eluted with 1:1 petrol:ether, 3-methylsulfanilide (4.9 g., 10%), m.p. 105-106° from chloroform, (Found: C, 58.9; H, 5.3; N, 10.5; S, 12.2. C₁₃H₁₄N₂O₂S requires C, 59.5; H, 5.4; N, 10.7; S, 12.0%).

ν_{\max} . 3260, 1500 (NH), 1620, 1600 (C=C), 1330, 1180, 1160 (SO₂), 790, 760, 690 cm.⁻¹ (m-disubst., and mono subst., benzene) m/e 262 (C₁₃H₁₄N₂O₂S), 107, 106, 93 base, 92.

p.m.r. (CDCl₃) 2.65-3.24 τ (11H, m); 7.83 τ (3H, s).

4-Chloroacetanilide-N-sulfochloride

Sodium hydride (50% dispersion in oil, 2.4 g., 0.05 mole) was added to a suspension of p-chloroacetanilide (8.5 g., 0.05 mole) in dry benzene (175 ml.). The reaction was heated under reflux for 12 hr., then cooled externally to 7° and sulfonyl chloride (4.05 ml., 0.05 mole) in dry petrol added dropwise with stirring. The reaction was stirred for 2 hr. at 7°, filtered, and the filtrate evaporated under reduced pressure to give an oil (13.3 g.). Trituration with petrol gave 4-chloroacetanilide-N-sulfochloride (10.0 g., 75%), m.p. 92.5-93.5° from CCl₄. (Found C, 35.5; H, 2.7; N, 5.4. C₈H₇Cl₂NO₃S requires C, 35.85; H, 2.6; N, 5.2%)
 ν_{max} . 1730, 1400, 1230, 1190, 1160, 1090, 1010, 910, 740, 710 cm.⁻¹
 m/e 271, 269, 267 (2-Cl) (C₈H₇Cl₂NO₃S); 229, 227, 225 (2-Cl); 171, 169 (1-Cl); 153; 151; 129, 127 (1-Cl); 64 (base).

4-Bromo-4'-chlorosulfanilide

p-Bromoaniline (2.6 g., 15 mmole) in dry ether (30 ml.) was added dropwise with stirring to p-chloroacetanilide-N-sulfochloride (1.3 g., 5 mmole) in dry ether (50 ml.) cooled to 3°. The reaction was heated under reflux overnight, then filtered and the filtrate evaporated to dryness to give an oil

(2.7 g.) $\nu_{\text{max.}}$ 3250, 1700 cm^{-1} . Analysis by t.l.c. showed two components. The oil in aqueous sodium hydroxide (1N, 100 ml.) was heated to 80° for 5 min., cooled, filtered, and acidified with 2N hydrochloric acid to precipitate 4-bromo-4'-chloro-sulfanilide (1.5 g., 83%), m.p. 119-121° from 1:1 chloroform:petrol (Found; C, 39.8; H, 2.7; N, 7.7; S, 8.6. $\text{C}_{12}\text{H}_{10}\text{BrClN}_2\text{O}_2\text{S}$ requires C, 39.85; H, 2.8; N, 7.75; S, 9.0%)
 $\nu_{\text{max.}}$ (Nujol) 3270, 1490, 1330, 1150, 1010, 805, 720, 700 cm^{-1}
 m/e 364, 362, 360 ($\text{C}_{12}\text{H}_{10}\text{BrClN}_2\text{O}_2\text{S}$, base); 263, 261, 236, 170-3127.

Total intensity of 408, 406, 404 (2-Br) and 320, 318, 316 (2-Cl) less than 0.5% of 364, 362, 360 (Br, Cl).

4-Chlorosulfanilide

By a similar procedure p-chloroacetanilide-N-sulfochloride (2.6 g., 10 mmole) and aniline (3.1 g., 30 mmole) gave an oil (3.1 g.) $\nu_{\text{max.}}$ 3250, 1700 cm^{-1} . After hydrolysis in aqueous sodium hydroxide, acidification with 2N hydrochloric acid and extraction with ether gave 4-chlorosulfanilide (2.7 g., 97%) as an oil. (Found C, 50.4; H, 3.8; N, 10.1. $\text{C}_{12}\text{H}_{11}\text{ClN}_2\text{O}_2\text{S}$ requires C, 51.0; H, 3.9; N, 9.9%).
 $\nu_{\text{max.}}$ 3250, 1600, 1500, 1340, 1220, 1160, 1100 cm^{-1}
 m/e 284, 282 (1-Cl), base 93.

N,N',4,4'-Tetrachlorosulfanilide

Chlorine (5.5 g.) was dissolved in aqueous sodium hydroxide (2N, 50 ml.) at 0-2°. ⁵⁵ Carbon tetrachloride (40 ml.), precooled to 2°, and then 4,4'-dichlorosulfanilide (3.1 g., 0.01 mole) were added and the reaction stirred vigorously for 4 hr. The aqueous layer was separated and extracted with more carbon tetrachloride (3 x 40 ml.). The combined extracts dried (MgSO₄) and evaporated to dryness gave N,N',4,4'-tetrachlorosulfanilide (3.7 g., 95%), m.p. 84-85° (decomp.)

$\nu_{\text{max.}}$ 1490, 1360, 1180, 1170, 1100, 1090, 1020, 900, 800, 730 cm.⁻¹

m/e 383.9062, C₁₂H₈³⁵Cl₄N₂O₂S requires 383.9061.

The freshly prepared product analysed iodimetrically for 90% purity on the basis of active chlorine. The product decomposed overnight at room temperature; but could be stored indefinitely at -40°.

4-Bromo-N,N',4'-trichlorosulfanilide

By a similar procedure, 4-bromo-4'-chlorosulfanilide (0.7 g.) gave 4-bromo-N,N',4'-trichlorosulfanilide (0.8 g., 97%), m.p. 90-92° (decomp.)

$\nu_{\text{max.}}$ (Nujol) 1170, 1090, 1020, 900, 800, 730 cm.⁻¹

m/e 432, 430, 428 (C₁₂H₈BrCl₃N₂O₂S); 398, 396, 394 (Br, 2-Cl); 362, 360, 358 (BrCl).

N,N'-Dichlorosulfanilide

a. By a similar procedure sulfanilide (2.4 g., 0.01 mole)

gave a yellow solid (3.1 g.) m.p. 60-68° from petrol.

$\nu_{\text{max.}}$ 1590, 1480, 1400, 1360, 1170, 1070, 950, 910, 770, 690,
670 cm.^{-1}

m/e 354, 352, 350 (3-Cl), 320, 318, 316 (2-Cl), 283, 281 (1-Cl),
93 (base),

consistent with a mixture of di-, and tri- chlorinated sulfanilides.

b) Sulfanilide (0.5 g., 2 mmole) and N-chlorosuccinimide

(0.54 g., 4 mmole) were shaken vigorously at room temperature
in dry carbon tetrachloride (100 ml.) for 24 hr. No reaction
occurred. The solution was heated under reflux for 12 hr.

Analysis by t.l.c. showed only sulfanilide and N-chlorosuccinimide
present. A similar result was obtained using N-bromosuccinimide
as the halogenating agent.

c. A solution of chlorine in aqueous 1molar sodium carbonate
was adjusted to be 1.6 molar in available chlorine.⁵⁷ One
equivalent (1.25 ml.) was added dropwise to a stirred, cooled
(5°) suspension of sulfanilide (500 mg., 2 mmole) in aqueous
sodium bicarbonate (0.075 M, 25 ml.).

After 3 hr. ether extraction gave, after drying (MgSO_4),

an oil (530 mg.) which evolved chlorine at room temperature.

ν_{max} . identical to authentic sulfanilide.

m/e 320, 318, 316 (2-Cl) (5%); 284, 282 (1-Cl) (10%), 248 (85%) of total parent ion currents.

Increasing the reaction time to e.g. 12 hr. did not increase the yield of chlorinated sulfanilides.

d. To sulfanilide (248 mg., 1 mmole) in dry benzene (10ml.) at 7° was added with stirring tert-butyl hypochlorite (0.10 ml., 0.84 mmole). After 3 hr. the reaction had turned pale yellow. Evaporation of the benzene under reduced pressure below 10° gave a viscous oil (280 mg.).

ν_{max} . (thin film) identical to sulfanilide.

m/e 320, 318, 316 (2-Cl) (10%); 284, 282 (1-Cl) (25%); 248 (65%) of total ion currents.

The product analysed iodimetrically for 25% active chlorine.

The difference between the mass spectral and iodimetric determinations may be due either to differences in sensitivity of the three compounds in the mass spectrometer, or to some chlorination of the aromatic ring.

e. Chlorine was passed into aqueous sodium bicarbonate (0.6 N, 50 ml.) at 2° until the solution gave no precipitate

with aqueous barium chloride.⁵⁶ Carbon tetrachloride (20 ml.) precooled to 2°, then sulfanilide (250 mg., 1.0 mmole) were added and the reaction stirred vigorously for 1 hr. The organic layer was separated, dried, (MgSO₄) and evaporated to dryness to give a yellow oil (245 mg.),
m/e 320, 318, 316 (C₁₂H₁₀Cl₂N₂O₂S); 284, 282 (1-Cl);
248, 93 (base).
 ν_{max} . 3260, 1490, 1610, 1340, 1150, 1090, 800, 730, 695 cm.⁻¹.
Analysis by t.l.c. (silica-benzene) consistent with a mixture of sulfanilide and N-chlorinated sulfanilides.

Pyrolysis of N,N'-Dichlorosulfanilide

The crude reaction product (145 mg.) from the preceding experiment was heated under reflux in dry carbon tetrachloride (25 ml.) for 12 hr., and the products chromatographed on a silica column (1 x 20 cm.). Elution with 1:10 ether:petrol gave azobenzene (19 mg., 23%) m.p. and mixed m.p. 67-68° (lit.⁸⁷ m.p. 68°). Elution with ether gave sulfanilide (40 mg., 16%), m.p. 110-112° (lit.⁴⁹ m.p. 112°), i.r. identical to an authentic specimen. Small amounts of chloroazobenzenes were detected on t.l.c. and from the mass spectrum of the crude azobenzene.

N,N',4-Trichlorosulfanilide

By a similar method to method (e) above, 4-chlorosulfanilide (2.3 g., 8.2 mmole) gave N,N',4-trichlorosulfanilide as an oil (2.8 g.) containing unchanged 4-chlorosulfanilide (i.r., t.l.c.).
 ν_{max} . (thin film) 3260, 1700, 1580, 1490, 1400, 1180, 1100, 830, 760, 720 cm^{-1}
 m/e 356, 354, 352, 350 ($\text{C}_{12}\text{H}_9\text{Cl}_3\text{N}_2\text{O}_2\text{S}$); 3.9, 317, 315 (2-Cl); 284, 282, 280.

The crude product (2.4 g.) after thermolysis in dry carbon tetrachloride gave on chromatographic workup:

- a) 4,4'-dichloroazobenzene (8 mg.) m.p. and mixed m.p. 180-185°, (lit.⁸⁷ m.p. 186°).
- b) A mixture of chlorinated azobenzenes (89 mg.). T.l.c. (silica-benzene) indicated 4,4'-dichloroazobenzene and azobenzene present, plus a product of intermediate Rf.
 ν_{max} . 1620, 1510, 1580, 1490, 1380, 1260, 1150, 1090, 1020, 840, 810, 780, 690 cm^{-1}
 m/e 254, 252, 250 (2-Cl); 218, 216 (1-Cl); 217, 215 (1-Cl); 183, 182, 181.
- c) Recovered 4-chlorosulfanilide (480 mg., 20%), identified by i.r. and t.l.c. (silica-ether).

Pyrolysis of N,N',4,4'-Tetrachlorosulfanilide

N,N',4,4'-Tetrachlorosulfanilide (1.05 g., 2.75 mmole) in dry carbon tetrachloride (50 ml.) was heated under gentle reflux for 24 hr., until reaction was complete. Chlorine was evolved, and the products chromatographed on a neutral alumina column. Elution with ether:petrol 1:20 gave 4,4'-dichloroazobenzene, (246 mg., 36%), m.p. and mixed m.p. 184-185° (lit.⁸⁷ m.p. 186°). The remainder of the material appeared to have formed polar polymers, eluting with ether:methanol mixtures. Analysis by mass spectrometry of the gases evolved during the pyrolysis gave m/e 74, 72, 70 (2-Cl, base); intensity of ion current at m/e 64 (SO₂) less than 2% of base.

4-Bromo-N,N',4'-trichlorosulfanilide

Under similar pyrolytic conditions, 4-bromo-N,N',4'-trichlorosulfanilide (430 mg., 1 mmole) gave a mixture of azobenzenes (55 mg., 26%) which were sublimed at 120-140°. The product could not be resolved by t.l.c. on silica. Analysis by mass spectroscopy gave m/e 339, 341, 343 (2-Br); 294, 296, 298 (1-Cl, Br); 250, 252, 254 (2-Cl) with total parent ion currents (i.e. approx. yields) in ratio 5:16:8.

Dechlorination of N,N',4,4'-tetrachlorosulfanilide

a. A solution of sodium iodide (435 mg., 2.9 mmole) in acetone

(5 ml.) was added dropwise at -45° to the tetrachlorosulfanilide (560 mg., 1.45 mmole) in acetone (50 ml.). Iodine was liberated. The solution was evaporated to small bulk, excess 2N aqueous sodium thiosulfate added, the mixture extracted with ether and the extract evaporated to dryness to give a dark tar. Chromatography on neutral alumina eluted with petrol 4,4'-dichloroazobenzene (< 5 mg.), m.p. and mixed m.p. $185-186^{\circ}$ after sublimation (lit.⁸⁷ m.p. 186°).

b. Zinc powder was activated by washing successively with 50% hydrochloric acid, distilled water, ethanol and ether. N,N',4,4'-tetrachlorosulfanilide (0.60 g., 1.57 mmole) and freshly prepared activated zinc powder (0.5 g.) in dry benzene (90 ml.) were stirred at room temperature for 1 hr. No reaction occurred. The reaction mixture was heated under reflux for 6 hrs. Chlorine was evolved, identified by acidity and smell; but no sulfur dioxide could be detected by potassium dichromate test paper.

Chromatography of the reaction product on silica gave 4,4'-dichloroazobenzene (120 mg., 30%) m.p. and mixed m.p. $184-186^{\circ}$ (lit.⁸⁷ m.p. 186°).

Pyrolysis of N,N',4,4'-tetrachlorosulfanilide

The tetrachlorosulfanilide (350 mg., 0.9 mmole) in dry

ether (100 ml.) was heated under reflux for 12 hr. The solvent was removed under reduced pressure to give a red oil $\nu_{\text{max.}}$ 3280 cm.^{-1} , which was chromatographed on neutral alumina. Petrol:ether, 20:1 eluted 4,4'-dichloroazobenzene (5 mg., 2%) m.p. 183-186° (lit.⁸⁷ m.p. 186°) i.r. spectrum identical to an authentic sample. Ether:methanol, 50:1 eluted 4,4'-dichlorosulfanilide (170 mg., 49%) m.p. and mixed m.p. 119-121° (lit.⁵⁰ m.p. 120-121°).

Photolysis of N,N',4,4'-tetrachlorosulfanilide

The tetrachlorosulfanilide (350 mg., 0.9 mmole) in dry carbon tetrachloride (30 ml.) was irradiated for 2.5 hr. using a Phillips 500 watt sun-lamp, until analysis by t.l.c. showed reaction complete. Chromatography on a silica column gave 4,4'-dichloroazobenzene (18 mg., 8%), m.p. 185° (lit.⁸⁷ m.p. 186°), i.r. identical to an authentic sample. A black tar (approx. 250 mg.) accounted for the remainder of the starting material.

Chlorination of Cyclic Sulfamides

1H,3H Dibenzo[df][2,1,3]thiadiazepine 2,2-dioxide

a. Attempts to chlorinate the cyclic sulfamide under reaction conditions a-c and e described above for sulfanilide, were unsuccessful. Starting material was recovered, identified by m.p. and mixed m.p., and i.r. spectrum.

b. Tert-butyl hypochlorite (0.24 ml., 2 mmole) was added to a cooled (0°), stirred suspension of the cyclic sulfamide (120 mg., 0.49 mmole) in carbon tetrachloride:chloroform 1:1 (50 ml.). The suspension gradually dissolved. Aliquots were removed at 1 hr. intervals and the disappearance of the amide absorption monitored at 3250 cm.⁻¹. Disappearance was complete after 12 hr.

Evaporation of the solvent under reduced pressure gave a waxy solid (164 mg.).

ν_{max} . 1480, 1300, 1150, 1030, 760, 700 (broad peaks)

m/e 386, 384, 382 (4-Cl); 352, 350, 348 (3-Cl); 351, 349, 347 (3-Cl); 318, 316, 314 (2-Cl).

The use of only 2 equivalents of tert-butyl hypochlorite, or of a shorter reaction time, failed to completely N-chlorinate the cyclic sulfamide.

Pyrolysis of chlorinated product

Pyrolysis of the chlorinated reaction product (150 mg.) in

dry carbon tetrachloride for 4 hr. gave, after removal of solvent, a black, water soluble tar. From an aqueous solution of the tar, ether extracted a brown gum (7 mg.). Analysis by t.l.c. (silica-ether) showed no chloro-benzo-[c]cinnolines present. (No fluorescence under u.v. visualisation).

c. Chlorine gas was passed into a stirred solution of the cyclic sulfamide (0.50 g., 2 mmole) in dry chloroform (100 ml.) at 5° for 30 min. The resulting orange solution was stirred for 3 hrs. at 5° until analysis by t.l.c. (silica-ether) showed no remaining starting material. Evaporation of the solvent under reduced pressure (temperature <15°) gave a dark tar (500 mg.), ν_{\max} . 3250, 1150 (broad peak).

1H,3H,Benzo[2,1,3]thiadiazoline 2,2-dioxide and

1H,3H,Naphtho[1,8-cd][1,2,6]thiadiazine 2,2-dioxide

a. The sulfamides were recovered from attempts to chlorinate under conditions b, c and e described above for sulfanilide.

b. Naphthothiadiazine dioxide (2.2 g., 0.01 mole) under the conditions⁵⁵ described above for preparing N,N',4,4'-tetrachlorosulfanilide gave a brown precipitate (2.1 g.) m.p. >330° (charred) insoluble in common organic solvents.

ν_{\max} . 3200, 1600, 1150, 800 cm^{-1} all peaks broad,
m/e parent > 1000.

Benzothiadiazoline dioxide (2.0 g., 0.017 mole) under the same conditions⁵⁵ gave a buff acidic precipitate, (2.0 g.) m.p. >260° (charred).

$\nu_{\text{max.}}$ 3550, 3200, 1300, 1150, 850, 750 cm.^{-1} all peaks broad.

No satisfactory recrystallisation solvent could be found.

c. Naphthothiadiazine dioxide (2.2 g., 0.01 mole) was suspended in a cooled (5°) solution of tert-butyl hypochlorite (4.8 ml., 0.04 mole) in dry chloroform (100 ml.). Aliquots were removed at intervals and the disappearance of the amide absorption at 3250 cm.^{-1} monitored. Disappearance was complete after 4 hrs. Evaporation of the solvent under reduced pressure gave an oil (2.5 g.),

m/e 360, 358, 356 (4-Cl); 336, 334, 332 (3-Cl); 291, 289, 287 (2-Cl).

Consistent with tri- and tetra-chlorinated products.

The product was unstable at room temperature, evolving chlorine.

Under similar conditions benzothiadiazoline dioxide (1.7 g., 0.01 mole) and tert-butyl hypochlorite (4.8 ml., 0.04 mole) gave a trichlorinated thermally unstable oil (2.0 g.).

m/e 276, 274, 272 (3-Cl); 241, 239, 237 (2-Cl); 204, 202 (1-Cl).

$\nu_{\text{max.}}$ 1600, 1480, 1300, 1150, 1030, 830, 740, 695 cm.^{-1}

Acyclic Diaryl Sulfamides

Oxidation of Sulfanilide with Sodium Hypochlorite

To a stirred solution of sulfanilide (5.0 g., 0.02 mole) in aqueous sodium hydroxide (1N, 50 ml.), cooled externally to 5°, was added dropwise an aqueous solution of sodium hypochlorite (2.2 N, 9.1 ml.) in aqueous sodium hydroxide (2N, 10 ml.).

An immediate reaction occurred. Extraction of the solution with ether (3 x 100 ml.) gave a deep red extract. The addition and extraction were repeated with four portions of alkaline hypochlorite until no further reaction occurred. The extracts after drying (CaSO₄) gave a dark red solid (1.01 g.) m.p. 85-90°.

Chromatography on a basic alumina column (2 x 20 cm.) with 3:1 petrol:ether gave p-benzoquinoneanil (823 mg., 23%) m.p. 102-103° (lit.⁸² m.p. 103-103.5°) (Found: C, 78.2; H, 4.9; N, 7.95. Calc. for C₁₂H₉NO C, 78.7; H, 4.95; N, 7.65%.

M.W. 183.2)

λ_{max} . 264 (ϵ 17,300), 290 (13,600), 460 n.m. (3,280)

ν_{max} . 1640 (C=O), 1610 (quinonoid C=C), 870, 790, 690 cm.⁻¹

m/e 183 (C₁₂H₉NO) base, 182, 155, 154, 129, 77.

Comparison by t.l.c. of the crude reaction products with an authentic sample failed to show the presence of azobenzene.

None was isolated in the chromatographic work up.

Oxidation of sulfanilide with sodium hypobromite

Oxidation of sulfanilide (0.5 g., 2 mmole) under similar conditions using alkaline sodium hypobromite⁸³ as oxidant, gave quinone-anil (40 mg., 22%). No azobenzene was detected on chromatographic work-up.

Oxidation of sulfanilide with potassium permanganate

- a. Sulfanilide (1.5 g., 6 mmole) in aqueous sodium hydroxide (2N, 50 ml.), cooled to 5° was oxidised by the dropwise addition of aqueous potassium permanganate (1.0 g., 6.3 mmole). Ethereal extraction gave a dark oil (50 mg.) containing six highly coloured components (t.l.c. silica-benzene). Chromatography gave quinone-anil (40 mg., 3.5 %), m.p. and mixed m.p. 103-104°. Acidification of the alkaline reaction mixture (conc. HCl) and ~~ether~~ethereal extraction, gave a dark tar (0.3 g.). t.l.c. (silica-benzene) showed no sulfanilide present.
- b. Under similar conditions sulfanilide (268 mg., 1.08 mmole) and potassium permanganate (120 mg., 0.76 mmole) gave quinone-anil (<5 mg.) and unchanged sulfanilide (100 mg., 0.4 mmole).

Attempted oxidation of sulfanilide with hydrogen peroxide

Sulfanilide (240 mg., 1 mmole) in aqueous sodium hydroxide (0.1 N, 20 ml.) was precipitated unchanged by the dropwise addition of hydrogen peroxide (100 vol., 5 ml.).

Oxidation of sulfanilide with sodium hypochlorite

Aqueous sodium hypochlorite (2M, 3.5 ml.) was added dropwise over 5 min. to a stirred, cooled (3°) solution of sulfanilide (840 mg., 3.4 mmole) in aqueous sodium carbonate (1M, 50 ml.). The reaction mixture was extracted with ether which gave, after drying (Na₂SO₄), a dark oil (358 mg.) which was chromatographed on a silica column. Benzene eluted *p*-benzoquinoneanil (17 mg., 2.7%) m.p. 99-100° (lit.⁸² m.p. 103-103.5°) i.r. identical to an authentic sample. Benzene-ether 1:1 eluted sulfanilide (150 mg., 18%) m.p. 110-111° (lit.⁴⁹ m.p. 112°).

The aqueous reaction layer was saturated with sodium chloride; but gave no precipitate of N-phenylbenzo-1,4-quinonediimine-N'-sulfonate.⁶² Acidification with 2N hydrochloric acid and extraction with ether gave, after drying, (Na₂SO₄), a gum (254 mg.). Chromatography on silica with benzene-ether 50:1 as eluent gave 1H,3H dibenzo[df][2,1,3]thiadiazepine 2,2-dioxide (99 mg., 12%) m.p. and mixed m.p. 211-213° (decomp.) (Found: C, 58.6; H, 4.0; N, 11.2; S, 13.1. C₁₂H₁₀N₂O₂S requires C, 58.5; H, 4.1; N, 11.3; S, 13.0%).

$\nu_{\text{max.}}$ 3250, 1490, 1290, 1150, 970, 760, 720 cm.⁻¹

m/e 246 (C₁₂H₁₀N₂O₂S base), 181, 167, 154.

Benzene-ether 20:1 eluted a buff solid (25 mg.) m.p. 130-135° (decomp.).

$\nu_{\text{max.}}$ 3220, 1600, 1310, 1270, 1150, 1030, 800, 750, 720
695 cm.^{-1}

m/e 487 (<5% base), 337 (base), 273, 246, 181, 93.

$337 \xrightarrow{*} 246 + 91 \quad (m^* = 179.5, \text{calc. } 179.6)$

$337 \xrightarrow{*} 273 + 64 \quad (m^* = 221.3, \text{calc. } 221.2)$

Oxidation of 4,4'-Dichlorosulfanilide with Sodium Hypochlorite

Aqueous sodium hypochlorite (1N, 10 ml.) was added over 5 min. with vigorous stirring to a solution of 4,4'-dichlorosulfanilide (1.6 g., 5 mmole) in aqueous sodium hydroxide (1N, 30 ml.) under ether (50 ml.). The reaction was cooled externally to 5°. After the addition was completed the ethereal layer was separated, the alkaline layer extracted with more ether (2 x 50 ml.), and the combined extracts dried (CaSO_4) and evaporated to dryness. The residue was a viscous red oil (0.64 g.). Chromatography on a silica column (2 x 25 cm.) eluted with petrol 4,4'-dichloroazobenzene (26 mg., 2%) m.p. and mixed m.p. 185-187° (lit.⁸⁷ m.p. 188°).

Elution with benzene gave N-(p-chlorophenyl)-p-benzoquinone imine (0.22 g., 20%) m.p. 82-83° (lit.¹⁵⁷ m.p. 83.5°).

m/e. 219, 217 (1-Cl, base).

Oxidation of 3,3'-Dimethylsulfanilide with Sodium Hypochlorite

Aqueous sodium hypochlorite (2N, 5 ml.) was added dropwise to a stirred, cooled (5°), solution of 3,3'-dimethylsulfanilide (0.94 g., 3.4 mmole) in aqueous sodium hydroxide (1N, 50 ml.) under a layer of ether (100 ml.). After 10 min. the aqueous layer was separated, extracted with more ether (3 x 50 ml.) and the combined ethereal extracts dried (CaSO₄) and evaporated to dryness. The residual viscous red oil (85 mg.) was chromatographed on a silica column (1 x 30 cm.). Benzene eluted N-m-tolyl-3-p-toluquinone-4-imine (65 mg., 10%), m.p. 37-39° (decomp.) (Found: C, 79.1; H, 5.9; N, 6.0. C₁₄H₁₃NO requires C, 79.6; H, 6.2; N, 6.6%, M.W. 211.25) ν_{\max} . 1640, 1620, 1580 (C=O and C=N), 800, 690 (m-disubst. benzene), 1290, 1090 cm.⁻¹

λ_{\max} . (EtOH) 265 (ϵ 15,000); 285 (10,200); 463 n.m. (2,100).
p.m.r. (CDCl₃) 2.7-3.7 τ (7H, m); 7.63 τ (3H,s); 7.73 τ (3H,s).

Oxidation of 3-Methylsulfanilide with Sodium Hypochlorite

Sodium hypochlorite (1N, 2 ml.) was added dropwise to a stirred solution of 3-methylsulfanilide (0.48 g., 1.85 mmole) in aqueous sodium hydroxide (1N, 12 ml.), cooled externally to 3°. The reaction mixture was shaken with ether (4 x 20 ml.) until the extract was colourless. The addition and extraction

were repeated until no further reaction occurred, and the combined extracts were dried (CaSO_4) and evaporated to dryness. The residual gum (95 mg.) analysed on t.l.c. (silica-benzene) for quinone-anil, R_f 1.8, dimethylquinone-anil R_f 2.8, and a third product R_f 2.4. Chromatography on a silica column (2 x 30 cm.) with petrol as eluant gave no azobenzene or substituted azobenzene. A polarity gradient from petrol to 1:10 benzene:petrol eluted a mixture of quinone-anils (76 mg.) analysed by t.l.c. and mass spectrometry. The chromatographed mixture was analysed by mass spectrometry; m/e 212, 211, 198, 197, 185, 183, 182 ratio of ion currents for m/e 211:197:183 = 19:33:18. An intermolecular reaction requires a ratio of 1:2:1. Analysis of the starting material 3-methylsulfanilide gave a ratio for m/e 276:262:248 of 0:100:2, and the mass spectrum of N-m-tolyl-3-p-toluquinone-4-imine showed no significant peaks for m/e 197 or 183.

Hydrolysis of N,N'-diarylsulfamides

a) Sulfanilide (330 mg., 1.3 mmole) in aqueous sodium hydroxide (1N, 50 ml.) was continuously extracted with ether at 30° for 12 hr. The ethereal extract dried (CaSO_4) and evaporated to dryness contained (i.r., t.l.c.) no aniline; but contained unchanged sulfanilide (12 mg.). Acidification of the aqueous layer and ethereal extraction (3 x 100 ml.)

completed recovery of sulfanilide, m.p. 111-112° (lit.⁴⁹ m.p. 112°). Similarly, no hydrolysis was observed over 24 hr. at 0°

b) Under similar conditions, 4,4'-dinitrosulfanilide (634 mg., 1.88 mmole) gave p-nitroaniline (92 mg., 0.67 mmole) m.p. 146-148° from methanol-benzene (lit.⁸⁷ m.p. 148°). infra-red spectrum identical to authentic p-nitroaniline.

c) The ultraviolet spectrum of sulfanilide (1×10^{-4} molar) in 0.1 N sodium hydroxide at 70° was monitored between 250 and 450 nm. for 12 hr. No change in the absorbance of the spectrum was observed.

Oxidation of p-nitroaniline with sodium hypochlorite

p-Nitroaniline (5.0 g., 0.036 mole) suspended in aqueous sodium hydroxide (1N, 100 ml.) and sodium hypochlorite (1M, 50 ml.) was heated at 90° for 1 hr. on a steam bath. The reaction mixture was then filtered while hot, and the residue digested with boiling ethanol (3 x 100 ml.) to remove p-nitroaniline, filtered and air dried to give 4,4'-dinitroazobenzene (2.0 g., 40%) m.p. and mixed m.p. 222-224° from benzene (lit. m.p. 216°^{34,84}, 222°⁸⁵). The aqueous filtrate on cooling precipitated p-nitroaniline. The total recovery of p-nitroaniline from this and the ethanolic washings was 2.0 g. (40%). No other products were detected (t.l.c. silica-benzene) from the reaction.

4,4'-Dinitroazobenzene

p-Nitroaniline (0.9 g., 6.5 mmole) and activated manganese dioxide⁸⁶ (6.0 g.) were heated in benzene (200 ml.) under reflux for 48 hr. The reaction mixture was filtered and chromatographed on silica. Benzene eluted 4,4'-dinitroazobenzene (0.3 g., 33%) m.p. 227-228° from benzene (lit. m.p. 216°^{34,84}, 222°⁸⁵)
 $\nu_{\text{max.}}$ 1610, 1540, 1350, 1005, 870, 810, 760, 690 cm.^{-1}
 m/e 272 ($\text{C}_{12}\text{H}_8\text{N}_4\text{O}_4$)

Oxidations with tert-butyl hypochloritea. 4,4'-Dichlorosulfanilide

Tert-butyl hypochlorite (182 mg., 2 mmole) and 4,4'-dichlorosulfanilide (534 mg., 2 mmole) in dry benzene (30 ml.) were stirred at 5° for 20 min. The addition of potassium tert-butoxide (2 mmole) in tert-butanol caused an instantaneous darkening of the reaction.

Chromatography on silica gave 4,4'-dichloroazobenzene (79 mg., 19%) m.p. and mixed m.p. 183-185° (lit.⁸⁷ m.p. 186°)

b. 4-Bromo-4'-chlorosulfanilide

Under similar conditions 4-bromo-4'-chlorosulfanilide (93 mg., 0.26 mmole) gave a mixture of halogenated azobenzenes (12 mg., 15%), m.p. 188-191°. m/e 342, 340, 388 ($C_{12}H_8Br_2N_2$); 298, 296, 294 ($C_{12}H_8BrClN_2$) 254, 252, 250 ($C_{12}H_8Cl_2N_2$). Ion currents (approx. yields) in ratio 1.33; 2.38; 1.00.

c. 3-Methylsulfanilide

Under similar conditions, 3-methylsulfanilide (225 mg, 0.86 mmole) gave a mixture of azobenzenes as an oil (38 mg., 23%), m/e: 210 ($C_{14}H_8N_2$), 196 ($C_{13}H_9N_2$, base), 182 ($C_{12}H_{10}N_2$). Ion currents (approx. yields) in ratio 1.0:2.2:0.95 respectively.

Cyclic Aryl SulfamidesOxidations with aqueous alkaline hypochlorite1H,3H,Dibenzo[df][2,1,3]thiadiazepine 2,2-dioxide

Aqueous sodium hypochlorite (2M, 7 ml.) was added dropwise over 10 min. to a stirred solution of the cyclic sulfamide (700 mg., 2.8 mmole) in aqueous sodium hydroxide (20 ml.), cooled externally to 5°. The reaction darkened during the addition and a brown precipitate formed. After 4 hr., ethereal extraction gave a yellow solid (80 mg.) which was chromatographed on a silica column. Benzene:ether, 20:1 eluted 2-chlorobenzo-[c]cinnoline (24 mg., 4%), m.p. 213-214° (lit. m.p. 211°,⁸⁹ 215.5-216°⁸⁸) (Found: C, 66.6; H, 3.4; N, 12.8. Calc. for C₁₂H₇ClN₂ C, 67.2; H, 3.3; N, 13.1%).

ν_{\max} (Nujol) 1615, 1600, 1575, 1550, 1415, 1360, 820, 780, 750 cm.⁻¹

m/e 216, 214 (C₁₂H₇ClN₂, base); 188, 186 (1-Cl), 151, 150, 93, 75.

p.m.r. (CDCl₃) 1.11-1.67 τ (m, 4H); 1.92-2.35 (sextet, 3H),

and benzo[c]cinnoline (10 mg., 2%), m.p. 150-155° (lit.⁸⁷ m.p.

156°), identical (t.l.c. and i.r.) to an authentic sample.

p.m.r. (CCl₄) 1.00-1.65 τ (m, 4H), 2.02-2.42 (q, 4H).

Acidification of the aqueous layer with dilute hydrochloric

acid, and ethereal extraction gave an orange gum (242 mg., 35%).

Analysis (t.l.c. and i.r.) consistent with unchanged starting

material. Filtration of the aqueous layer removed the original brown precipitate (240 mg.) formed during the oxidation. The filtrate gave a negative sulfate test with aqueous barium chloride.

The use of 90% dioxan, 10% water as a reaction solvent gave similar yields of chlorobenzocinnoline and benzocinnoline. Increasing the reaction time to 24 hours gave an increased yield of (9%) of the mixed benzocinnolines with no recovered starting material.

1H,3H,[2,1,3]Benzothiadiazoline 2,2-dioxide.

a. Aqueous sodium hypochlorite (0.42M, 3.6 ml., 1.51 mmole) was added during 5 min. to a stirred, cooled solution of benzothiadiazoline dioxide (0.506g., 2.98 mmole) in aqueous sodium hydroxide (2N, 10 ml.). The reaction was stirred for a further 3 min. acidified (HCl) and extracted with ether. The extract was treated immediately with an excess of ethereal diazomethane, evaporated to dryness and chromatographed on silica to give (i) N,N'-dimethyl-2,1,3-benzothiadiazoline 2,2-dioxide (0.118 g., 20%) m.p. 81-82°. (Found: C, 49.0; H, 5.2; N, 14.0; m/e 198. $C_8H_{10}N_2O_2S$ requires C, 48.5; H, 5.1; N, 14.1% M 198) ν_{\max} 1610, 1490, 1290, 1210, 1155, 870, 730 cm^{-1} . p.m.r. ($CDCl_3$) τ 2.9-3.4 (4H,m); 6.73 (6H,s)

(ii) 1,3-dimethyl-4 or 5-(3'-methyl-2,1,3'-benzothiadiazolin-1'-yl 2,2'-dioxide)-2,1,3-benzothiadiazoline 2,2-dioxide (0.385g., 67%) m.p. 180-190° (from benzene-cyclohexane) (Found: C, 47.7; H, 4.3; N, 14.6;

m/e 380; $C_{15}H_{16}N_4O_4S_2$ requires C, 47.4; H, 4.2; N, 14.7%; M, 380).

ν_{\max} 1600, 1480, 1320-1260, 1150, 850, 745 cm^{-1}

p.m.r. (CDCl_3) τ 2.7-3.6 (7H, m); 6.72, 6.73, 6.77 (9H, s, s, s).

b. Oxidation of benzothiadiazoline dioxide (0.6g., 3.5 mmole) under similar conditions using an excess (5 fold) of sodium hypochlorite gave a polymeric solid on ethereal extraction (0.6g., 100%) m.p. 140-160° charred. (Found: C, 42.6; H, 3.7; N, 14.1, S, 17.9% m/e 64).

ν_{\max} 3520, 3180, 2660, 1720, 1600, 1260, 1150, 740 cm^{-1} .

p.m.r. ($(\text{CD}_3)_2\text{CO}$) τ 0.0 (1H, exch. with D_2O); 2.6-3.4 (4.5H, m);

5.1 (1H, exch. with D_2O)

λ_{\max} (EtOH) 210 ($E_{1\text{cm}}^{1\%}$ 1.39×10^7); 288 nm. (2.1×10^6).

Methylation of the polymer with diazomethane gave quantitatively a

further polymer m.p. 185-195° decomp. (Found: C, 46.4; H, 3.8; S, 17.3;

m/e 64. $(C_7H_6N_2O_2S)_m$ requires C, 46.2; H, 3.3; S, 17.6%).

ν_{\max} 1730, 1600, 1480, 1320, 1270, 1150, 740 cm^{-1} .

p.m.r. (CDCl_3) τ 2.8-3.4 (3.8H, m); 4.65, 4.75 (3H, s, s)

1H,3H,Naphtho[1,8-cd][1,2,6]thiadiazine 2,2-dioxide

a. Oxidation of this cyclic sulfamide (1.1 g., 5 mmole) under similar conditions to those in the previous experiment gave an acid insoluble product (1.1 g.) m.p. $>290^{\circ}$ (charred)

$\nu_{\text{max.}}$ 3200, 1600, 1310, 1150, 820, 740 cm.^{-1} , all peaks broad.

No neutral products were isolated from the reaction mixture by extraction with ether.

b. Aqueous sodium hypochlorite (2M, 10 ml.) was added dropwise with stirring over 1.5 hr. to a cooled (5°) solution of the cyclic naphthothiadiazine dioxide (1.1 g., 5 mmole), tetracyclone (2.4 g., 6.3 mmole) and sodium hydroxide (1.0 g., 25 mmole) in dioxan (50 ml.) and water (7 ml.). A tar separated during the addition. The reaction was stirred overnight at room temperature, then poured into water (200 ml.). Ether extracted tetracyclone (2.4 g.) m.p. and mixed m.p. 219-220°. Analysis of the extract by t.l.c. (silica/alumina-ether/benzene) showed only tetracyclone present.

Acidification of the aqueous layer with 2N hydrochloric acid gave a black ether insoluble precipitate (1.0 g.) m.p. $>160^{\circ}$ (charred) $\nu_{\text{max.}}$ 1160 cm.^{-1} . The filtrate gave a negative sulfate ion test with aqueous barium chloride.

Oxidation with *tert*-butyl hypochlorite

1H,3H,Dibenzo[*df*][2,1,3]thiadiazepine 2,2-dioxide

The cyclic sulfamide (158 mg., 0.64 mmole) was dissolved in a mixture of dry benzene (100 ml.) and potassium *tert*-butoxide in *tert*-butanol (1M, 1.5 ml.). The solution was cooled (5°), and *tert*-butyl hypochlorite (0.15 ml., 1.2 mmole) in benzene (10 ml.) added dropwise. The reaction darkened instantly. The reaction was stirred at room temperature for 6 hrs. Analysis (t.l.c., silica-ether) showed no benzo[*c*]cinnoline or 2-chlorobenzo[*c*]cinnoline present. The reaction solution was extracted with dilute sodium hydroxide, and the extract acidified to recover dibenzothiadiazepine dioxide (50 mg., 31%), identified by t.l.c. and i.r. spectrum.

1H,3H,[2,1,3]Benzothiadiazoline 2,2-dioxide

Under similar conditions the cyclic sulfamide (1.70 g., 0.01 mmole), potassium *tert*-butoxide (20 mmole) and *tert*-butyl hypochlorite (1.1 ml., 10 mmole) in dry benzene, gave a dark precipitate (1.1 g.). T.l.c. showed one component present. No satisfactory recrystallising solvent could be found. Evaporation of the filtrate under reduced pressure gave an oil (600 mg.), t.l.c. showed both starting material and the

above product present.

The complete reaction product was chromatographed on a silica column. Ether eluted:

- a) benzothiadiazoline 2,2-dioxide (430 mg., 25%), m.p. and mixed m.p. 180-182° (lit.⁵¹ m.p. 181-183°)
- b) red amorphous solid (1.1 g.) m.p. >160° (charred)
(Found: C, 38.2; H, 2.6; N, 12.3; S, 13.0%)
 $\nu_{\text{max.}}$ 3500, 3200, 1610, 1490, 1300, 1150 cm.^{-1}
m/e 78, 74, 64 (base), 45, 31, 29, run down to 4eV. Inlet temperature = 80-100°.

Photolysis of 3-methylsulfanilide

3-Methylsulfanilide (263 mg., 1 mmole) in absolute methanol (10 ml.) was irradiated in quartz apparatus in a Rayonet reactor for 20 hr. The reaction solution was poured into aqueous sodium hydroxide (0.1 N, 50 ml.). Extraction with ether gave a viscous black oil (62 mg.) which was chromatographed on silica. Petrol eluted 3-methyl azobenzene (18 mg., 9%) m.p. 15-18° (lit.⁸⁷ m.p. 18-19°).

ν_{max} . (thin film) 3040, 2920, 2850, 1600, 1470, 790, 695 cm^{-1}
 p.m.r. τ 2.0-2.9 (m, 9H), 7.85 (s, 3H).

m/e 196 ($\text{C}_{13}\text{H}_{12}\text{N}_2$) (base), 91, 77.

Acidification of the alkaline layer and ether extraction gave unchanged 3-methylsulfanilide (110 mg., 42%) m.p. and mixed m.p. 104-105°.

Photolysis of sulfanilide

Sulfanilide (873 mg., 3.5 mmole) in deoxygenated absolute methanol (100 ml.) was irradiated for 8 hr. in quartz apparatus with a Hanovia medium pressure lamp. Analysis (t.l.c. silica and alumina/benzene) showed azobenzene, hydrazobenzene and aniline present. The solution was concentrated to 5.00 ml. and aniline (88 mg., 27%) estimated by g.l.c. on Carbowax: KOH:chromosorb W, 8:2:90. The solution was evaporated to dryness and partitioned

between aqueous sodium hydroxide and ether. The ethereal layer washed with dilute hydrochloric acid and evaporated to dryness, gave azobenzene (90 mg., 28%) m.p. and mixed m.p. 65-68° (lit.⁸⁷ m.p. 68°). Acidification of the alkaline aqueous layer and ethereal extraction gave unchanged sulfanilide (177 mg., 20%) m.p. 110-112°, (lit.⁴⁹ m.p. 112°), i.r. spectrum identical to an authentic sample.

Photolysis of 3-methylsulfanilide

Under similar conditions 3-methylsulfanilide (635 mg., 2.4 mmole) gave unchanged 3-methylsulfanilide (15%), 3-methylazobenzene (80 mg., 34%), m.p. 15-17° (lit.⁸⁷ m.p. 18-19°). m/e 196 ($C_{13}H_{12}N_2$) base, 182, 181, 91, 77. Intensity at m/e 182 correct for ^{13}C and ^{15}N isotopes of $C_{12}H_9N_2$ and a basic oil (85 mg., 35%), t.l.c. (alumina-benzene) identical to authentic aniline. Analysis (i.r.) identical to a 1:1 mixture of aniline and *m*-toluidine. The mixture was unresolved by g.l.c. on a Carbowax:KOH:chromosorb W, 8:2:90 column.

Pyrolysis of Sulfanilide

Sulfanilide (680 mg., 2.74 mmole) in dry diglyme (50 ml.) was heated under reflux (165°) for 16 hr. The cooled solution poured into water (400 ml.) and ether extracted gave a brown tar (180 mg.) containing 8-10 products. No aniline, azobenzene

or hydrazobenzene were present (t.l.c. alumina-benzene). Basification of the aqueous layer and ethereal extraction gave a multicomponent tar (40 mg.) containing no aniline or hydrazobenzene (t.l.c.). Acidification and ethereal extraction gave no acidic material.

Bipthalimid sulfone

a. Potassium phthalimide (23.3 g., 0.126 mole) in dry benzene (200 ml.) was cooled (10°) and stirred while sulfuryl chloride (8.5 g., 0.063 mole) was added dropwise over 1 hr. The reaction was stirred at room temperature for 24 hr., then filtered. The residue (16 g.) contained potassium phthalimide and phthalimide (i.r. spectrum) m/e 276; 247, 245 (1-Cl); 147 (base).

The filtrate was evaporated under reduced pressure to give a colourless solid (8.3 g.) m.p. 75-85°.

m/e 276; 247, 245 (1-Cl); 183, 181 (1-Cl) base.

The solid in dry benzene (150 ml.) was saturated with HCl gas, the resulting precipitate of phthalimide removed by filtration and the filtrate evaporated to dryness to give a colourless solid (4.1 g.) m.p. 70-80°.

Recrystallisation from benzene gave a first crop of phthalimide, and a second crop of a colourless solid (2.3 g., 13%), m.p. 173-175°

$\nu_{\text{max.}}$ 2220, 1800, 1740, 1690, 1600, 1285, 1250, 880, 780, 760,
720 cm.^{-1}

m/e 276 base, 248, 234, 220, 204, 174, 147, 130, 104, 102, 76.

276 $\xrightarrow{*}$ 248 + 28 ($m^* = 223$, Calc. 222.9)

248 $\xrightarrow{*}$ 220 + 28 ($m^* = 195$, Calc. 195.1)

b. Phthalimido-N-sulfonyl chloride⁷⁸ (12.2 g., 0.05 mole)
in dry benzene (200 ml.) was added over 2 hr. to a stirred
cooled (10°) suspension of potassium phthalimide (9.3 g.,
0.05 mole) in dry benzene (100 ml.). The reaction was stirred
at room temperature for 12 hr., then filtered. The residue
(14.7 g.) consisted of phthalimide and potassium phthalimide
(i.r. spectrum). The filtrate was evaporated to dryness to
give a colourless solid (5.8 g.) m.p. 60-75°.

m/e 276; 247, 245 (1-Cl, base), 183, 181 (1-Cl), 147.

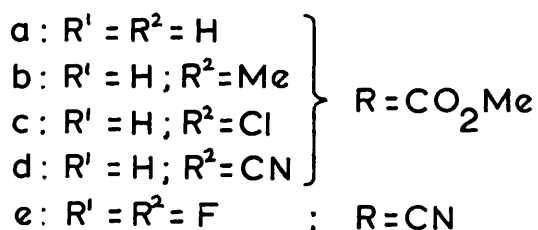
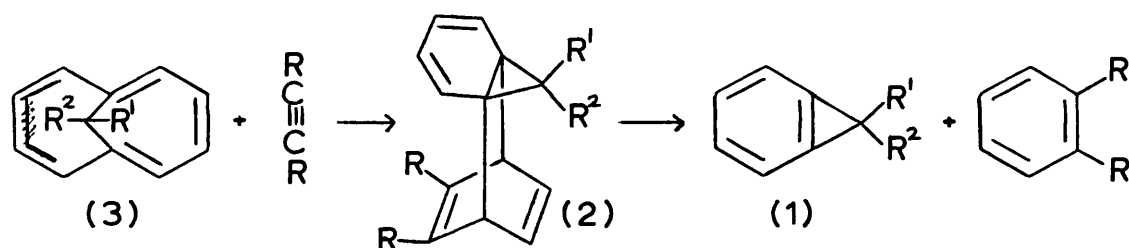
PART II

OXIDATION OF TRIAZINONES

INTRODUCTION

Introduction

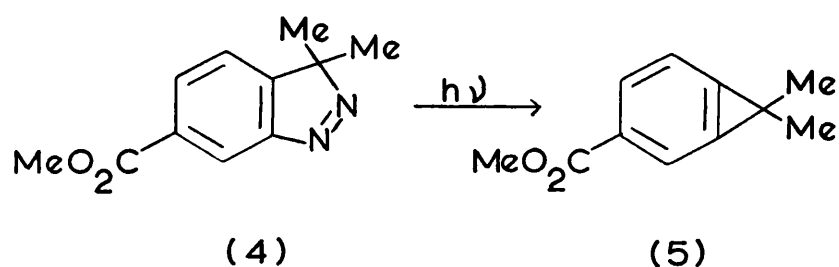
There are few methods available for the synthesis of three membered carbon rings fused to benzene, and these are either of considerable synthetic difficulty or of rather limited generality. The parent hydrocarbon, benzocyclopropene (1a) has been synthesised by gas phase pyrolysis of the adduct (2a) from dimethylacetylenedicarboxylate with 1,6-methano-[10] annulene (3a)¹¹⁶. This method (Scheme 1) was also successful with the difluorin-



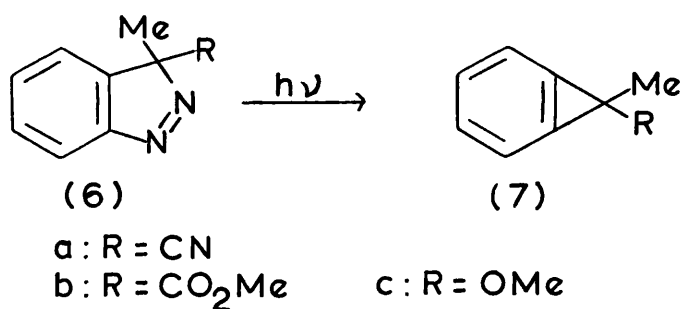
(Scheme 1)

ated adduct (2e); but although the adducts (2 b-d) could be synthesised, their pyrolysis did not lead to the appropriate benzocyclopropene¹¹⁷. It is as yet uncertain which structural parameters are essential for the above synthesis.

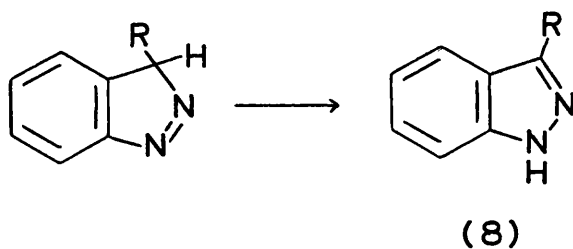
An alternative approach involves the photolytic extrusion of nitrogen from the appropriately substituted 3-H indazole¹¹⁸. Thus photolysis of 3,3-dimethyl-6-carbomethoxyindazole (4) gave 1,1-dimethyl-3-carbomethoxybenzocyclopropene (5)¹¹⁹ and low temperature



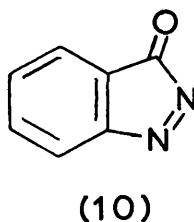
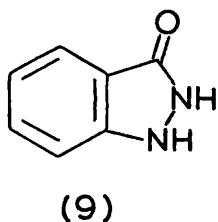
photolysis of the indazoles (6 a-c) gave the benzocyclopropenes (7 a-c) all in unspecified yields¹²⁰.



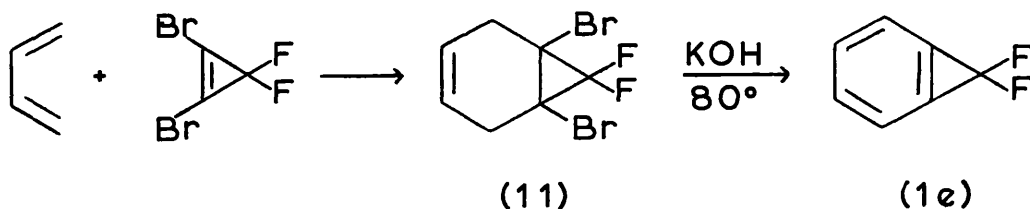
Extensions of this synthesis to benzocyclopropenes unsubstituted at C₁ are limited by the ready tautomerism of 3-H indazoles to the 1-H isomers (8)



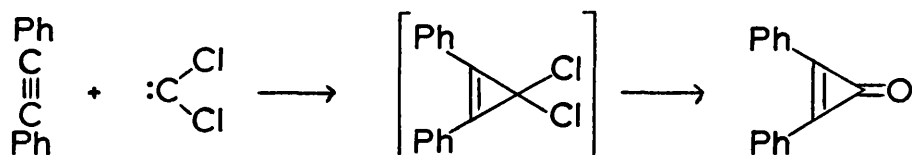
It is also of significance that 3-indazolone (10) generated by the oxidation of 3-indazolinone (9) has been reported as being stable to irradiation - albeit under unspecified reaction conditions¹⁰⁷.



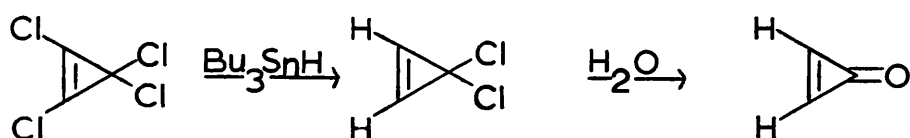
A third preparative route has been briefly reported by Vogel. Base catalysed dehydrobromination of the tetrahalocyclopropane (11) previously reported by Law and Tobey¹²¹ gave 1,1-difluorobenzocyclopropene (1e) in 40% yield¹¹⁷.



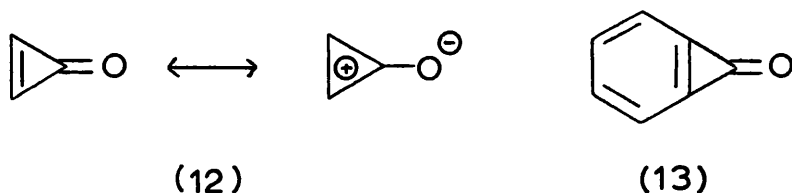
This is of significance as 3,3-dihalocyclopropenes are in general easily hydrolysed to the corresponding cyclopropenones. Examples include the isolation of diphenylcyclopropenone from the reaction of toluene and dichlorocarbene generated in the presence of base¹²²;



and the generation of cyclopropenone itself by the ready hydrolysis of 3,3-dichlorocyclopropene;¹²³

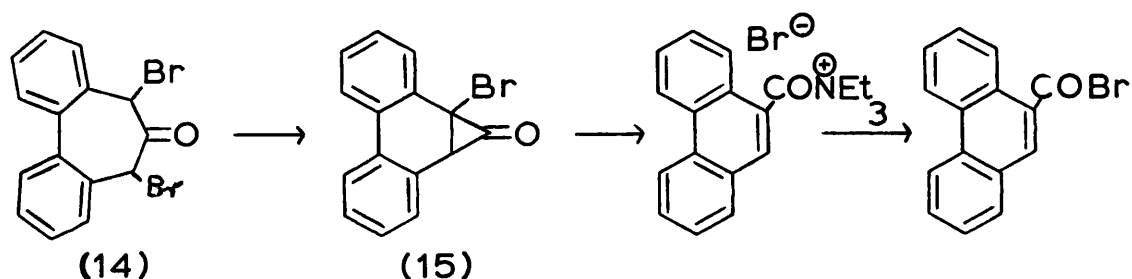


Although no report of the hydrolysis of 3,3-difluorocyclopropenes is available, it seems likely that the isolation of 1,1-difluorobenzocyclopropene from the basic reaction conditions shown above is an indication that the greater stability of cyclopropenones relative to the cyclopropenes due to the contribution of the aromatic 2 π electron doublet (12)^{124 125} is not paralleled to the same extent in the benzo-fused derivative (13).



To date the ketone benzocyclopropenone (13) has not been isolated, though it has been postulated as an intermediate in the pyrolysis and mass spectral fragmentation of indanetrione¹²⁶, and in the pyrolysis of phthalic anhydride¹²⁷.

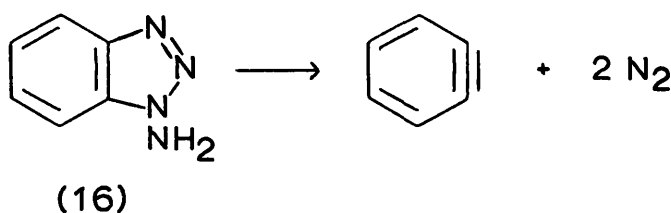
Attempts at synthesising related systems by methods developed for unfused cyclopropenones have been unsuccessful. Thus dehydrobromination of the dibromoketone (14) with triethylamine gave the cyclopropane (15) which ring opened on nucleophilic attack by triethylamine (Scheme 2). No elimination to phenanthrocyclopropenone could be observed¹²⁸ although the dehydrobromination of



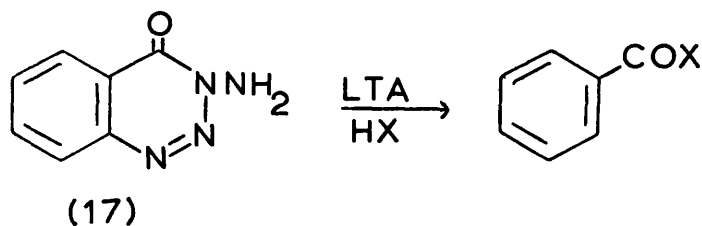
(Scheme 2)

α, α' -dibromoketones to cyclopropenones is well documented^{7 129}.

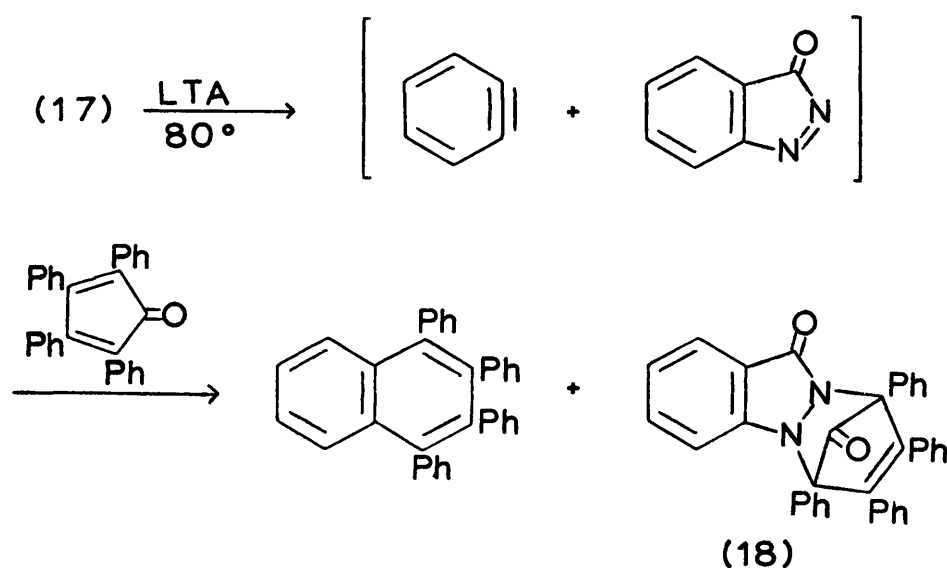
Studies by Campbell and Rees on the oxidative generation of benzyne from 1-aminobenzotriazole (16)³



led to an extension to the oxidation of 1-amino-1,2,3-benzo[e]triazin-4-one (17)¹³⁰. Oxidation with lead tetraacetate (L.T.A.) in the presence of nucleophiles led to good yields of the corresponding benzoyl derivatives:



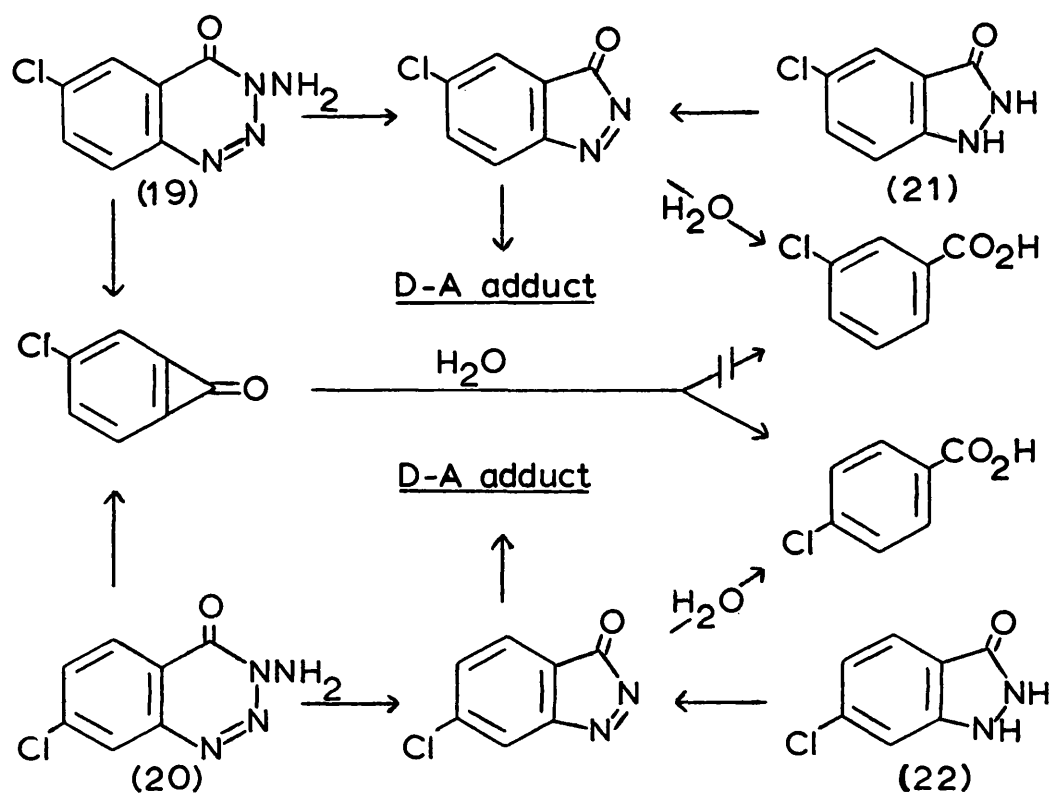
Oxidation in boiling benzene in the presence of tetraphenylcyclopentadienone (tetracyclone) gave a small (4%) yield of the benzyne adduct, tetraphenylnaphthalene and a good yield of the Diels-Alder adduct (18) with 3-indazolone, which is also formed in the reaction (Scheme 3).



(Scheme 3)

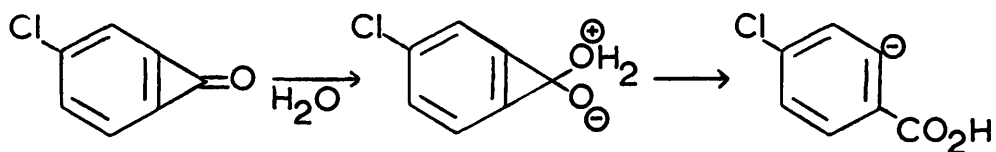
Subsequent work by Adamson¹³¹ using the substituted 3-amino-6- and 7-chlorobenzotriazinones (19) and (20) showed that if the indazolone was preferentially removed from the oxidation in an inert solvent by forming the tetracyclone adduct, then subsequent addition of water gave only p-chlorobenzoic acid from either isomeric triazinone.

Independent generation of the chloroindazolones by oxidation of the indazolinones¹⁰⁷ (21) and (22) and reaction with water gave exclusively unrearranged acids in each case (Scheme 4).



(Scheme 4)

It followed that a symmetrical intermediate, probably a cyclopropenone, was responsible for the rearrangement product obtained from 3-amino-6-chlorobenzotriazinone and that the direction of ring opening on nucleophilic attack was strongly influenced by the combined inductive and mesomeric effects.

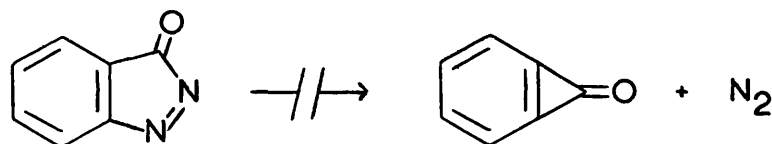


The present work was undertaken to observe the life-time in solution and the influence of substituents on the direction of ring opening of the intermediate benzocyclopropenones. We wished also to study the mechanisms by which the 3-aminobenzotriazinones fragmented on oxidation, and, finally, to see whether the reaction could be extended as a general synthetic method for three membered rings fused to benzene.

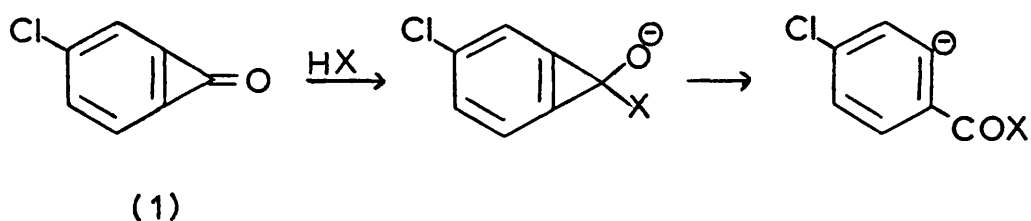
DISCUSSION

Discussion

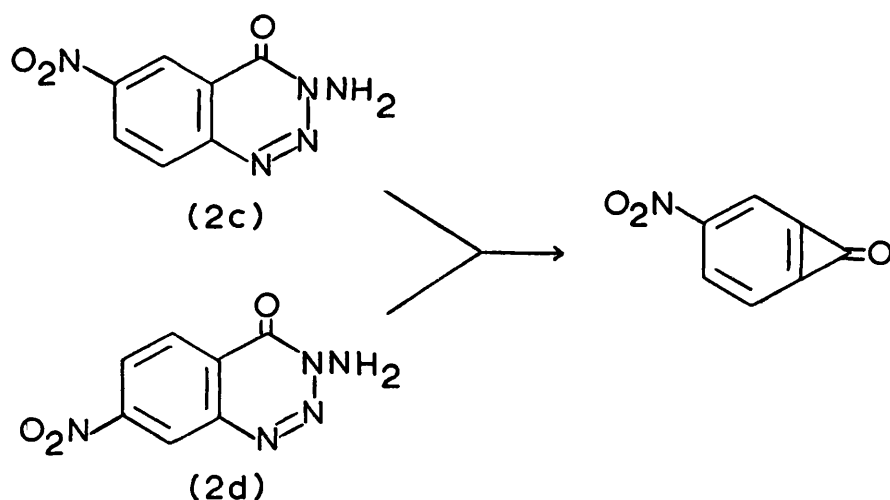
It has been mentioned in the introduction that Campbell¹³⁰ and subsequently Adamson¹³¹ showed that the products obtained from the lead tetra-acetate oxidation of 3-aminobenzotriazin-4-ones, were best rationalised as coming from two intermediates, 3-indazolone and benzocyclopropenone. It was also shown^{130 131}, and confirmed by the present study, that these two intermediates were formed by independent competing reactions. In particular, the indazolone could not be rationalised as a precursor of the benzocyclopropenone:



Adamson¹³¹ noted that 3-chlorobenzocyclopropenone (1) generated by oxidation of 3-amino-6-chlorobenzotriazinone, opened on nucleophilic attack to give exclusively derivatives of p-chlorobenzoic acid. This direction of ring opening can be considered as either inductively or mesomerically controlled - both processes favouring a developing carbanion meta rather than para to the chlorine;



The oxidation of the 3-amino-6-and -7-nitrobenzotriazinones (2c) and (2d) was expected to determine the relative importance of the two effects. Thus for the 3-nitrobenzocyclopropenone ring opening under nucleophilic

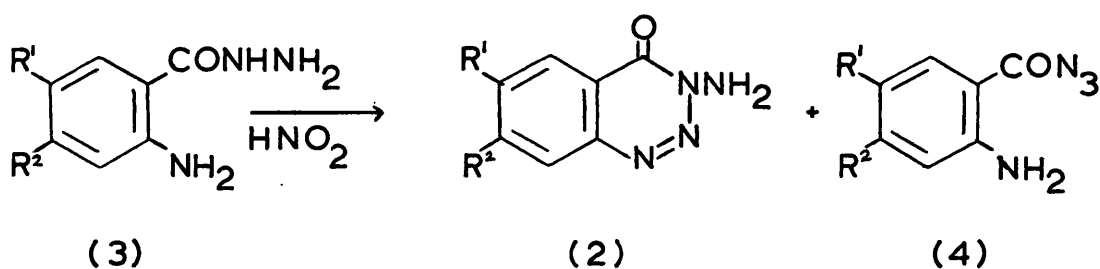


attack should give meta benzoyl derivatives if mesomerically stabilised and para benzoyl derivatives if inductively stabilised. The oxidation of 6-methyl-3-aminobenzotriazinone was also studied to determine the effect of an inductively donating substituent on the reaction. The substituents considered were limited to

the 6- and 7- positions of the benzotriazinone as the electronic directing effect from the 3- or 8- positions, i.e. ortho to the resulting benzocyclopropenone ring, would be difficult to separate from the steric directing effect. Such steric effects would be particularly serious with the very bulky nitro substituent. They have been postulated as an explanation of the difficulty of obtaining satisfactory Hammett σ constants for ortho substituents.¹³²

Preparation of Aminotriazinones and Indazolinones.

3-Aminobenzotriazinone (2a) and the unknown 6-methyl derivative (2b) were prepared by the literature procedure of diazotisation of the corresponding 2-aminobenzoylhydrazides (3a) and (3b). The 2-aminoben-

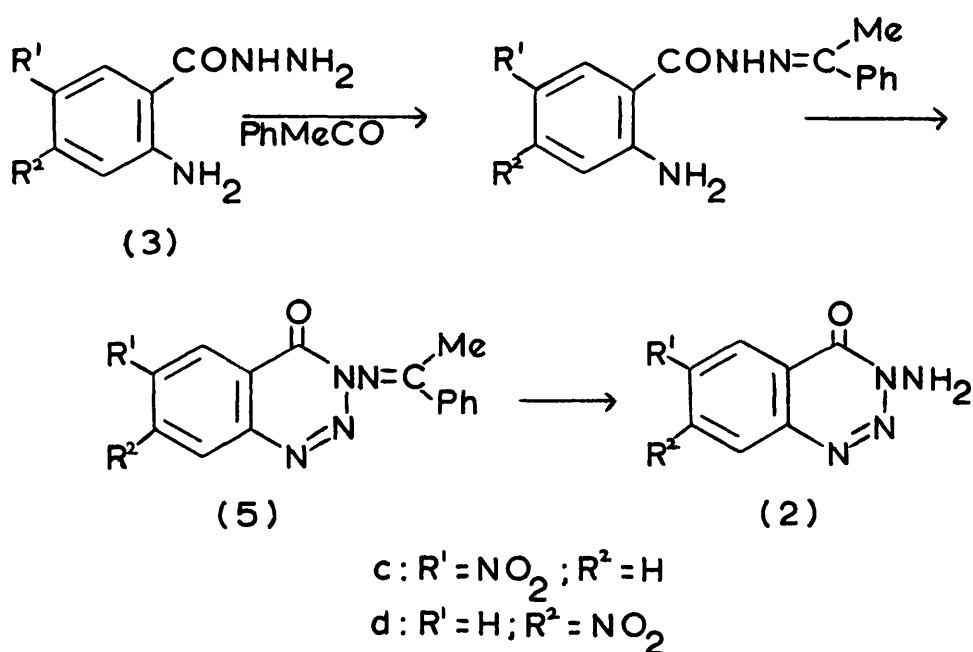


- a : R' = R² = H
 b : R' = Me ; R² = H
 c : R' = NO₂ ; R² = H
 d : R' = H ; R² = NO₂

zoyl azides (4a) and (4b) were formed in a competing reaction, and although they could easily be removed by washing the reaction product with ether, the yield of the triazinone was reduced to about 50%. For the

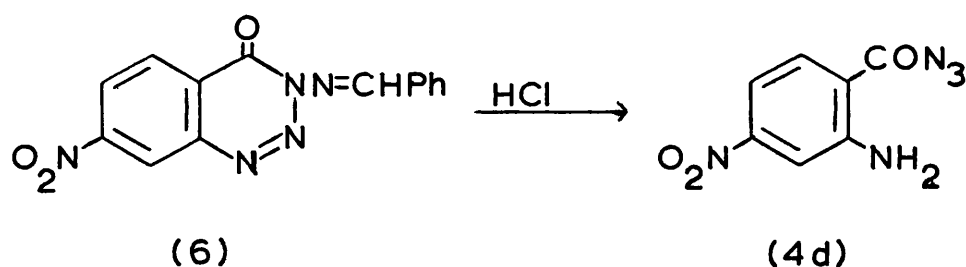
nitrotriazinones (2c) or (2d), diazotisation of the aminohydrazides (3c) or (3d) was not successful - these hydrazides gave exclusively the 2-aminonitrobenzoyl azides (4c) and (4d). Presumably the aryl amino groups in (3c) and (3d) are deactivated by the nitro substituents. These aminotriazinones were therefore prepared by longer routes.

It was found that the hydrazides (3c) and (3d) could be protected by condensation with acetophenone, diazotised to form the triazinones (5c) and (5d) and the protecting group removed by hydrolysis with aqueous trichloroacetic acid (Scheme 1).

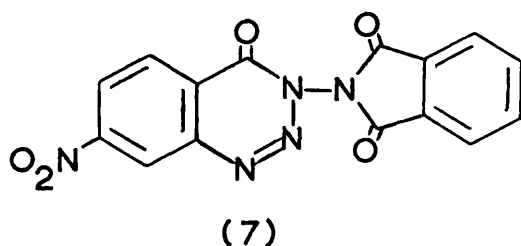


(Scheme 1)

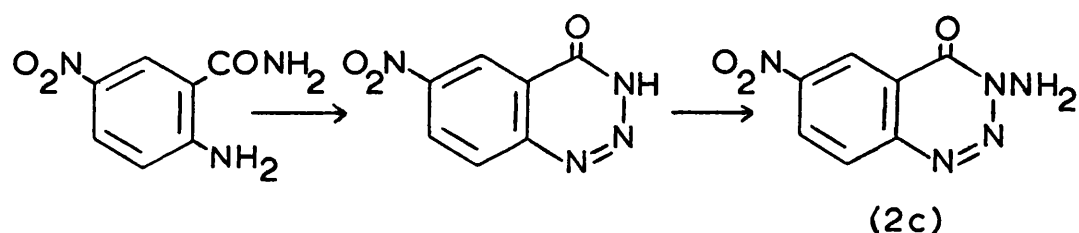
The conditions specified in the literature¹³³ to hydrolyse the 1-phenylethylidene protecting group - 18% aqueous hydrochloric acid - were found to degrade the triazinone ring which is both base and acid labile¹³⁴. The product isolated from hydrolysis of (5d) was 2-amino-4-nitrobenzoyl azide (⁴~~3d~~).



Similar problems were encountered with other protecting groups. Although the benzylidene (6) and phthaloyl (7) protected triazinones could be prepared by procedures analogous to those above, attempts to generate the aminotriazinones by acid catalysed hydrolysis failed. The first gave the benzoyl azide as shown, the second gave no characterisable products.

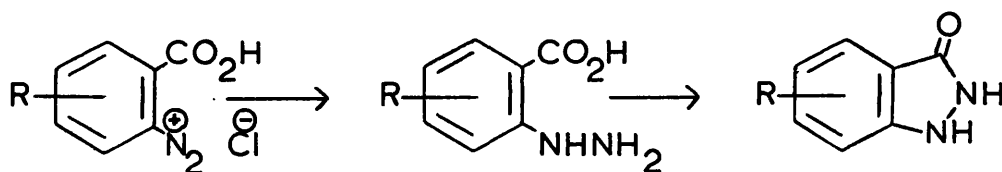


An alternative synthesis of the 3-amino-6-nitro-benzotriazinone was devised, based on the readily available 5-nitroanthranilamide. Diazotisation of the amide to give 6-nitrobenzotriazin-4-one followed by amination with hydroxylamine -O-sulfonic acid in aqueous potassium carbonate gave the required 3-amino-6-nitrobenzotriazinone (2c) in an overall yield of 47%. (Scheme 2)



(Scheme 2)

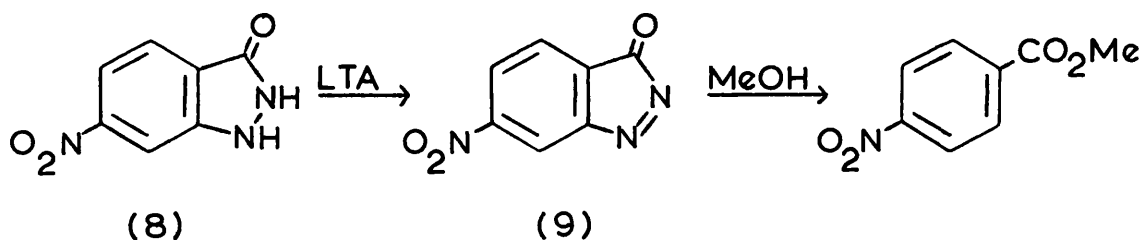
The 3-indazolinones were prepared by the literature procedure, which involves ring closure of the corresponding 2-hydrazinobenzoic acid by boiling with dilute hydrochloric acid¹⁰⁵,



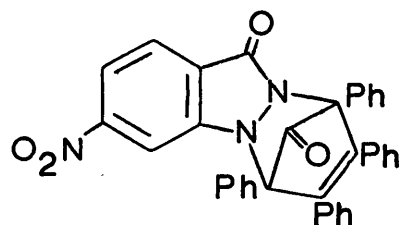
Oxidation of Benzotriazinones and Indazolinones

As pointed out in the Introduction, the 3-indazolones were probable intermediates in the oxidative fragmentation of the corresponding 3-aminobenzotriazinones.^{131 132} A preliminary study of 6-nitroindazolone (9) formed by oxidation of 6-nitroindazolinone (8) was undertaken.

Oxidation of (8) with lead tetra-acetate (L.T.A.) in methanol gave methyl p-nitrobenzoate (55%). No methyl m-nitrobenzoate (< 0.01%) was detected by g.l.c., although authentic mixtures could be resolved. As appreciable amounts of both meta and para isomers were obtained from oxidation of the corresponding 3-amino-7-nitrobenzotriazinone, see p.129, this confirmed to a greater degree of accuracy Adamson's conclusion that 3-indazolones do not lose nitrogen under these reaction conditions to give the symmetrical benzocyclopropenones.¹³¹

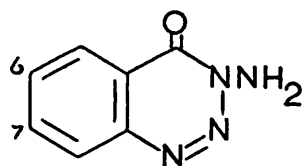


When the 6-nitroindazolinone was oxidised in an inert solvent in the presence of tetracyclone, the 6-nitroindazolone (9) could be trapped as the Diels-Alder adduct (10d).



(10 d)

Oxidation of the 3-aminobenzotriazinones (2a-d) with L.T.A. in methanol gave the methyl esters shown in Table 1.

Table 1.

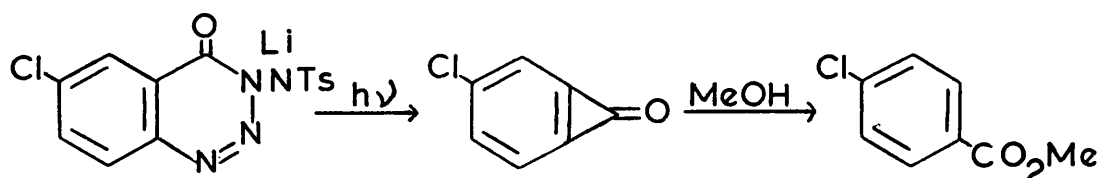
| <u>Aminotriazinone</u> | | <u>Product and Yield (%)</u> |
|------------------------|------|--|
| 3-amino | (2a) | methyl benzoate (75) |
| 6-methyl | (2b) | methyl <u>p</u> -toluate (9) methyl <u>m</u> -toluate (57) |
| 6-nitro | (2c) | methyl <u>p</u> -nitrobenzoate (13) methyl <u>m</u> -nitrobenzoate (59) |

Table 1 continued.

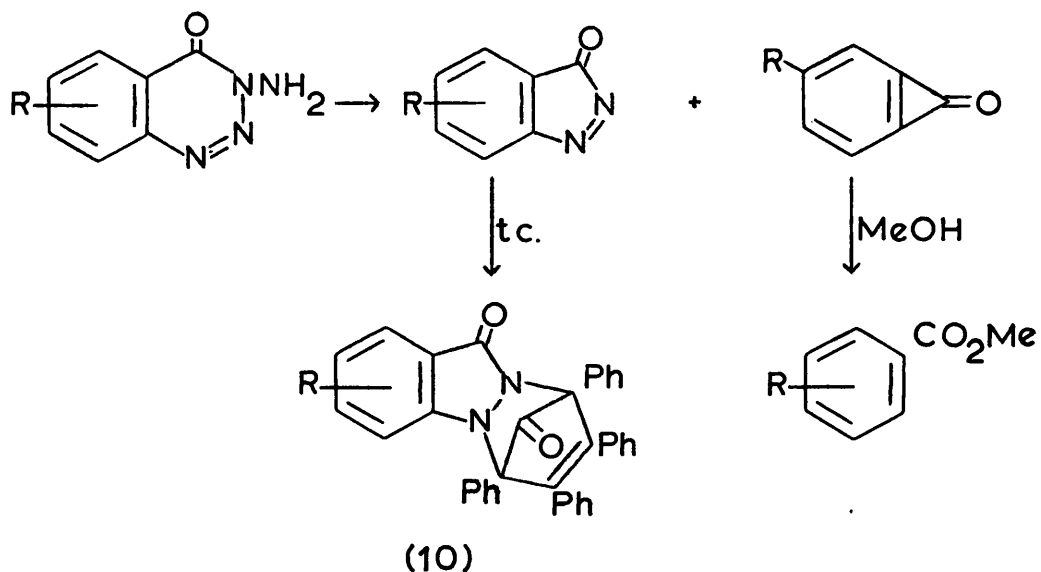
| | |
|-------------------------|--------------------------------------|
| 7-nitro (2d) | methyl <u>p</u> -nitrobenzoate (73) |
| | methyl <u>m</u> -nitrobenzoate (7) |
| 6-chloro ¹³¹ | methyl <u>m</u> -chlorobenzoate (58) |
| | methyl <u>p</u> -chlorobenzoate (11) |
| 7-chloro ¹³¹ | methyl <u>p</u> -chlorobenzoate (68) |

Comparison of the products obtained from the 6-substituted triazinones shows an isomer ratio remarkably insensitive to the substituent; but the product ratios from the 7-nitro and 7-chlorotriazinones, differ significantly. The detection of 7% rearranged product from the nitrotriazinone and none from the chlorotriazinone suggests that both mesomeric and inductive stabilisation is required for the direction of ring opening of the benzocyclopropenone to be specific.

Related work by Burgess has shown that 3-chlorobenzocyclopropenone generated in methanol by photolysis of lithium 3-tosylaminobenzotriazinone also opens to give exclusively methyl p-chlorobenzoate, no meta isomer being detected.¹³⁵



In our oxidations an attempt was made to study the benzocyclopropenones separately from the indazolones. The aminotriazinones (2b-d) were oxidised in methylene chloride in the presence of tetracyclone which trapped the indazolones as the Diels-Alder adducts. Subsequent to the oxidations methanol was added to trap the benzocyclopropenones. The yield of tetracyclone adducts (10) and the benzoate esters obtained are shown (Scheme 3 and Table 2).



(Scheme 3)

Table 2

| <u>Aminotriazinone</u> | <u>D.A.Adduct (%)</u> | <u>Methyl Esters (%)</u> |
|------------------------|-----------------------|--|
| 6-methyl (2b) | 26 | methyl <u>p</u> -toluate (2) methyl <u>m</u> -toluate (11) |
| 6-nitro (2c) | 45 | methyl <u>p</u> -nitrobenzoate (6) methyl <u>m</u> -nitrobenzoate (14) |
| 7-nitro (2d) | 53 | methyl <u>p</u> -nitrobenzoate (4.2) methyl <u>m</u> -nitrobenzoate (1.3) |

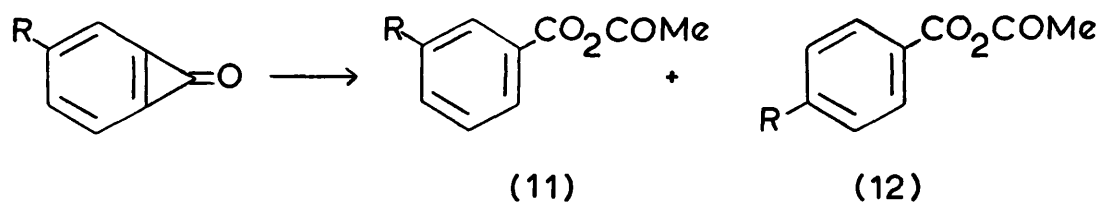
Again, in contrast to the 6- and 7-chlorotriazinones, there was no clear preference for a particular direction of ring opening. The observed preponderance of the unrearranged ester from both the 6- and 7-nitrotriazinones (2c) and (2d) probably reflects the efficiency of trapping of the indazolones, although as α -carbonylazo compounds these are expected to undergo Diels-Alder addition extremely readily.^{107 136}

It was noted from the oxidations in methylene

chloride that the yields of methyl benzoates were variable, not reaching their maximum values until up to 12 hours after the addition of methanol. These observations contrasted with the apparent susceptibility of the reactive species towards hydrolysis. Thus Campbell had found that even under anhydrous conditions, both benzoic acid (15%) and benzamide (5%) were formed when 3-amino-benzotriazinone (2a) was oxidised and the reaction mixture subsequently quenched with ammonia.¹³⁰

It was also noted that the addition of methanol up to 20 minutes after the oxidation of the 6-nitrobenzotriazinone (2c) still gave both methyl *m*- and *p*-nitrobenzoates.

These apparently conflicting observations can be resolved, as it is not necessary for the long lived intermediate to be the benzocyclopropenone. In the absence of stronger nucleophiles, acetate ion or acetic acid could attack the intermediate cyclopropenone to form the isomeric mixed benzoic acetic anhydrides (11) and (12).

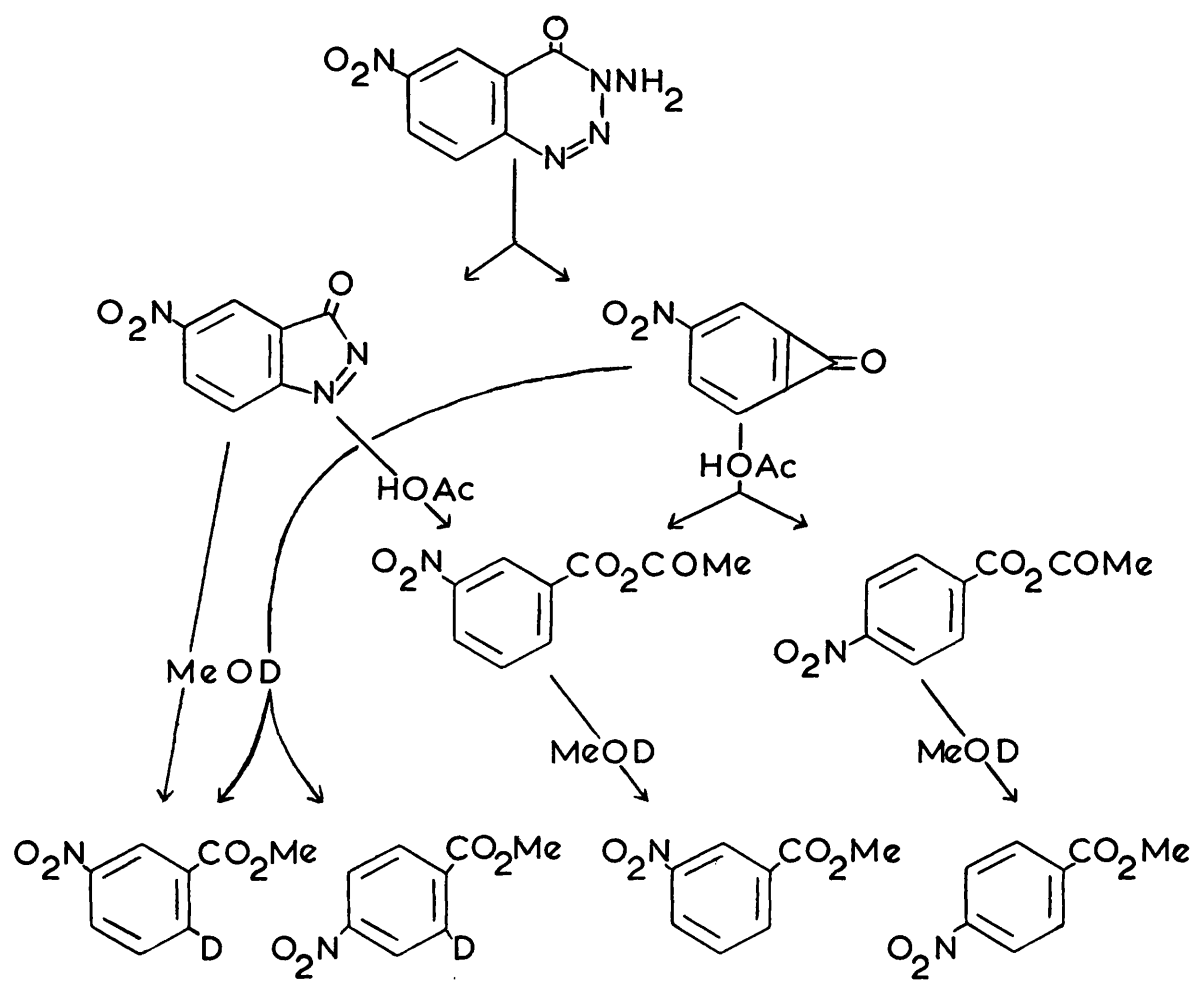


These would react subsequently with methanol to give the observed methyl benzoates. This possibility had previously been dismissed on the grounds that benzoic acetic anhydride underwent methanolysis to give mainly methyl acetate and benzoic acid, and that oxidation of 3-amino-6-chlorobenzotriazinone in acetonitrile followed by addition of D_2O gave chlorobenzoic acids incorporating deuterium on the ring.¹³¹

This latter observation must be discounted, however, as much of the deuterium incorporation could have arisen via the 3-chloroindazolone which was not selectively removed from the reaction. As regards the former, Bailey and Chang have shown that methanolysis of acetic benzoic anhydride gave methyl benzoate (14%)¹³⁷. In our hands, *p*-nitrobenzoic acetic anhydride underwent methanolysis to give methyl *p*-nitrobenzoate (20%) and methyl acetate (80%). Although the amounts of rearranged esters obtained from oxidising the aminotriazinones in methanol require direct trapping of the benzocyclopropenone, the much smaller amounts obtained from the oxidations in methylene chloride are adequately explained by methanolysis of an intermediate mixed anhydride.

That formation of a mixed anhydride was indeed the fate of the 3-nitrobenzocyclopropenone was shown by an

oxidation of 3-amino-6-nitrobenzotriazinone in methylene chloride and tetracyclone, with subsequent addition of MeOD. A pure sample of the rearranged methyl p-nitrobenzoate was obtained, and found to contain 8.1% deuterium. Examination of Scheme 4 shows that methyl 2-deutero-4-nitrobenzoate can only come from benzocyclopropenone remaining when the methanol was added. Thus after 3 minutes 92% of the 3-nitrobenzocyclopropenone had been ring opened by acetate or acetic acid.

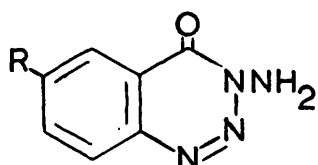


(Scheme 4)

Infra-red Spectroscopic Studies.

The origins of the characteristic infra-red absorption bands of cyclopropenones at 1600-1660 cm^{-1} and 1840-1865 cm^{-1} have been the subject of much debate. The solvent dependence of the absorbance maximum at 1600-1660 cm^{-1} has been interpreted as being due to a carbonyl stretching frequency, and the absorbance at 1840-1865 cm^{-1} as due to the cyclopropenone ring coupled to the carbonyl¹³⁸. More recent analysis by solvent dependence, isotopic substitution and calculation, has shown that for dimethyl- or diphenylcyclopropenone, the bands at 1850, 1640 and 880 cm^{-1} have 40-50%, 20-30% and 15-20% respectively of vibrational energy due to the carbonyl group.¹³⁹ Thus benzocyclopropenone would be expected to show an infra-red stretching frequency at high ($> 1850 \text{ cm}^{-1}$) wavenumber, whether or not there is electron delocalisation around the three membered ring.

Solution infra-red spectra of the reaction mixture taken immediately after oxidation of the 3-aminotriazinones (2b, c, e) showed no absorption above 1825 cm^{-1} .



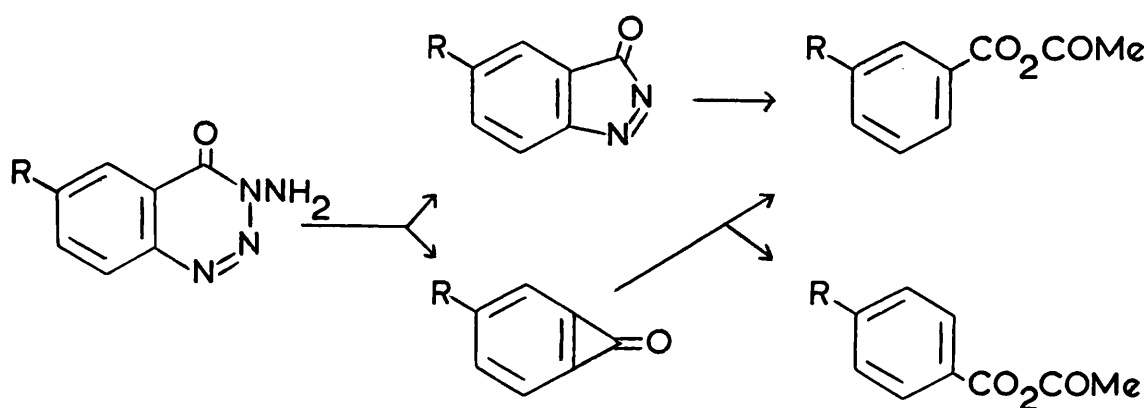
(2)

b : R = Me
 c : R = NO₂
 e : R = Cl

The reaction mixtures all showed absorbance around 1800-1825 cm⁻¹ which did not decrease with time. These maxima correspond exactly to those of the mixed benzoic acetic anhydrides. Subsequent addition of methanol to the reaction mixtures from the triazinones (2c) and (2b) led to the estimation of both rearranged and unrearranged methyl esters, showing that the ester precursor was present when the infra-red spectra were run.

It was of interest to check the infrared spectra of the indazolones for which Ullman and Bartkus report absorbance at 5.58 μ (1790 cm⁻¹).¹⁰⁷ Oxidation of 5-chloroindazolinone in methylene chloride gave a solution with absorbance at 1790 cm⁻¹. This peak disappeared over 3 hours and was replaced by a peak at 1825 cm⁻¹ - corresponding to the mixed benzoic acid anhydride.

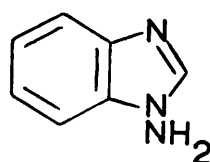
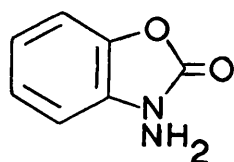
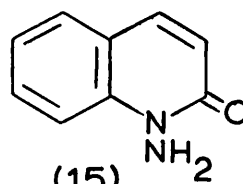
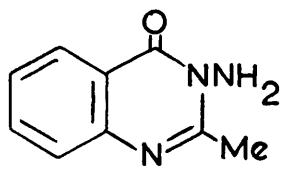
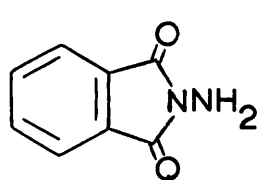
Thus it can be said that oxidation of 3-amino-benzotriazin-4-ones with L.T.A. gives both benzocyclopropenone and indazolone. In the absence of added nucleophiles both will react with acetate or acetic acid to give a mixed benzoic acetic anhydride.



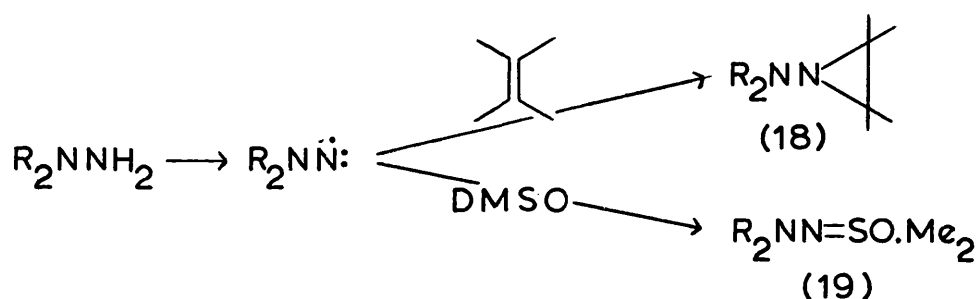
The lifetime of the benzocyclopropenone in the reaction medium is too short to make this synthesis of preparative importance; but the indazolone was trapped by nucleophiles or by dienes in yields which compare favourably with those obtained by us by oxidation of the indazolinones.

Fragmentation of 3-aminobenzotriazinone.

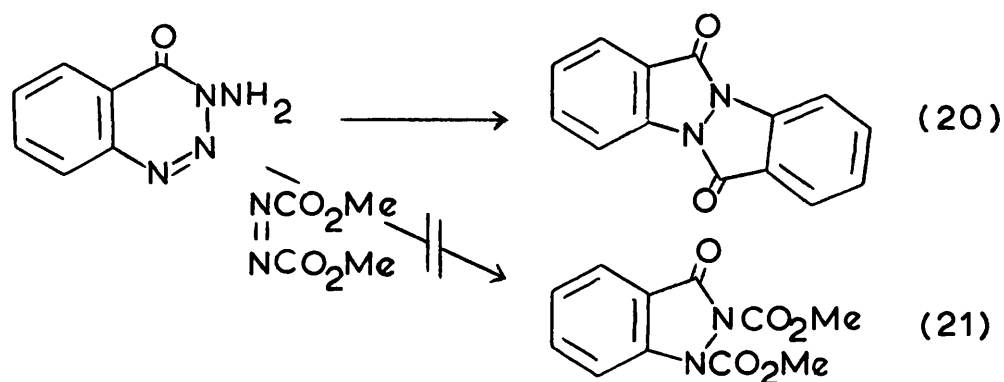
It has been shown recently, that oxidation of the heterocycles (13-16)¹⁴⁰ and (17)¹⁴¹ generates the amino



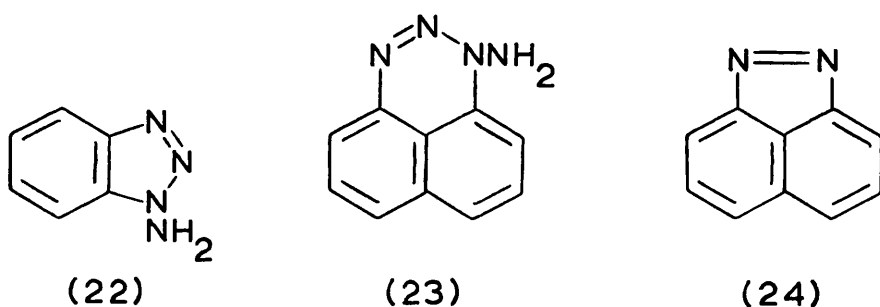
nitrene which can be trapped with olefins as the aziridine (18) or with dimethyl sulfoxide as the sulfoximine (19);



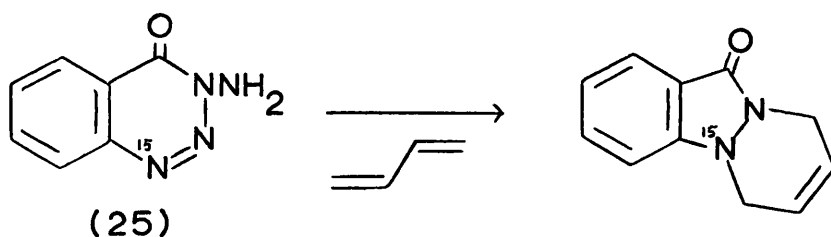
Oxidation of 3-aminobenzotriazinone (2a) in the presence of olefins or of dimethyl sulfoxide did not give aziridines or sulfoximines. The products isolated in all cases were benzoic acid and the indazoloindazolone (20). This latter is also formed in low yield in the oxidation of 3-aminobenzotriazinone in methylene chloride¹³⁰. It is formally the adduct of benzocyclopropenone with 3-indazolone; but oxidation of 3-aminobenzotriazinone in the presence of dimethyl azodicarboxylate failed to give the corresponding 1,2-dicarbomethoxyindazolin-3-one (21).



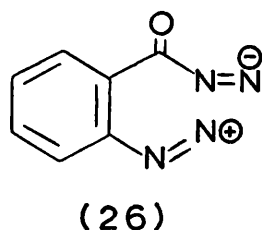
Thus 3-aminobenzotriazinone in its oxidative fragmentation resembles 1-aminobenzotriazole (22) and 1-aminonaphthotriazine (23) in that the nitrene cannot be trapped before fragmentation occurs. No products containing nitrogen, however, were obtained from the oxidation of (22) or (23). In particular the analogue of 3-indazolone, benz[c,d]indazole (24) is not obtained from (23).



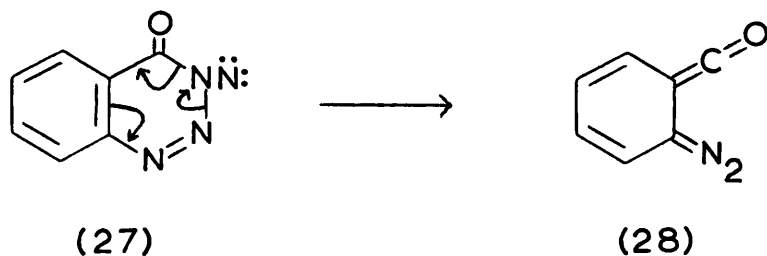
The origin of the nitrogen remaining in our 3-indazolone was therefore of interest. Oxidation of 3-aminobenzotriazinone-1- ^{15}N (25) in the presence of butadiene gave the indazolone adduct with complete retention of the ^{15}N label.



This probably rules out the zwitterion (26) as an intermediate since this should lose the labelled nitrogen. A similar diradical intermediate cannot be rigorously excluded, but the complete retention of the ^{15}N seems to favour a concerted mechanism for fragmentation of the nitrene (27)

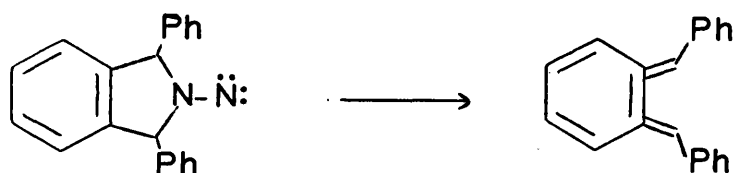


Two concerted mechanisms can be postulated for formation of the indazolone, both with analogies. One is a pericyclic ($\sigma^2s + \sigma^2s + \pi^2s$) process¹⁴² to give the diazoketene (28) which is a valence tautomer of the indazolone (Scheme 5). This is analogous to the



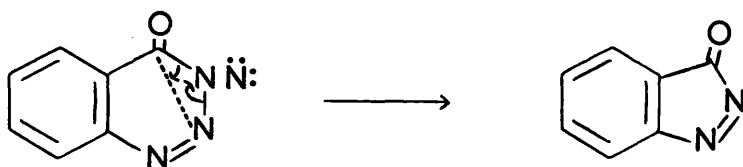
(Scheme 5)

stereospecific loss of nitrogen from the nitrene (29) which was investigated by Carpino.¹⁴³



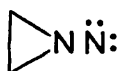
(29)

The alternative (Scheme 6) is a direct formation of the indazolone by a ($\sigma^2s + \sigma^2a$) process.

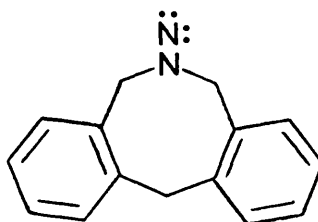


(Scheme 6)

Similar mechanisms have been suggested to account for the stereospecific loss of nitrogen from aziridinyl nitrenes (30)¹⁴² and from the nitrene (31), a system where o-quinonoid derivatives cannot be formed.¹⁴⁴

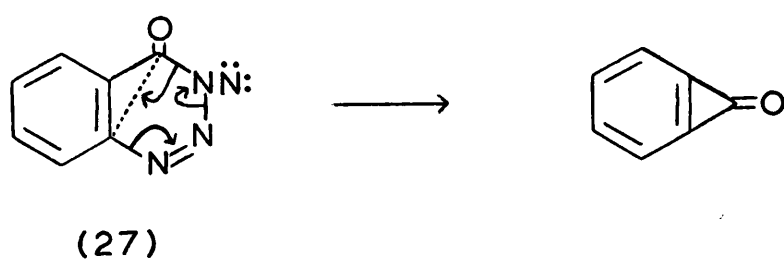


(30)



(31)

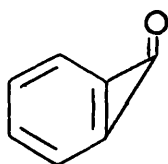
Finally, the nitrene (27) can fragment concertedly to form benzocyclopropenone ; a ($\sigma^2s + \sigma^2s + \sigma^2s$) pericyclic reaction would give the cyclopropenone directly (Scheme 7).



(Scheme 7)

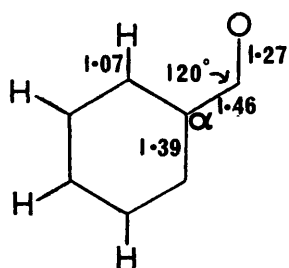
Extended Hückel Molecular Orbital Calculations.

The concerted fragmentation depicted in Scheme 7 requires the formation of the benzocyclopropenone in a geometrically distorted form (32).

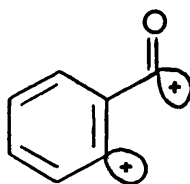


(32)

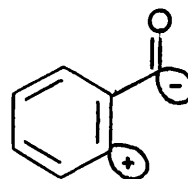
It was of interest to see whether the formation of the required symmetric σ orbital (S) was energetically feasible for this geometry. Extended Hückel M.O. calculations^{145 146} were carried out on the ring opened cyclopropenone (33), using the bond lengths and angles shown (Table 3). The exocyclic C-C and C-O bond lengths



(33)



S



A

were those found in benzamide.¹⁴⁷ It was found that for $\alpha = 100^\circ$ or 104° , the symmetric σ orbital (S)

is the highest occupied orbital (H.O.M.O.) and the antisymmetric σ orbital (A) is the lowest unoccupied orbital (L.U.M.O.). At $\alpha = 108^\circ$ to 120° , however, the energies of these orbitals are reversed, so that (A) is the H.O.M.O.

The energy differences however, are small between (S) and (A) (0.554 eV at $\alpha = 120^\circ$) so that the concerted loss of nitrogen and formation of the symmetric singlet (S) (which can collapse smoothly to benzocyclopropenone) seems energetically reasonable.

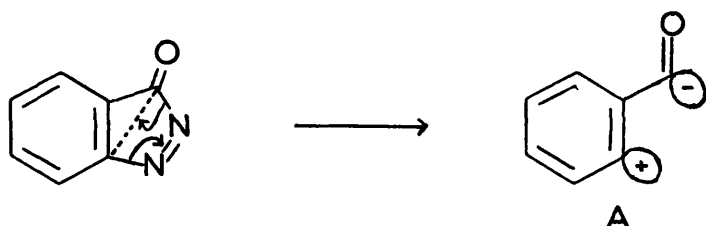
Table 3

Hückel energies (eV)

| <u>$\alpha^{(o)}$</u> | <u>(S)</u> | <u>(A)</u> | <u>ΔeV</u> |
|----------------------------------|------------|------------|------------------------------|
| 100 | -11.182 | *10.612 | 0.770 |
| 104 | -11.062 | *10.773 | 0.289 |
| 108 | *10.836 | -11.016 | 0.180 |
| 112 | *10.787 | -11.095 | 0.308 |
| 116 | *10.711 | -11.139 | 0.428 |
| 120 | *10.616 | -11.170 | 0.554 |

* LUMO

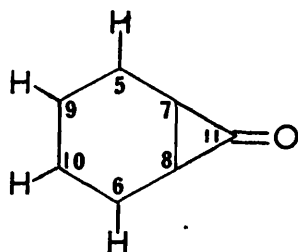
Concerted loss of nitrogen from 3-indazolone in a
 ($\sigma^2_s + \sigma^2_s$) process would give the corresponding



antisymmetric singlet (A) which could not close to the cyclopropenone. Thus orbital symmetry provides a possible explanation for the observed reaction pathways.

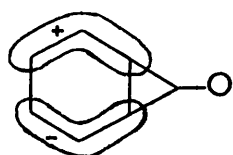
The use of the extended Hückel method, with its necessary neglect of electron-electron interactions has been criticised¹⁴⁸; but the method is at its strongest when used as here, to examine the effect of small changes in molecules on the ordering of molecular orbital energies¹⁴⁹.

A calculation by the method on benzocyclopropenone, using the geometry,

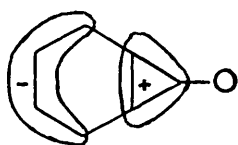


C-H = 1.07 Å
 C-C = 1.39 Å
 C-O = 1.22 Å

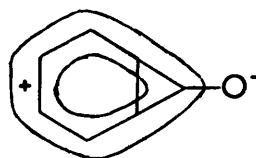
gave the H.O.M.O. (-11.979 eV) as the bonding orbital between C₇ and C₈; the second highest (-12.581 eV) was the bonding σ orbital over C₇, C₈ and C₁₁. Next came the two highest occupied π M.O.'s, the first (-12.809 eV) with symmetry as shown in (34) the second (-13.285 eV) as shown in (35). The lowest π orbital



(34)



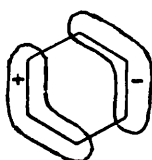
(35)



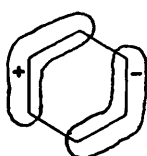
(36)

(-14.699 eV) was delocalised over all the carbon atoms (36).

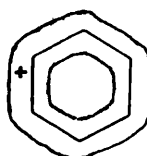
It is of interest that the degeneracy of the two H.O.M.O.'s of benzene¹⁴⁵ has been split by the presence of the fused cyclopropene ring. Thus (37) and (38) of benzene correspond to (34) and (35) of benzocyclopropenone and the lowest π orbital of benzene (39)



(37)



(38)



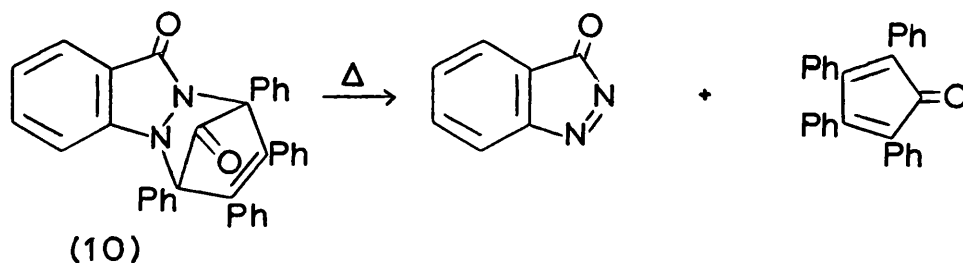
(39)

corresponds to (36). This calculation, therefore, suggests that the π electrons in benzocyclopropanone are disturbed by the fused ring and that some delocalisation over seven carbon atoms occurs. The chemistry of the molecule as ascertained so far, shows that any resulting enhanced stability of the carbonyl towards nucleophilic attack is not of preparative significance.

Pyrolysis of α -Carbonyl Azo Adducts.

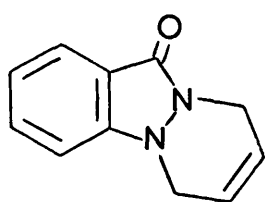
Campbell observed that oxidation of 3-aminobenzo-triazin-4-one or 3-indazolinone in boiling benzene gave small (4%) amounts of benzyne¹³⁰.

The indazolone-tetracyclone adducts (10) on attempted sublimation underwent a retro Diels-Alder reaction to give tetracyclone and products derived from the indazolone¹³¹.

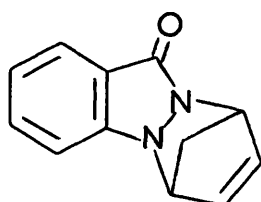


These two observations prompted an investigation to generate the indazolone at high temperature in the gas phase when intramolecular loss of nitrogen and carbon monoxide to give benzyne might be expected to occur.

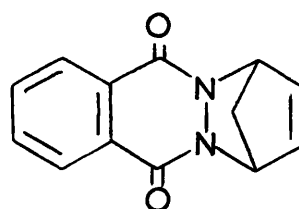
The indazolone adducts with butadiene (40) and cyclopentadiene (41) and the adduct from phthalaz-1,4-dione and cyclopentadiene (42) were prepared.



(40)



(41)



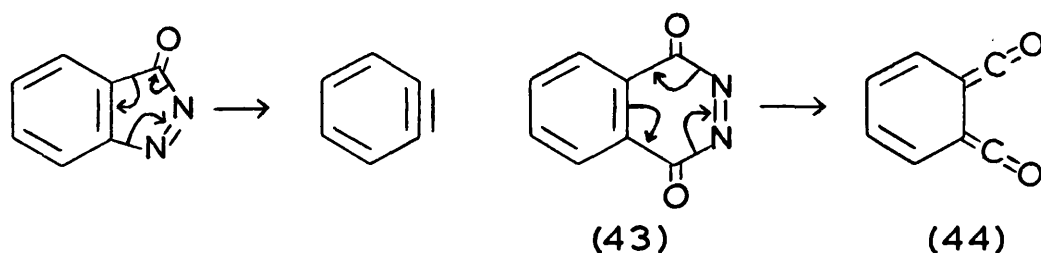
(42)

These fragmented smoothly on heating in the vapour phase at temperatures between 380° and 610°. The products are given in Table 4 with yields based on recovered starting material.

Table 4

| <u>Adduct</u> | <u>Temp.</u> | <u>Product and yield (%)</u> |
|---------------|--------------|---|
| (40) | 610° | biphenylene (38%) |
| (41) | 380° | biphenylene (32%) |
| (42) | 530° | 1,2-benzocyclobuta- dienequinone (33%) |

The isolation of biphenylene in good yield from the adducts of 3-indazolone, indicates that benzyne is a likely intermediate in the fragmentation of the indazolone.



(Scheme 8)

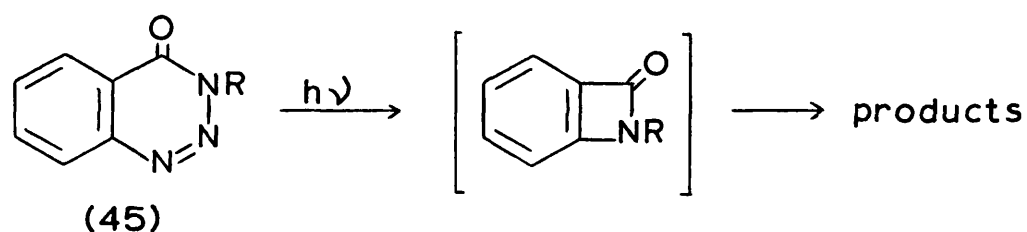
A pericyclic ($\sigma^2s + \sigma^2s + \sigma^2s$) pathway is possible for this fragmentation; a similar concerted mechanism for the phthalaz-1,4-dione (43) would give the bisketene (44) (Scheme 8) which is a valence tautomer of benzocyclobutenedione, though it has never been detected in reactions of that compound.¹⁵⁰ An alternative step-wise loss of nitrogen is also possible, however, to give benzocyclobutenedione via a diradical intermediate.

The use of the retro Diels-Alder reaction in this way may have more general application to the production of unstable species in the absence of solvent. Wittig and Hoffmann have used the same technique to generate benzyne from benzothiadiazole-1,1-dioxide.¹⁵¹

Pyrolysis of benzotriazinones.

It has been shown that photolytic extrusion of nitrogen from benzotriazin-4-ones is general when the triazinone is substituted with a π electron containing group at the 3-position.

Thus loss of nitrogen (Scheme 9) was observed for



a : R = H

b : R = Me

c : R = CH₂COPh

d : R = Ph

e : R = mesityl

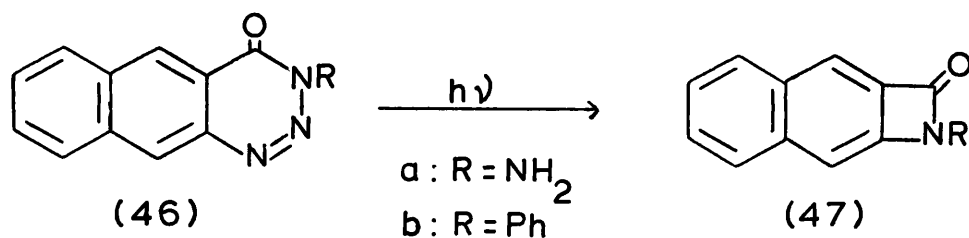
f : R = tosyl

g : R = COPh

(Scheme 9)

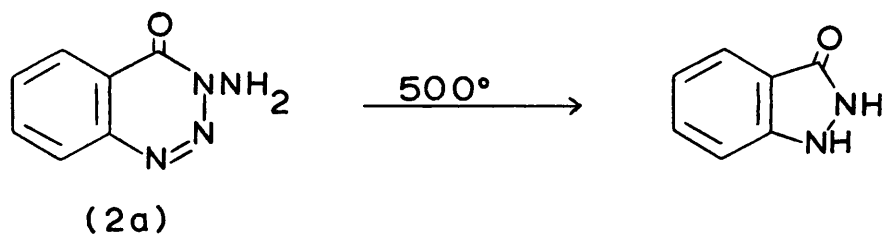
(45d-g) but not for (45a-c).^{152 135}

Photolysis of 3-aminonaphtho[2,3,e]triazin-4-one (46a)¹⁵³ and of the 3-phenyl derivative¹⁵⁴ (46b) have recently been shown to give the naphthoazetidinones (47a, b)

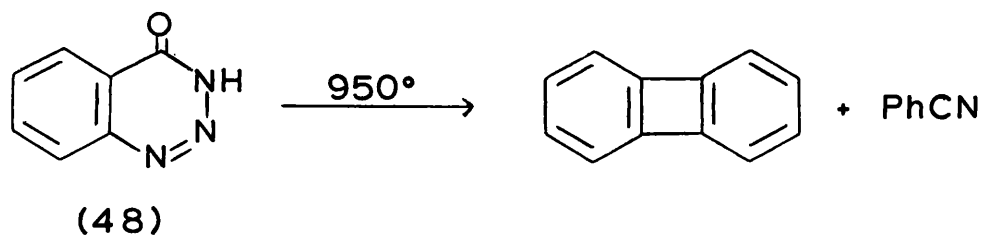


Photolysis of 3-aminobenzotriazinone, however, gave 3-indazolinone; benzotriazinone, for which this pathway is not open, was photostable¹⁵³.

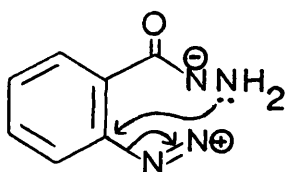
Pyrolysis of 3-aminobenzotriazinone (2a) at 500° and 0.05 mm. gave a quantitative yield of 3-indazolinone.



Benzotriazinone (48) was stable up to 720°; but underwent extensive degradation at 950° to give small amounts of biphenylene and benzonitrile.



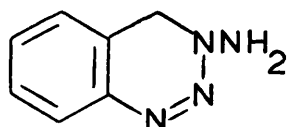
The mechanism of this degradation is as yet uncertain; but the differing ease of pyrolysis of (2a) and (48), mirroring their ease of photolysis, suggests that in the transition state for loss of nitrogen, nucleophilic attack by the lone pair of the hydrazide nitrogen is well advanced;



Dihydrobenzo-1,2,3-triazines.

As pointed out in the Introduction, benzocyclopropenes are accessible compounds, the parent hydrocarbon being stable for weeks at room temperature.

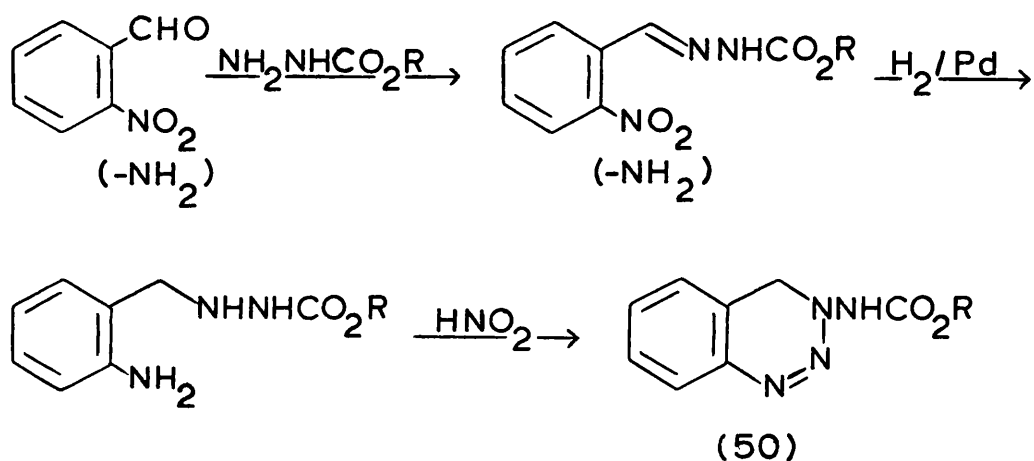
In an attempt to extend the oxidative fragmentation route to the synthesis of other benzo-fused three membered rings, the synthesis of (49) was undertaken.



(49)

A direct synthesis by diazotisation of 2-aminobenzylhydrazine was considered impracticable, as the unknown starting material would diazotise extensively at the more basic hydrazine nitrogen. Simple synthetic routes to the protected triazines (50a) and (50b) were effected starting from 2-nitro- or 2-aminobenzaldehyde. (Scheme 10)

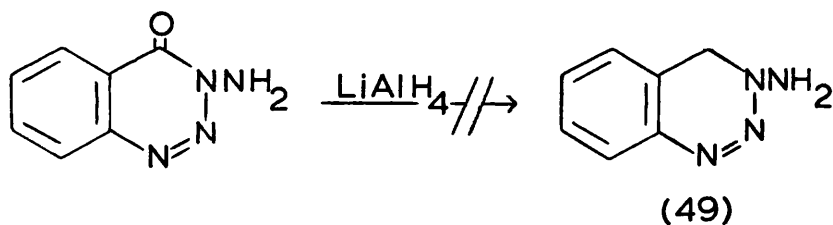
The removal of the protecting ethoxycarbonyl or butoxycarbonyl groups by base or acid catalysis^{115 155}, proved impossible without concomitant degradation of the triazine ring to complex mixtures in which azides were predominant.



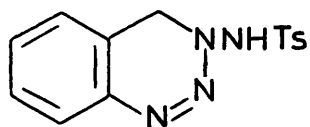
a: R = Et
b: R = Bu^t

(Scheme 10)

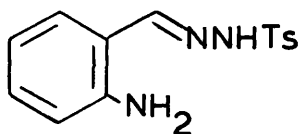
Attempts to synthesise triazine (49) by reduction of 3-aminobenzotriazinone with lithium aluminium hydride were similarly unsuccessful, again giving azides as products.



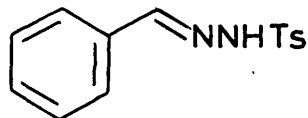
Attempts to synthesise the tosyl derivative (51) by a sequence similar to Scheme 10, were unsuccessful. The aminotosylhydrazone (52) could not be catalytically reduced to the hydrazine by methods successful with



(51)



(52)



(53)

the unsubstituted tosyl hydrazone (53).¹¹⁴ Reduction with metal hydrides gave only o-toluidine.¹⁵⁶

Thus although the scope of the oxidative fragmentation is extendable in principle, the practical application of the method is hampered by the present absence of a suitable synthetic route to the aminotriazines.

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

Experimental

Preparation of Benzotriazinones and Indazolinones

3-Amino-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one

2-Aminobenzoylhydrazide (22.6 g., 0.15 mole) was dissolved in acetic acid (35 ml.) and water (125 ml.). Sodium nitrite (10.3 g., 0.15 mole) in water (50 ml.) was added dropwise to the stirred solution at 3-5°. The resulting yellow precipitate was filtered, washed with water, and stirred with ethanol (2 x 50 ml.). The alcohol insoluble fraction was crystallised from ethanol to give 3-amino-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one (10.0 g., 41%) m.p. 154-155° decomp., (lit.⁹⁶ m.p. 152-153° decomp.). The ethanol solution was poured into water and the precipitate crystallised from petroleum-benzene (5:1) to give 2-aminobenzoyl azide as yellow plates, m.p. 81-83° decomp. (lit.⁹⁶ m.p. 82-83° decomp.).

3-Amino-6-methyl-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one

a. 2-amino-5-methylbenzoylhydrazide Methyl 2-amino-5-methylbenzoate (20 g., 0.12 mole) and hydrazine hydrate (20 ml.) were heated under reflux in ethanol (20 ml.) for 12 hr. The reaction mixture was cooled and recrystallised from benzene to give 2-amino-5-methylbenzoylhydrazide (12.6 g., 63%) m.p. 140-140.5° (Found: N, 25.5. $C_8H_{11}N_3O$ requires N, 25.4%).

$\nu_{\text{max.}}$ 3460, 3300, 1640, 1590, 890, 830, 720 cm.^{-1}

b. To a solution of the hydrazide (6.5 g., 0.039 mole) in 50% aqueous acetic acid (40 ml.) at 4° was added sodium nitrite (2.7 g., 0.039 mole) in water (15 ml.). After 0.5 hr. the precipitate was filtered off and crystallised from methanol to give 3-amino-6-methyl-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one (3.6 g., 51%) m.p. $173-175^{\circ}$ (Found: C, 54.3; H, 4.5; N, 32.1. $\text{C}_8\text{H}_8\text{N}_4\text{O}$ requires C, 54.5; H, 4.6; N, 31.8%).

$\nu_{\text{max.}}$ 3280, 3220, 3150, 1680, 1280, 1060 cm.^{-1}

3-Amino-6-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one

Method A

a. 5-Nitroanthranilamide 5-Nitroisatoic anhydride (Aldrich) (20.8 g., 0.1 mole) was suspended in aqueous ammonia (s.g. 0.88, 50 ml.) and water (250 ml.), and warmed to 70° . The anhydride dissolved and a precipitate of 5-nitroanthranilamide (14.5 g., 80%) formed; m.p. $237-238^{\circ}$ (from ethanol) (lit.⁹⁷ m.p. 236°).

b. 6-Nitro-3,4-dihydrobenzo[e]-1,2,3-benzotriazin-4-one 5-Nitroanthranilamide (14 g., 0.077 mole) was diazotised with sodium nitrite in dilute acetic acid to give 6-nitro-1,2,3-benzotriazin-4-one (11.8 g., 80%) m.p. $189-190^{\circ}$ decomp. (from ethanol) (lit.⁹⁸ m.p. 185°).

c. Amination The triazinone (5.8 g., 0.029 mole) was stirred in aqueous potassium carbonate (20%, 100 ml.) at 3° and hydroxylamine-O-sulfonic acid⁹⁹ (10 g., 0.09 mole) was added in portions. After 2 hr. the precipitate was filtered off and crystallised from methanol to give 3-amino-6-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one (2.8 g., 47%) m.p. 188-190° decomp. (Found: C, 40.8; H, 2.4; N, 32.9. $C_7H_5N_5O_3$ requires C, 40.6; H, 2.4; N, 33.8%)
 ν_{\max} . 3340, 3260, 3110, 1700, 1620, 1600, 1540, 1350 cm^{-1}

Method B

a. 2-Amino-5-nitrobenzoylhydrazide 5-Nitroanthranilic acid was converted to the methyl ester (100%) m.p. 167-168° (lit.¹⁰⁰ m.p. 168°) with an excess of ethereal diazomethane. The methyl ester (7.2 g., 0.037 mole) was stirred with hydrazine hydrate (25 ml.) in dioxan (150 ml.) at 25° for 6 hr. The solution was concentrated at 40° under reduced pressure and the resulting precipitate air-dried to give 2-amino-5-nitrobenzoylhydrazide (7.0 g., 97%) m.p. 215-218° decomp. (lit.¹⁰¹ m.p. 214-218° decomp.).

b. 2-Amino-5-nitro-N'-(1-phenylethylidene)benzoylhydrazide 2-Amino-5-nitrobenzoylhydrazide (6.2 g., 0.032 mole), acetophenone (3.8 g., 0.032 mole) and hydrochloric acid (2 N, 0.5 ml.) were shaken in ethanol (50 ml.) for 18 hr. at 25°. The resulting precipitate was filtered and washed with ether to give 2-amino-5-nitro-N'-(1-phenyl-

ethylidene)benzoylhydrazide (8.3 g., 88%) m.p. 228-230° (from ethanol-dioxan) (Found: N, 18.9. $C_{15}H_{14}N_4O_3$ requires N, 18.8%).
 ν_{\max} . 3440, 3340, 3200, 1665, 1630, 1535, 1320 cm^{-1}

c. Diazotisation The above protected hydrazide (6.1 g., 0.02 mole) in 50% aqueous acetic acid was diazotised at 5° by the addition of sodium nitrite (2.1 g., 0.03 mole). After 15 hr. the reaction mixture was filtered, and the precipitate washed with water and air-dried to give 3-(1-phenylethylideneamino)-6-nitrobenzo[e]-1,2,3-triazin-4-one (3.8 g., 60%) m.p. 211-213° decomp. Recrystallisation from chloroform gave needles, m.p. 214-215° decomp. (Found: C, 58.4; H, 3.8; N, 23.1. $C_{15}H_{11}N_5O_3$ requires C, 58.25; H, 3.6; N, 22.65%).
 ν_{\max} . 1690, 1620, 1535, 1355, 1345 cm^{-1} .

d. 3-Amino-6-nitrobenzo[e]-1,2,3-triazin-4-one The protected triazinone (0.45 g., 1.46 mole) in water (10 ml.) and trichloroacetic acid (3 g.) was stirred at room temperature for 10 hr. The reaction solution was poured into water (50 ml.) and the precipitate filtered, washed with water and ether, and dried to give 3-amino-6-nitrobenzo-1,2,3-triazin-4-one (0.243 g., 80%) m.p. and mixed m.p. 185-188°.

3-Amino-7-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one

Method A

a. Methyl 2-amino-4-nitrobenzoate 4-Nitroanthranilic acid was

converted quantitatively by an excess of ethereal diazomethane to the methyl ester m.p. 155° (lit.¹⁰² m.p. 157°).

b. 2-Amino-4-nitrobenzoylhydrazide A solution of methyl 2-amino-4-nitrobenzoate (6.0 g., 0.031 mole) and hydrazine hydrate (20 ml.) in dioxan (50 ml.) was shaken at 25° for 24 hr. The resulting precipitate was 2-amino-4-nitrobenzoylhydrazide (4.0 g., 67%) m.p. 221-223° (lit.¹⁰³ m.p. 224-225°). (Found: C, 43.1; H, 4.3; N, 28.3; m/e 196. Calc. for $C_7H_8N_4O_3$: C, 42.9; H, 4.1; N, 28.6%; \bar{M} , 196). ν_{\max} . 3480, 3360, 3300, 1660, 1620, 1350, 820, 730 cm^{-1} .

c. Protection of the hydrazide A suspension of 2-amino-4-nitrobenzoylhydrazide (5.7 g., 0.029 mole) and acetophenone (3.6 g., 0.030 mole) in hydrochloric acid (2 N, 2 ml.) and ethanol (50 ml.) was shaken for 6 hr. at room temperature to give a precipitate of 2-amino-4-nitro-N¹-(1-phenylethylidene)benzoylhydrazide (8.2 g., 92%) m.p. 241-242° (from ethanol) (Found: C, 60.0; H, 4.4; N, 19.3. $C_{15}H_{14}N_4O_3$ requires C, 60.4; H, 4.7; N, 18.8%). ν_{\max} . 3340, 3300, 3220, 1655, 1520, 1345, 1265 cm^{-1} .

d. Diazotisation The phenylethylidene derivative (8.2 g., 0.027 mole) was suspended in 50% aqueous acetic acid (100 ml.) at 3°, and sodium nitrite (3.6 g., 0.052 mole) added to the stirred suspension over 1 hr. The reaction was stirred for a further 3 hr. at room temperature, filtered and the solid product washed with water and air-dried to give 3-(1-phenylethylideneamino)-7-nitro-3,4-dihydrobenzo[e]-1,2,3-

triazin-4-one (7.6 g., 90%) m.p. 191-193° from chloroform) (Found: C, 58.6; H, 3.6; N, 22.0; m/e 309. $C_{15}H_{11}N_5O_3$ requires C, 58.25; H, 3.6; N, 22.6%; \underline{M} 309).
 ν_{\max} . 1700, 1540, 1345 cm^{-1} .

e. Removal of protecting group The phenylethylideneaminotriazinone (7.6 g., 0.025 mole) was allowed to stand in aqueous trichloroacetic acid (33%, 150 ml.) for 5 days. The precipitate (2.5 g.) was filtered off and the filtrate neutralised with sodium carbonate and continuously extracted with ether to give more solid (0.9 g.). The combined product was 3-amino-7-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one (3.4 g., 66%) m.p. 191-192° decomp. (from ethanol) (Found: C, 40.2; H, 2.4; N, 32.9; m/e 207. $C_7H_5N_5O_3$ requires C, 40.6; H, 2.4; N, 33.8%; \underline{M} 207).
 ν_{\max} . 3300, 3170, 3100, 1700, 1670, 1530, 1340, 730 cm^{-1} .

Method B

a. 2-Amino-4-nitro-N-phthalimidobenzamide N-Carbethoxyphthalimide¹⁰⁴ (0.49 g., 2.24 mmole) was added to a stirred suspension of 2-amino-4-nitrobenzoylhydrazide (0.388 g., 1.98 mmole) in aqueous sodium carbonate (0.2 \underline{M} , 20 ml.) at 20°. After 1 hr. the solid product (0.426 g., 66%) was filtered, washed with water and air dried to give 2-amino-4-nitro-N-phthalimidobenzamide, m.p. 266° (from ethanol). (Found: C, 54.8; H, 2.9; N, 17.1. $C_{15}H_{10}N_4O_5$ requires C, 55.2;

H, 3.1; N, 17.2%).

$\nu_{\text{max.}}$ 3440, 3350, 3200, 1800, 1765, 1755, 1650, 1600, 1530, 1350 cm^{-1} .

m/e 326, 296, 200, 165 (base), 135, 119, 104, 91, 76.

b. 3-Phthalimido-7-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one

2-Amino-4-nitro-N-phthalimidobenzamide (0.070 g., 0.52 mmole) in 50% aqueous acetic acid (20 ml.) was diazotised with excess sodium nitrite at 5° and stirred for 40 min. The yellow product was filtered off, washed with water and dried in air to give 3-phthalimido-7-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one (0.165 g., 87%) m.p. 247-249° (from ethanol). (Found C, 53.2; H, 2.4; N, 21.2. $\text{C}_{15}\text{H}_7\text{N}_5\text{O}_5$ requires, C, 53.5; H, 2.1; N, 20.8%).

$\nu_{\text{max.}}$ 1765, 1740, 1720, 1540, 1340, 1280, 1030, 880, 800, 740, 710 cm^{-1} .

m/e 337, 309, 263, 251, 235, 207, 179, 150.

c. Cleavage of phthaloyl protecting group 3-Phthalimido-7-nitrobenzo-

[e]-1,2,3-triazin-4-one (0.138 g., 0.41 mole) and hydrazine hydrate (0.5 ml.) in ethanol (20 ml.) were shaken for 5 min. The solid dissolved. The ethanol was removed under reduced pressure and the residue partitioned between aqueous sodium carbonate and ether. The ethereal layer, dried (MgSO_4) and evaporated to dryness gave a gum (15 mg.).

$\nu_{\text{max.}}$ 3480, 3260, 1600, 1520, 1350 cm^{-1}

m/e 221, 206, 192, 181, 150.

Method C

a. 2-Amino-4-nitro-N¹-benzylidenebenzoylhydrazide 2-Amino-4-nitrobenzoylhydrazide (0.340 g., 1.74 mmole), and benzaldehyde (0.190 g., 1.81 mmole) were shaken in ethanol (20 ml.) for 48 hr. at 20°. The resulting precipitate crystallised from ethanol to give 2-amino-4-nitro-N¹-benzylidenebenzoylhydrazide (0.380 g., 77%) m.p. 215-217°. (Found: C, 59.3; H, 4.7; N, 20.5. $C_{14}H_{12}N_4O_3$ requires C, 59.15; H, 4.3; N, 19.7%).

ν_{\max} . 3450, 3350, 3240, 1650, 1580, 1550, 1520, 1355 cm^{-1}

m/e 284, 236, 221, 164 (base), 119.

The use of an excess of benzaldehyde, together with acid catalysis or a higher temperature (refluxing ethanol) gave 2-benzylideneamino-4-nitro-N¹-benzylidenebenzoylhydrazide m.p. 224-226° (from ethanol) (Found: C, 68.0; H, 4.3; N, 15.2. $C_{21}H_{16}N_4O_3$ requires C, 67.7; H, 4.3; N, 15.05%).

ν_{\max} . 3280, 1660, 1530, 1350 cm^{-1}

m/e 372, 295, 268, 253, 192.

b. 3-Benzylideneamino-7-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one

The mono-protected hydrazide (0.30 g., 1.06 mmole) in 50% acetic acid (20 ml.) at 3° was diazotised by the addition of solid sodium nitrite (0.10 g., 1.45 mmole). After stirring for 1 hr., the resulting precipitate was filtered off and crystallised from ethanol to give 3-benzylideneamino-7-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one (0.24 g., 77%) m.p. 257-259° (decomp) (Found: C, 56.55; H, 3.3;

N, 24.0. $C_{14}H_9N_5O_3$ requires C, 56.95; H, 3.1; N, 23.7%)

ν_{\max} . 1710, 1600, 1530, 1350 cm^{-1}

m/e 295, 267, 266 (base), 165.

c. Removal of protecting group

(i) 3-Benzylideneamino-7-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one was recovered after 24 hr. at 25° in 17% w/w hydrochloric acid.

(ii) The protected triazinone (0.045 g.) in ethanol (10 ml.) and conc. hydrochloric acid (5 ml.) was stirred at 40° for 15 min. The reaction mixture was poured into cold water, neutralised (NaHCO_3), and extracted with ether to give 2-amino-4-nitrobenzoyl azide (0.025 g., 78%) m.p. and mixed m.p. 133° decomp.

An authentic specimen was prepared by diazotisation of 2-amino-4-nitrobenzoylhydrazide in acetic acid to give 2-amino-4-nitrobenzoyl azide (63%) m.p. 133° decomp. (from ether-petrol) (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%)

ν_{\max} . 3460, 3440, 2160, 1700, 1530, 1350 cm^{-1}

m/e 207.

1- ^{15}N -3-Amino-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one

^{15}N -Anthranilic acid (0.200 g., 1.45 mmole) was converted to the methyl ester with diazomethane, and then to its hydrazide by heating the ester with an excess of hydrazine hydrate. The hydrazide was protected by stirring for 15 min. with acetophenone (0.175 g., 1.45 mmole) in acetic acid (30%, 4 ml.). The protected hydrazide

was not isolated, but was diazotised in situ by the addition of aqueous sodium nitrite (1.1 equiv.). The precipitate was filtered off and washed with water to give the protected triazinone (ν_{max} . 1680 cm^{-1}). The protected triazinone was then dissolved in conc. hydrochloric acid (3 ml.) and the solution stirred at 0°. The solution was washed with ether (2 ml.) to remove acetophenone, then neutralised with aqueous sodium bicarbonate and extracted with ether (3 x 10 ml.). This ethereal solution was dried and evaporated to give 1-¹⁵N-3-Amino-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one (0.126 g., 53% overall) m.p. 149-151° identical (by infra-red spectrum and t.l.c.) to an authentic specimen.

m/e 163, 162, relative intensities 1.1:1.0.

3-Indazolinones

These were prepared by the literature method from the corresponding anthranilic acids, by diazotisation and reduction to the 2-hydrazinobenzoic acid and followed by ring closure in boiling dilute hydrochloric acid.

3-Indazolinone (79%), needles from methanol, m.p. 249-251° (lit.¹⁰⁵ m.p. 250-252°).

6-Nitro-3-indazolinone (60%), orange needles from ethanol, m.p. 244-245° (lit.¹⁰⁶ m.p. 244°).

Oxidation of Triazinones and Indazolinones

Oxidations of Indazolinones in Methanol

- a. 3-Indazolinone 3-Indazolinone (1.0 g., 7.5 mmole) in methanol (50 ml.) was stirred at 25°. Lead tetra-acetate (3.3 g., 7.5 mmole) was added during 20 min. Nitrogen was slowly evolved. After 24 hr. methyl benzoate (0.5 g., 49%) was estimated by g.l.c. (d.e.g.s. - Chromosorb P, 100°).
- b. 6-Nitro-3-indazolinone Under similar conditions to those above, 6-nitro-3-indazolinone gave methyl p-nitrobenzoate (55%), m.p. 93-95° (lit.⁸⁷ m.p. 96°) isolated by chromatography on silica. G.l.c. (d.e.g.s. - Chromosorb P, 160°) failed to detect any methyl m-nitrobenzoate in the crude reaction mixture.

Oxidation of Aminotriazinones in Methanol

- a. 3-Amino-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one The triazinone (0.325 g., 2.0 mmole) in dry methanol (10 ml.) was oxidised by the addition of lead tetra-acetate (0.890 g., 2.0 mmole) during 5 min. at 25°. Gas was evolved, and after 1 hr., methyl benzoate (0.204 g., 75%) was estimated by g.l.c. (d.e.g.s. - Chromosorb P, 100°).
- b. 3-Amino-6-methyl-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one Under similar conditions to those above, this triazinone gave methyl p-toluate (9%) and methyl m-toluate (57%), separated and estimated

by g.l.c. (d.e.g.s. - Chromosorb P, 100°).

c. 3-Amino-6-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one Under similar conditions to those above, this triazinone gave methyl m-nitrobenzoate (59%) and methyl p-nitrobenzoate (13%), separated and estimated by g.l.c. (d.e.g.s. - Chromosorb P, 160°).

d. 3-Amino-7-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one Under similar conditions to those above, this triazinone gave methyl m-nitrobenzoate (7%) and methyl p-nitrobenzoate (73%), separated and estimated by g.l.c. (d.e.g.s. - Chromosorb P, 160°).

Oxidation of Indazolinones in Methylene chloride

a. 3-Indazolinone 3-Indazolinone (1.0 g., 7.5 mmole) in methylene chloride (50 ml.) was stirred at 25°. Lead tetra-acetate (3.3 g., 7.5 mmole) was added in one portion, followed by tetracyclone (2.9 g., 7.5 mmole) in methylene chloride (50 ml.). After 24 hr. the reaction solution was chromatographed on alumina to give 1,4-carbonyl-1,4-dihydro-1,2,3,4-tetraphenyl-4a,9a-diazafluoren-9-one (0.78 g., 20%) m.p. 179-181°. (Found: C, 83.0; H, 5.0; N, 5.8; m/e 516. $C_{36}H_{24}N_2O_2$ requires C, 83.7; H, 4.7; N, 5.4%; M, 516). ν_{\max} . 1725, 1710, 1635, 1560, 1500 cm^{-1} .

b. 6-Nitro-3-indazolinone Under similar conditions to those above, 6-nitro-3-indazolinone gave 1,4-carbonyl-1,4-dihydro-6-nitro-1,2,3,4-tetraphenyl-4a,9a-diazafluoren-9-one (32%) m.p. 161-163°. (Found:

C, 76.9; H, 4.3; N, 7.3; m/e 561. $C_{36}H_{23}N_3O_4$ requires C, 77.0; H, 4.1; N, 7.5%; \underline{M} , 561).
 ν_{\max} . 1730, 1635, 1550, 1345 cm^{-1} .

Oxidations of Aminotriazinones in Methylene chloride

I. 3-Amino-3,4-dihydrobenzo-1,2,3-triazin-4-one

a. In the presence of butadiene 3-aminobenzotriazin-4-one (2.0 g., 12.4 mmole) in methylene chloride (50 ml.) was cooled externally to -50° and butadiene (5 g.) added. Lead tetra-acetate (5.5 g., 12.4 mmole) in methylene chloride (100 ml.) was added dropwise. After the addition, the reaction mixture was stirred for 1 hr. then warmed to room temperature and filtered. The filtrate was washed with 2 \underline{N} sodium hydroxide, then with water and chromatographed on silica. Ether - 10% ethanol eluted a red oil (0.5 g.) which was chromatographed on neutral alumina. Ether eluted 1,4-dihydro-4a,9a-diazafluoren-9-one (0.450 g., 20%) m.p. $114-115^\circ$ from benzene-cyclohexane (lit.¹⁰⁷ m.p. $96-97^\circ$). (Found: C, 70.5; H, 5.6; N, 15.4. Calc. for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.4; N, 15.0%).
 ν_{\max} . 1670, 1640, 1610, 760 cm^{-1} .
 p.m.r. (CDCl_3) τ 2.0-3.0 (4H, m); 3.95 (2H, s); 5.60 (2H, s); 6.00 (2H, s).
 m/e 186, 171, 158, 132, 104, 76.

b. In the presence of cyclopentadiene Under similar conditions to those given above, but using cyclopentadiene, was obtained

1,4-methano-1,4-dihydro-4a,9a-diazafluoren-9-one (18%) m.p. 93-94°
(from benzene-cyclohexane) (lit.¹⁰⁷ m.p. 117-117.5°).

ν_{\max} . 1660, 1610, 1315, 1100, 980, 920, 780, 765, 750 cm^{-1} .

n.m.r. (CDCl_3) τ 2.2-3.1 (4H, m); 3.97 (2H, d, d); 4.72 (1H, s);

4.98 (1H, s); 7.85 (2H, d, d).

c. In the presence of furan Under similar conditions to those above, but using furan as the diene, was obtained benzoic acid (21%) m.p. and mixed m.p. 121-3°. No other products could be characterised.

d. In the presence of olefins 3-Amino-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one (4.0 mmole) and the olefin (5 g.) in methylene chloride (20 ml.) was oxidised by the dropwise addition of lead tetra-acetate (4.0 mmole) in methylene chloride (50 ml.). The reaction mixture was chromatographed on silica to give benzoic acid, m.p. and mixed m.p. 121-123° (from benzene), and 6H,12H,indazolo[1,2-a]indazole-6,12-dione m.p. 300° (sublimed) (lit.¹⁰⁸ m.p. 300-300.8°) in the yields shown:

| <u>Olefin</u> | <u>Benzoic Acid</u> | <u>Indazolo-indazolone</u> |
|------------------------|---------------------|----------------------------|
| Cyclohexene | 14% | 5% |
| <u>cis</u> -2-butene | 18% | 2% |
| <u>trans</u> -2-butene | 20% | 3.5% |

e. In the presence of dimethyl azodicarboxylate Under the conditions outlined above, using dimethyl azodicarboxylate as trap, chromatography of the reaction mixture on neutral alumina gave benzoic acid, (23%) m.p. and mixed m.p. 121-123°. No other aromatic products were obtained (i.r. and n.m.r. analysis).

f. In the presence of dimethyl sulfoxide 3-Amino-3,4-dihydrobenzo[e]-1,2,3,-triazin-4-one (0.650 g., 4.0 mmole) in dry dimethyl sulfoxide (10 ml.) at 25° was stirred while lead tetra-acetate (1.69 g., 3.8 mmole) was added. An exothermic reaction took place, with gas evolution. The reaction mixture was poured into water (50 ml.) and filtered. The filtrate was made alkaline with 2 N sodium hydroxide, and extracted with methylene chloride to give crude 6H-12H-indazolo[1,2-a]indazole-6,12-dione (0.037 g., 1.6%) m.p. 295-300° (sublimed) (lit.¹⁰⁸ m.p. 300-300.8°) ν_{\max} . 1690 cm^{-1} .

g. 1-¹⁵N-3-Amino-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one in the presence of butadiene The ¹⁵N-labelled triazinone (0.083 g., 0.51 mmole) was added to a solution of butadiene (5 ml.) in methylene chloride (5 ml.) at -5°. Lead tetra-acetate (0.250 g., 0.56 mmole) in methylene chloride (3 ml.) was then added dropwise and the reaction mixture allowed to warm to room temperature. Chromatography on silica gave 1,4-dihydro-4a,9a-diazafluoren-9-one (0.034 g., 36%) m.p. 113-114° (lit.¹⁰⁷ m.p. 96-97°) i.r. and n.m.r. identical to an authentic specimen.
m/e 187, 186, relative intensities 1.1:1.0.

II. 3-Amino-6-methyl-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one

The triazinone (0.422 g., 2.4 mmole) and tetracyclone (0.950 g., 2.4 mmole) were dissolved in dry methylene chloride (25 ml.). Lead tetra-acetate (1.1 g., 2.4 mmole) was added and nitrogen was evolved vigorously. After 5 min. dry methanol (2.0 ml.) was added. After 24 hr. the mixture was filtered and the filtrate examined by g.l.c. (d.e.g.s. - Chromosorb P, 100°). Comparison with standard solutions indicated the presence of methyl m-toluate (39 mg., 11%) and methyl p-toluate (7 mg., 2%). Chromatography of the reaction mixture on silica gave tetracyclone (0.730 g., 77%), and 1,4-carbonyl-7-methyl-1,2,3,4-tetraphenyl-4a,9a-diazafluoren-9-one (0.340 g., 26%) m.p. 80-90° decomp. A sample purified by chromatography on neutral alumina had m.p. 90-95° decomp. (Found: C, 83.7; H, 5.2; N, 5.2. $C_{37}H_{26}N_2O_2$ requires C, 83.75; H, 4.9; N, 5.3%). ν_{\max} . 1720, 1635, 790, 760, 710, 680 cm^{-1}
m/e 530, 384, 264.

The adduct decomposed on attempted recrystallisation from benzene, liberating tetracyclone (t.l.c.).

III. 3-Amino-6-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one

a. In the presence of tetracyclone The triazinone (0.206 g., 1.0 mmole) and tetracyclone (0.385 g., 1.0 mmole) were stirred in methylene chloride (5 ml.) at 25° and lead tetra-acetate (0.50 g.,

1.1 mmole) added in portions. After 2 min., dry methanol (2 ml.) was added. The reaction mixture was stirred for 5 min. and then made up to 10.0 ml. with dry methanol. Methyl m-nitrobenzoate (25.2 mg., 14%) and methyl p-nitrobenzoate (10.6 mg., 6%) were estimated on g.l.c. (d.e.g.s. - Chromosorb P, 160°). Chromatography on silica gave (with benzene) tetracyclone (0.155 g., 40%), m.p. and mixed m.p. 219-220°. Benzene-ether (9:1) gave a mixture of methyl m- and p-nitrobenzoates (30 mg.). Benzene-ether (1:1) gave 1,4-carbonyl-1,4-dihydro-7-nitro-1,2,3,4-tetraphenyl-4a,9a-diazafluoren-9-one (0.252 g., 45%), m.p. 210-211° (from benzene) (Found: C, 77.0; H, 4.45; N, 7.2. $C_{36}H_{23}N_3O_4$ requires C, 77.0; H, 4.1; N, 7.5%).

ν_{max} . 1720, 1625, 1525, 1500, 1330 cm^{-1}

A second experiment under similar conditions in which methanol was added 20 min. after the oxidation gave methyl m-nitrobenzoate (11%) and methyl p-nitrobenzoate (6.5%).

b. In the presence of tetracyclone, and MeOD The triazinone (1.64 g., 7.95 mmole) and tetracyclone (3.08 g., 8.02 mmole) were stirred in methylene chloride (25 ml.). Lead tetra-acetate (8.15 mmole) in methylene chloride (25 ml.) was added dropwise. 5 min. after the oxidation was complete, MeOD (5 ml.) was added. The reaction mixture was stirred for 1 hr. then heated under reflux for 2 hr. Chromatography on silica gave a mixture of methyl m- and p-nitrobenzoates (0.162 g., 11%) ratio 4.5:5.5 respectively

by g.l.c. (d.e.g.s. - Chromosorb P, 160°), and 1,4-carbonyl-1,4-dihydro-7-nitro-1,2,3,4-tetraphenyl-4a,9a-diazafluoren-9-one (1.708 g., 40%) m.p. and mixed m.p. 210-211°. A sample was obtained from the ester mixture by preparative t.l.c. (silica-benzene) and sublimed to give methyl p-nitrobenzoate, m.p. 92-94°. Found: m/e 182:181 = 0.176:1.00. A specimen of undeuterated ester had m/e 182:181 = 0.095:1.00 (theoretical ratio = 0.092:1.00). Thus deuterium incorporation = 8.1%.

IV. 3-Amino-7-nitro-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one

a. In the presence of butadiene Lead tetra-acetate (0.6 g., 1.3 mmole) was added to the triazinone (0.090 g., 0.435 mmole) and butadiene (1 ml.) in methylene chloride (20 ml.) at -5°. The reaction mixture was allowed to warm to room temperature, filtered and chromatographed on silica to give 6-nitro-1,4-dihydro-4a,9a-diazafluoren-9-one (0.033 g., 33%), m.p. 248° decomp. (Found: C, 56.9; H, 3.9. $C_{11}H_9N_3O_3$ requires C, 57.1; H, 3.9%).

ν_{\max} . 1670, 1650, 1520, 1340, 770, 730 cm^{-1}

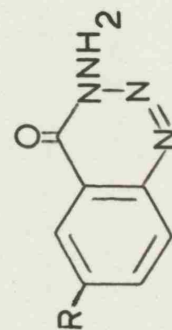
m/e 231, 216, 185, 184, 149, 103, 75.

b. In the presence of tetracyclone The triazinone (0.426 g., 2.06 mmole) and tetracyclone (0.772 g., 2.01 mmole) in methylene chloride (25 ml.) at 25° were oxidised by the addition of lead

tetra-acetate (1.5 g., 3.4 mmole). 2 min. after the oxidation was complete, methanol (2 ml.) was added. After 24 hr., methyl m-nitrobenzoate (4.9 mg., 1.3%) and methyl p-nitrobenzoate (15.6 mg., 4.2%) were estimated by g.l.c. (d.e.g.s. - Chromosorb P, 160°). Chromatography on silica gave (with benzene) tetracyclone (18%) m.p. and mixed m.p. 219-220°, and 1,4-carbonyl-1,4-dihydro-6-nitro-1,2,3,4-tetraphenyl-4a,9a-diazafluoren-9-one (0.607 g., 53%) m.p. and mixed m.p. 157-159°.

Solution Infra-red Spectra of 3-Aminobenzotriazinone Oxidations

| Triazinone | Initial Trap | Spectrum | | MeOH added (min) | Spectrum | | Products |
|---------------------|--------------|------------|------------------------------|------------------|------------|------------------------------|--------------|
| | | Time (min) | $\nu_{\max}(\text{cm}^{-1})$ | | Time (min) | $\nu_{\max}(\text{cm}^{-1})$ | |
| R = Cl | None | 3 | 1810, 1760 | 3 | 6 | 1810sh, 1760 | |
| | | 20 | 1810, 1760 | | 23 | - | |
| R = Cl | tetracyclone | 3 | 1810, 1760 | 5 | 8 | 1810, 1760 | |
| | | 20 | 1810, 1760 | | 25 | - | |
| R = NO ₂ | tetracyclone | 8 | 1820, 1760 | 10 | 12 | 1820, 1760sh | m-ester (9%) |
| | | 30 | 1820, 1760 | | 40 | 1760sh. | p-ester (8%) |
| R = Me | tetracyclone | 8 | 1810 1760 | 18 | 29 | 1810, 1760 | m-ester (3%) |
| | | | | | 39 | 1810, 1760 | p-ester (1%) |
| | | | | | 78 | 1810sh, 1760 | |
| | | | | | 108 | 1760 sh | |
| | | | | | 138 | - | |



Infra-red spectroscopic studies

a. 3-Aminobenzotriazinones General method

The oxidations, additions of trap and transfer to infra-red liquid cells were all performed in a glove box under a nitrogen atmosphere dried by molecular sieves type 3A. The aminotriazinone (1 mmole) with tetracyclone (1 mmole) in dry methylene chloride (10 ml.) was oxidised by the addition of lead tetra-acetate (1 mmole) in methylene chloride (20 ml.). The infra-red spectrum of a sample withdrawn immediately after the oxidation via serum cap and syringe was monitored in the range 2000 to 1500 cm^{-1} . Methanol (2 ml.) was then added to the bulk reaction mixture and the infra-red spectrum of a sample similarly monitored as a function of time (Table, p.178). Analysis of the resultant methyl esters was carried out by g.l.c. Infra-red spectra of lead tetra-acetate in methylene chloride had ν_{max} at 1760 and 1710 cm^{-1} . Lead di-acetate was transparent from 2000 to 1600 cm^{-1} .

b. 4-Chloroindazolinone

The indazolinone (0.220 g., 1.3 mmole) in methylene chloride (10 ml.) was oxidised by the addition of lead tetra-acetate (0.580 g., 1.3 mmole) in methylene chloride (10 ml.). The reaction solution was monitored in the infra-red. The initial absorbance at 1790 cm^{-1} disappeared over 3 hr. and was matched by the appearance of a new absorbance at ν_{max} , 1825 cm^{-1} . The addition of methanol to the reaction

mixture caused the absorbance at 1825 cm.^{-1} to disappear over 12 hr.

p-Nitrobenzoic acetic anhydride

Ketene and p-nitrobenzoic acid reacted as in the literature method¹⁰⁹ gave p-nitrobenzoic acetic anhydride (100%) m.p. $71-73^{\circ}$ decomp. Recrystallisation from benzene-ether below 20° gave the mixed anhydride as cream crystals (45%) m.p. $75.5-77^{\circ}$ decomp. (lit.¹⁰⁹ m.p. $75.5-77^{\circ}$).
 $\nu_{\text{max.}}$ (CH_2Cl_2) $2920, 2860, 1820, 1730, 1605\text{ cm.}^{-1}$
 (Nujol) $3110, 1800, 1730, 1605\text{ cm.}^{-1}$

Benzoic acetic anhydride

Ketene and benzoic acid give similarly benzoic acetic anhydride (100%) as a mobile oil.
 $\nu_{\text{max.}}$ (CH_2Cl_2) $3100, 1820, 1730, 1600\text{ cm.}^{-1}$

Methanolysis of p-nitrobenzoic acetic anhydride

The mixed anhydride (1.28 g.,) was allowed to stand in dry methanol (50 ml.) at 25° for 20 hr. Analysis by g.l.c. then showed the presence of methyl p-nitrobenzoate (0.047 g.) (on d.e.g.s. - Chromosorb P) and of methyl acetate (0.075 g.) (on Porapak Q). Molar ratio of methyl p-nitrobenzoate:methyl acetate, 20:80; overall solvolysis 20.5%.

Pyrolysis of α -Carbonylazo adducts

General Method The apparatus consisted of an evacuated pyrex or silica tube heated externally by an electric sample heater and furnace heater as shown in the diagram (p.183). The tube was connected to a cold trap and the complete system evacuated by an oil pump to 0.04 torr. The furnace was heated to the required temperature, then the apparatus assembled as above and evacuated, ensuring that the sample was surrounded only by the sample heater. Controlled heating of the sample heater caused the sample to sublime, pass through the furnace, and collect in the final cold traps. In practice, a temperature of 960° in the furnace and 50° in the adjacent sample could be maintained indefinitely.

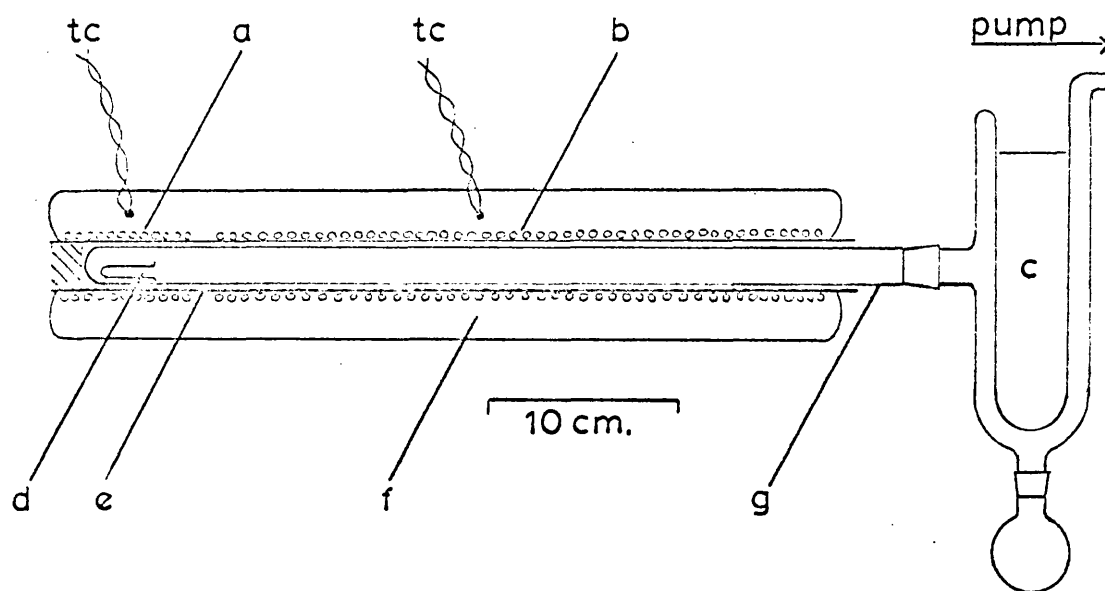
a. 1,4-Dihydro-4a,9a-diazafluoren-9-one

(i) The butadiene adduct was recovered (100%) from heating to 450°. The sample sublimed as an oil which crystallised, m.p. and mixed m.p. 104-106°, infra-red spectrum identical to that of an authentic specimen.

(ii) The butadiene adduct (0.141 g., 0.76 mmole) pyrolysed at 610° gave recovered starting material (50%), identical infra-red spectrum to an authentic specimen, and biphenylene (0.023 g., 19%), m.p. and mixed m.p. 107-109°, (lit.¹¹⁰ m.p. 110-111°), identical by g.l.c. (Silicone gum rubber), t.l.c. (silica-petrol) and infra-red spectrum to an authentic specimen.

b. 1,4-Methano-1,4-dihydro-4a,9a-diazafluoren-9-one The cyclopentadiene adduct (0.102 g., 0.515 mmole) was pyrolysed at 380° to give recovered starting material (0.060 g., 59%), and biphenylene (0.010 g., 13%) m.p. and mixed m.p. 105-107°. Infra-red spectrum, g.l.c. and t.l.c. were identical to an authentic specimen. Three trace components of shorter retention time were observed in the g.l.c. The yield of these additional compounds was increased on pyrolysis of the adduct at 480°, as was the yield of biphenylene (18%).

c. 1,4-Methano-1,4-dihydro-4a,9a-diaza-9,10-anthraquinone The phthalazinedione adduct was recovered after heating at 380°. The adduct (0.064 g., 0.23 mmole) was pyrolysed at 530° to give a yellow pyrolysate (0.055 g.), m.p. 120-127°. Chromatography on neutral alumina gave 1,2-benzocyclobutadienequinone (0.010 g., 33%), m.p. 132-133° (lit.^{111a} m.p. 132-135°)
 ν_{max} . 3070, 1870, 1805, 1780, 1760, 1580, 1430, 1360, 1280, 1170, 1135, 935, 850, 775 cm^{-1} identical to the published spectrum.^{111b}



- a: sample heater 500w.
- b: furnace 1100w.
- c: cold trap
- d: sample
- e: quartz furnace support
- f: fireclay
- g: pyrolysis tube
- tc: thermocouple

PYROTRON Mk.3

Miscellaneous Experiments

Pyrolysis of 3-aminobenzo-1,2,3-triazin-4-one

The aminotriazinone (0.246g., 1.52 mmole) was pyrolysed at 500° and 0.05 torr. The pyrolysate was 3-indazolinone (0.200g., 98.5%) m.p. and mixed m.p. 245-250°, infra-red spectrum identical to that of an authentic specimen.

Pyrolysis of 3,4-dihydrobenzo-1,2,3-triazin-4-one

The triazinone was recovered from heating in vacuo to 720°. The triazinone (0.176g., 1.2 mmole) on pyrolysis at 950° underwent extensive charring. The pyrolysate (11.3 mg) on analysis by g.l.c. and t.l.c. showed both biphenylene and benzonitrile present. The infra-red spectrum was consistent with a mixture of these compounds. ν_{\max} 3060, 2120, 1440, 1420, 1260, 1150, 1130, 960, 730 cm^{-1} .

Oxidation of 3-aminobenzo-1,2,3-triazin-4-one with nickel peroxide

The triazinone (0.440g., 2.7 mmole) and nickel peroxide (2.5g.) were stirred in a methanol (20 ml.) at 25° for 48 hours. Slow gas evolution occurred. The reaction mixture was filtered and the filtrate chromatographed on silica to give methyl 2-azidobenzoate (0.192g., 40%) identical (i.r. spectrum and t.l.c.) to an authentic specimen. No starting material was recovered.

3-Amino-7-nitrobenzo-1,2,3-triazin-4-one with sodium methoxide

The triazinone (0.104g., 0.5 mmole) was stirred in dry methanol (5 ml.) and sodium methoxide (4 mmole) for 12 hours. Chromatography on

silica gave methyl 2-azido-4-nitrobenzoate (0.071g., 64%) m.p. and mixed m.p. 93-96°, identical (i.r. spectrum and t.l.c.) to an authentic specimen.

Methyl 2-azido-4-nitrobenzoate

Methyl 2-amino-4-nitrobenzoate (0.5g., 2.5 mmole) was diazotised in 2N hydrochloric acid at 5° by the addition of sodium nitrite (0.27g., 4 mmole). The solution was filtered and aqueous sodium azide added. The resulting precipitate crystallised from ether - petrol to give methyl 2-azido-4-nitrobenzoate (0.33 g., 60%) m.p. 96-98°. (Found: C, 43.2; H, 2.8; N, 23.2. $C_8H_6N_4O_4$ requires C, 43.25; H, 2.7; N, 25.2%) ν_{\max} 2120, 1730, 1535, 1350, 1250, 880, 810, 735 cm^{-1} .

Methyl 2-azidobenzoate

By a similar procedure methyl anthranilate gave methyl 2-azidobenzoate as an oil (95%).

ν_{\max} (thin film) 2940, 2120, 1725, 1300, 1260, 750 cm^{-1} .

1,4-Methano-1,4-dihydro-4a, 9a-diaza-9,10-anthraquinone

Lead tetra-acetate (5.5g., 12.4 mmole) was added in portions to phthalazine -1,4-dione (2.0g., 12.4mmole) and cyclopentadiene (5g.) in methylene chloride (100 ml.) at -50°. After 2 hours the reaction mixture was warmed to room temperature and filtered. The filtrate was evaporated to small bulk, when petrol precipitated the adduct (0.58 g., 21%). Crystallisation from methylene chloride - benzene gave 1,4-methano-1,4-dihydro-4a, 9a-diaza-9, 10-anthraquinone (0.40 g., 14%) m.p. 216-219°.

ν_{max} 1630, 1605, 1310, 1120, 960, 770, 690 cm^{-1}

p.m.r. (CDCl_3) τ 1.6-2.3 (4H,m); 3.25 (2H,s); 4.0 (2H,s); 7.83 (2H,s).

Dihydrobenzo-1,2,3-triazines

A. Protected benzylidene hydrazines.

a. 1-Ethoxycarbonyl-2-(2-aminobenzylidene)hydrazine. 2-aminobenzaldehyde¹¹² (4.0g., 0.033 mole) and ethyl carbazate (3.45g., 0.033 mole) in ethanol (100 ml.) and dil. acetic acid (1 ml.) were stirred at 70° for 3 hours. The reaction mixture was evaporated to dryness and the residue crystallised from benzene to give 1-ethoxycarbonyl-2-(2-aminobenzylidene)hydrazine (4.3g., 63%) m.p. 130-131°. (Found: C, 58.3; H, 6.1; N, 19.8. $C_{10}H_{13}N_3O_2$ requires C, 58.0; H, 6.3; N, 20.3%).
 ν_{\max} 3360, 3200-3280, 1735, 1610, 1540, 1250, 760 cm^{-1} .

b. 1-Ethoxycarbonyl-2-(2-nitrobenzylidene)hydrazine. Under similar conditions to those above, 2-nitrobenzaldehyde (10.0 g., 0.066 mole) and ethyl carbazate (6.9 g., 0.066 mole) gave 1-ethoxycarbonyl-2-(2-nitrobenzylidene)hydrazine (16.0 g., 100%) which was used without further characterisation.

c. 1-p-Toluenesulfonyl-2-(2-aminobenzylidene)hydrazine. Under similar conditions to those above, 2-aminobenzaldehyde (3.5 g., 0.029 mole) and tosyl hydrazide (5.5 g., 0.029 mole) gave 1-p-toluenesulfonyl-2-(2-aminobenzylidene)hydrazine (5.5 g., 65%) m.p. 162-163° (from ethanol). (Found: c, 58.0; H, 5.2; N, 14.6. $C_{14}H_{15}N_3O_2S$ requires C, 58.1; H, 5.2; N, 14.5%).

ν_{\max} 3390, 3290, 3170, 1615, 1600, 1495, 1340, 1170 cm^{-1} .

m/e 289, 226, 157, 156, 143, 106, 91.

d. 1-p-Toluenesulfonyl-2-(2-nitrobenzylidene)hydrazine was prepared by the literature method¹¹³ as yellow crystals (73%) m.p. 154-155° (from ethanol), (lit.¹¹³ m.p. 154-156°).

ν_{\max} 3180, 1595, 1520, 1340, 1170, 1160, 930, 810, 740 cm^{-1} .

e. 1-tert-Butoxycarbonyl-2-(2-aminobenzylidene)hydrazine. 2-Aminobenzaldehyde (4.0 g., 0.033 mole) and tert-butyl carbazate (4.35 g., 0.033 mole) in tert-butanol was heated under reflux for 48 hours.

Work up as above followed by recrystallisation from benzene gave 1-tert-butoxycarbonyl-2-(2-aminobenzylidene)hydrazine (5.0 g., 65%), m.p. 93-94°. (Found: C, 61.0; H, 7.2; N, 17.8. $\text{C}_{12}\text{H}_{17}\text{N}_3\text{O}_2$ requires C, 61.25; H, 7.3; N, 17.9%).

ν_{\max} 3430, 3400, 3300, 3200, 1720, 1690, 1620, 1250, 1170, 750 cm^{-1} .

p.m.r. (CDCl_3) τ 1.7 (1H, s exchangeable with D_2O); 2.2 (2H, s); 2.7-3.5 (4H, m); 4.05 (2H, s, exchangeable with D_2O); 8.45 (9H, s).

f. 1-tert-Butoxycarbonyl-2-(2-nitrobenzylidene) hydrazine. 2-Nitrobenzaldehyde (9.8 g., 0.066 mole), tert-butyl carbazate (8.6 g., 0.066 mole) and pyridine (10 ml.) were heated under reflux in tert-butanol (100 ml.) for 12 hours. The solvent was removed under reduced pressure and the residue crystallised from benzene to give 1-tert-butoxycarbonyl-2-(2-nitrobenzylidene)hydrazine (13.6 g., 79%) m.p. 153-154°. (Found: C, 54.2; H, 5.6; N, 15.8. $\text{C}_{12}\text{H}_{15}\text{N}_3\text{O}_4$ requires C, 54.3; H, 5.7; N, 15.8%).

ν_{\max} 3260, 1700, 1520, 1350, 1330, 1250, 1150 cm^{-1} .

B. Protected Benzylhydrazines.

a. 1-Ethoxycarbonyl-2-(2-aminobenzyl)hydrazine.

(i) 1-Ethoxycarbonyl-2-(2-aminobenzylidene)hydrazine (2.28 g., 0.011 mole) in ethanol (100 ml.) was hydrogenated at 1 atmosphere over 10% Pd/C at 25°, to give 1-ethoxycarbonyl-2-(2-aminobenzyl)hydrazine (1.9 g., 83%) m.p. 81-81.5° from benzene. (Found: C, 57.4; H, 7.2; N, 19.05. $C_{10}H_{15}N_3O_2$ requires C, 57.4; H, 7.2; N, 20.1%).

ν_{\max} 3460, 3370, 3250, 1700, 1615, 1560, 1275, 750 cm^{-1} .

(ii) 1-Ethoxycarbonyl-2-(2-nitrobenzylidene)hydrazine (16 g., 0.067 mole) in ethanol (200 ml.) was hydrogenated at 4 atmosphere over 10% Pd/C at 50°, to give 1-ethoxycarbonyl-2-(2-aminobenzyl)hydrazine (12.5 g., 91%) m.p. and mixed m.p. 81-81.5° (from benzene).

b. 1-tert-Butoxycarbonyl-2-(2-aminobenzyl)hydrazine.

1-tert-Butoxycarbonyl-2-(2-aminobenzylidene)hydrazine (5.0 g., 0.021 mole) in benzene (100 ml.) was hydrogenated at 4 atmospheres over 10% Pd/C at 50° for 4 days. Chromatography of the product on silica gave recovered benzylidenehydrazine (3.0 g., 60%) and 1-tert-butoxycarbonyl-2-(2-aminobenzyl)hydrazine (2.0 g., 40%) m.p. 67-69°. (Found: C, 59.3; H, 7.5. $C_{11}H_{17}N_3O_2$ requires C, 59.2; H, 7.7%).

ν_{\max} 3420, 3370, 3230, 1710, 1690, 1610, 1290, 1250, 1150, 745 cm^{-1} .

p.m.r. (CDCl_3) τ 2.7-3.6 (4H,m); 5.73 (4H,s, exchangeable with D_2O); 6.05 (2H,s); 8.53 (9H,s).

Hydrogenation of 1-tert-butoxycarbonyl-2-(2-nitrobenzylidene)hydrazine under similar conditions to those above gave the same mixture of products, isolated in similar yields by column chromatography.

c. Attempted reduction of 1-p-toluenesulfonyl-2-(2-aminobenzylidene)-hydrazine.

(i) The hydrazine was recovered in fair to good yield (60-90%) from hydrogenation for up to 7 days in ethanol or methanol at 4 atmospheres over either 10% Pd/C or Pt. The addition of HCl gas to the reaction mixture¹¹⁴ did not assist reduction. The crude reaction mixtures were analysed by p.m.r. and mass spectrometry; but no benzylic proton resonance at τ 4-7 or parent ions at m/e 291 were observed.

(ii) Attempted reduction of 1-p-toluenesulfonyl-2-(2-nitrobenzylidene)-hydrazine under the above conditions gave only 1-p-toluenesulfonyl-2-(2-aminobenzylidene)-hydrazine (60-90%).

(iii) The aminosylhydrazine (0.29 g., 1 mmole) was stirred with sodium borohydride (1 equivalent) in ethanol for 1 hour. Chromatography on neutral alumina gave recovered hydrazone (0.13 g., 45%) and o-toluidine (0.03 g., 28%).

C. Protected Dihydrobenzo-1,2,3-triazines.

a. 3-Ethoxycarbonylamino-3,4-dihydrobenzo-1,2,3-triazine.

A solution of 1-ethoxycarbonyl-2-(2-aminobenzyl)-hydrazine (3.3 g., 0.016 mole) in 50% aqueous acetic acid (50 ml.) at 3° was diazotised by the addition of sodium nitrite (1.1 g., 0.016 mole) in water (20 ml.).

After the addition was completed, the mixture was stirred for 30 minutes then extracted with ether (3 x 100 ml.). The ethereal extract was washed with aqueous sodium bicarbonate and dried (MgSO_4); it gave a yellow oil (2.8 g.) which solidified on trituration with petrol. Chromatography on neutral alumina gave 3-ethoxycarbonylamino-3,4-dihydrobenzo-1,2,3-triazine (2.1 g., 60%) m.p. $105-106^\circ$. (Found: C, 54.5; H, 5.7; N, 26.0. $\text{C}_{10}\text{H}_{12}\text{N}_4\text{O}_2$ requires C, 54.5; H, 5.5; N, 25.4%).

ν_{max} 3170, 1740, 1250, 930, 840, 780 cm^{-1} .

m/e 220, 192, 190, 119, 118, 91

p.m.r. (CDCl_3) τ 2.4-3.5 (4H,m); 5.55(2H,s); 5.85 (2H,q); 8.82(3H,t).

b. 3-tert-Butoxycarbonylamino-3,4-dihydrobenzo-1,2,3-triazine.

Under similar conditions to those above, diazotisation of 1-tert-butoxycarbonyl-2-(2-aminobenzyl)-hydrazine gave 3-tert-butoxycarbonylamino-3,4-dihydrobenzo-1,2,3-triazine (70%) m.p. $116-117^\circ$ (from benzene).

(Found: C, 58.4; H, 6.8; N, 22.4; $\text{C}_{12}\text{H}_{16}\text{N}_4\text{O}_2$ requires C, 58.05; H, 6.5; N, 22.6%).

ν_{max} 3160, 1730, 930, 840, 780, 760 cm^{-1} .

Attempted preparation of 3-amino-3,4-dihydrobenzo-1,2,3-triazine.

a. From 3-ethoxycarbonylamino-1,2,3-triazine.

The triazine was recovered from solution in 10% potassium hydroxide in 90% aqueous ethanol, and from solution in cold 50% HCl or cold 50% aqueous CCl_3COOH . On warming the solutions until the starting material had disappeared (t.l.c.), neutralising the acid (NaHCO_3) and extracting

with ether, low (5-15%) yields of multicomponent tars (ν_{\max} 2160, 2120, 1630 cm^{-1}) were obtained.

The triazine in ether was precipitated quantitatively as the hydrochloride by the addition of hydrogen chloride. Aqueous ammonia (0.880) liberated the protected triazine quantitatively.

b. From 3-tert-butoxycarbonylaminobenzotriazine.

(i) The triazine (2.0 g., 0.008 mole) was dissolved in conc. hydrochloric acid (10 ml.) at 5° and stirred for 10 minutes. The reaction was basified with excess sodium bicarbonate and extracted with ether to give an oil, (100 mg.)

ν_{\max} 3300, 2100, 1610, 750 cm^{-1} . Chromatography on neutral alumina gave a red oil (4 mg.) ν_{\max} 3400 (broad) 2100, 1610 cm^{-1} which liberated a gas on admixture with lead tetra-acetate.

(ii) The triazine and trifluoroacetic acid in nitromethane¹¹⁵ were mixed at -20°, and then poured into cold 2N NaOH. Ether extraction gave a multicomponent tar in low yield (8%), ν_{\max} 2100 cm^{-1} . The crude tar did not visibly react with lead tetra-acetate.

c. From 3-amino-3,4-dihydrobenzo[e]-1,2,3-triazin-4-one.

The aminotriazinone (2.0 g., 12.3 mmole) in dry tetrahydrofuran (50 ml.) was added dropwise to lithium aluminium hydride (1.0 g., 26 mmole) in dry tetrahydrofuran at 0°. Water (1 ml.); sodium hydroxide (2N, 3 ml.) and water (1 ml.) were added consecutively dropwise and the

mixture filtered. The red filtrate on evaporation gave an oil (1.1 g., 55%) (ν_{\max} 2850, 2110 cm^{-1}). Chromatography on neutral alumina did not resolve the products; but all the fractions had ν_{\max} 2110 cm^{-1} and none gave any visible reaction with lead tetraacetate.

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