HETEROCYCLES, Vol. 15, No. 1, 1981

RECENT PROGRESS IN THE CHEMISTRY OF AZAAZULENES: SYNTHETIC METHODOLOGY AND CHEMICAL REACTIONS

Tarozaemon Nishiwaki and Noritaka Abe
Department of Chemistry, Faculty of Sciences, Yamaguchi
University, Yamaguchi City 753, Japan

Abstract- Synthetic methods of azaazulenes including some of their hydro and oxo derivatives and the cyclazines incorporating an azaazulene ring are surveyed. Nucleophilic and electrophilic substitutions and pericyclic reactions of azaazulenes and their derivatives are reviewed.

INTRODUCTION

Azaazulenes are a class of the compounds that have been receiving continual interest of chemists particularly for their relationship with the chemistry of azulenes. The studies pioneered by Nozoe and his associates and topics of relevance were comprehensively surveyed in 1960.[1] The last two decades saw enormous development in this field, including MO calculations[2] and spectroscopic (mass,[3a] ^{13}C n.m.r.,[3b] and electronic spectra[3c]) studies. The azaazulene rings are of importance in nature, where they are found in zoanthoxanthins (highly fluorescent metabolites of colonial anthozoans),[4] and coformycin[5a] and pentostatin[5b] that are the powerful inhibitors of adenosine deaminase. They are also a structural feature of the medicines that are currently used as hypnotics and sedatives.[6] Nevertheless, only brief coverage of the literature since 1960 is available.[7-10]

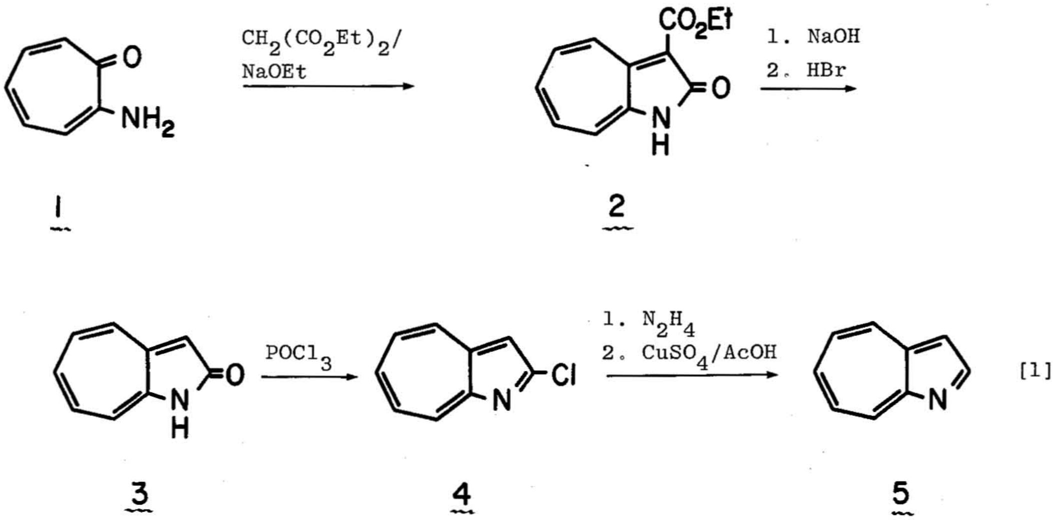
This review covers the recent progress in the chemistry of fully-conjugated azaazulenes including some of their hydro and oxo derivatives, with particular reference to their synthetic methods and chemical reactions, but it leaves out the chemistry of oxaza- and thiaza-azulenes. Among cyclazines, those incorporating an azaazulene ring are also referred to in this review.

The nomenclature adopted by CHEMICAL ABSTRACTS is used for the ring systems, but for the sake of convenience the replacement names (e.g. 1-azaazulenes) and the name of azulane proposed for 1,2-dihydroazulene by Nozoe (see Ref. 1, p. 536) are frequently used as well.

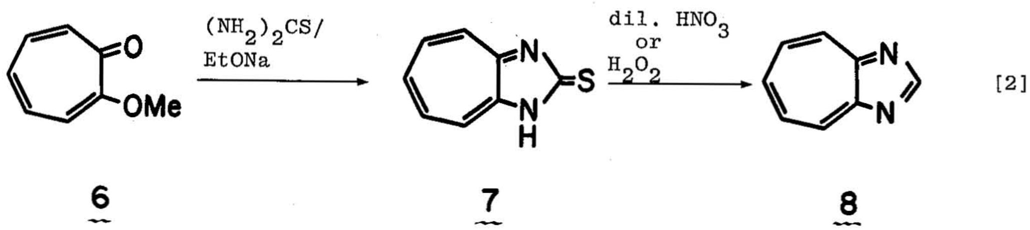
I. Syntheses of Azaazulenes

A. Syntheses From Reactive Troponoids

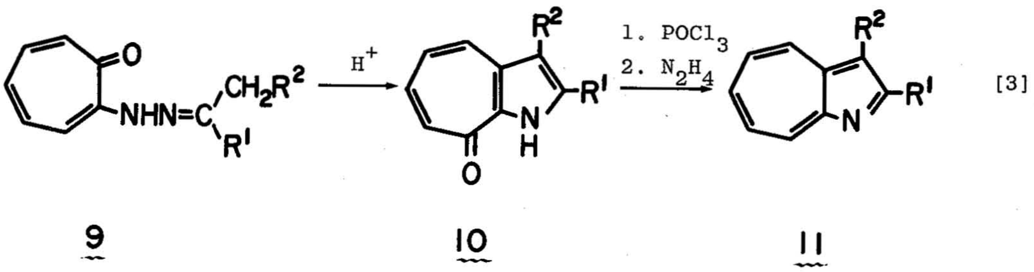
Azaazulenes containing nitrogen atom(s) in the five-membered ring are conveniently prepared starting from reactive troponoids [*e.g.* 2-amino- (1) and 2-methoxy-tropones (6)]. The Eqs. [1-3] are the representative synthetic methods of cyclohepta[b]pyrroles (1-azaazulenes) (*e.g.* 5 and 11) and cycloheptimidazole (1,3-diazaazulene) (*e.g.* 8). The substituents of 2, 3, 4, 7, and 10 are readily displaced or removed by the reagents shown. These methods were discovered in the



[1]



[2]

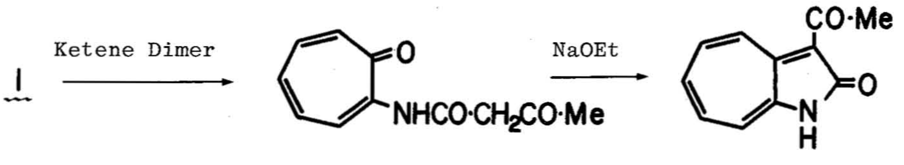


[3]

1950s[1] and have been still held importance even in recent studies. As shown in Eqs. 1 and 2, 2-amino- (1), 2-methoxy- (6), 2-chloro-tropones, and 2-troponylhydrazides (9) have been often used as the reactive troponoid in these annelation reactions, but recent studies have revealed that the tosylate of tropolone[11] and 2-dimethylaminotropones[12] are used as well.

Some tropones bearing a mobile group at C-2 were found to undergo regiospecific cyclisation with arylamidines to give 2-arylcycloheptimidazoles with loss of the C(2)-substituent. An electron-attracting group (*e.g*. Cl and R_3N^+) at C-2 induces cyclisation at C(7)-C(1), whereas a mesomerically electron-donating group (*e.g*. MeO) induces cyclisation at C(2)-C(1).[13a] Cyclisations of 2-ethylthio-[13c] and 2-dimethylsulphonio-tropones[13c] probably follow the latter course. For tropones carrying MeO or MeS groups at C-3, regiospecific nuclear hydride replacement at C-7 takes place affording 5-substituted 2-arylcycloheptimidazoles.[13b] 4-Methylthiotropone also undergoes regiospecific cyclisation to yield 6-methylthio-2-arylcycloheptimidazole.[13c]

Although in earlier studies,[1] active methylene compounds, amidines, or thiourea were employed for the annelations depicted in Eqs. 1 and 2, successful uses of acylhydrazines,[14] ketene dimer,[15] and pyridinium ylide[16] were subsequently reported. From the reaction of 2-chlorotropone with cyanoacetohydrazide, 1-amino-2-oxo-1,2-dihydrocyclohepta[b]pyrrole-3-carbonitrile was formed, whereas the reaction of 1 with ketene dimer gave 2-acetoacetamidotropone (12), which then cyclised in the presence of base to 3-acetylcyclohepta[b]pyrrol-2(1H)-one (13) [Eq. 4]. Notable is the one-step synthesis of azaazulenes from tropone and pyridinium ylide in the presence of ammonium bromide, but it leaves much to be desired with respect to the yield of the product.

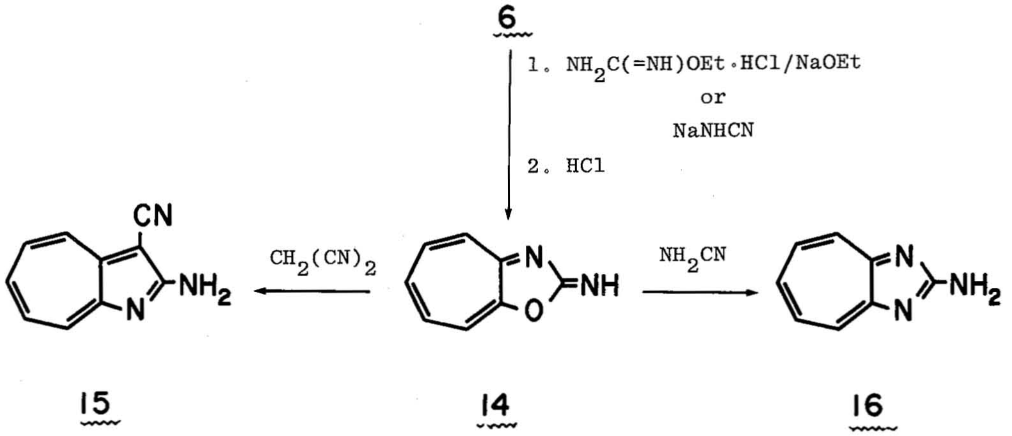


12

13

[4]

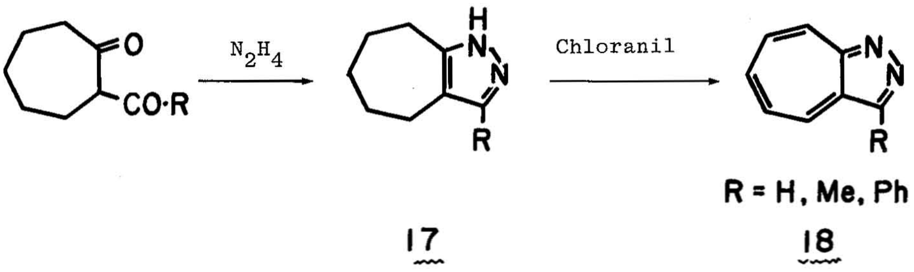
In 1968, Sunagawa *et al*. found interesting reactions of 6 and 2-ethylisourea hydrochloride. When the reaction was performed in the presence of sodium ethoxide equivalent to the hydrochloride, 2-ethoxy-derivative of **8** was formed in a moderate yield.[17a] However, if an excess of the base was used, the sodium salt of 2-cyanaminotropone was produced, from which 2-imino-2H-cycloheptoxazole (**14**) was obtained in a good overall yield.[17b] The compound **14** reacted with active methylene compounds (e.g. malononitrile),[17c] thiols,[17c] and cyanamide[17d] to afford 2-aminocyclohepta[b]pyrrole-3-carbonitrile (**15**), 2-alkylthiocycloheptimidazole, and 2-aminocycloheptimidazole (**16**) [Eq. 5].



[5]

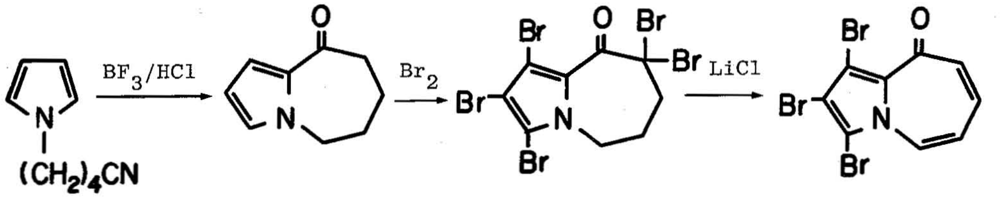
B. Syntheses via Hydroazaazulenes

Dehydrogenation of hydroazaazulenes, if they are readily prepared, may be very practicable for the syntheses of fully-conjugated azaazulenes. As a supplement to the examples cited in the previous review,[1] it will suffice to record the dehydrogenation of **17**, obtained from 2-acylcycloheptanone and hydrazine, to cycloheptapyrazole (1,2-diazaazulene) (**18**) [Eq. 6].[18]



[6]

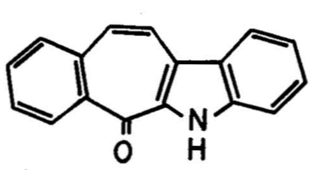
1,2,3-Tribromopyrrolo[1,2-a]azepin-9-one (3a-azaazulan-8-one derivative) (21) was prepared by the dehydrobromination of 20 synthesised from N-(4-cyanobutyl)pyrrole via 19, as depicted in Eq. 7.[19a] A similar sequence of reactions permitted an access to 11-methylazepino[1,2-a]indol-10-one.[19b]



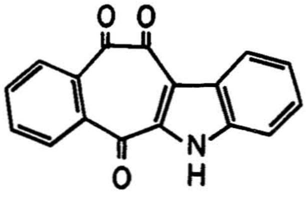
19 20 21

Inasmuch as Fischer indolisation of the hydrazone (9) derived from 2-hydrazino-2,4,6-cycloheptatrien-1-one proved to be a versatile synthetic method of cyclohepta[b]pyrrol-8(1H)-one (10) [Eq. 3],[1] a number of condensed azaazulanones have since been prepared by this method in combination with the halogenation-dehydrohalogenation or the oxidation of hydroazaazulanones. They are benzo[5,6]-cyclohept[1,2-b]indol-6(5H)-one (22)[20] and its 11,12-dioxo derivative (23),[21] and 5H-benzo[5,6]cyclohepta[1,2-b]cyclohepta[d]pyrrol-5,9(6H)-dione (24),[21] 5H-dicyclohepta[b,d]pyrrol-5-one (25),[22] cyclohept[b]pyrido[3,4-d]pyrrol-6(5H)-one (26),[22] cyclohept[b]indol-6(5H)-one (27),[23] cyclohept[b]indol-10(5H)-one (28),[23] and benzo[6,7]cyclohept[1,2-b]indol-7-one (29) derivatives.[24]

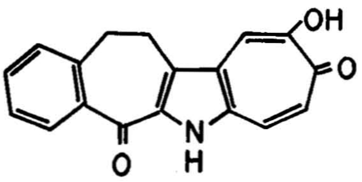
A recent synthesis of 4-ethoxyindeno[1,2-d]azepine (30) also involves the bromination-dehydrobromination of 4-oxo-1,2,3,4,5,10-hexahydroindeno[1,2-d]azepine as a key step.[25]



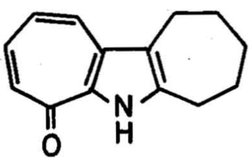
22



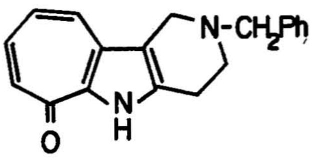
23



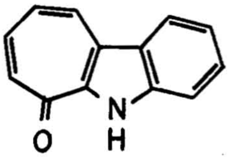
24



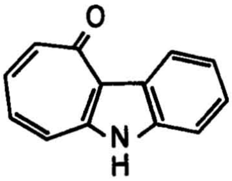
25



26



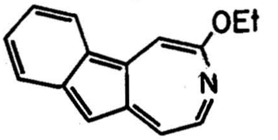
27



28

R = H, Me ; X = Cl, Br

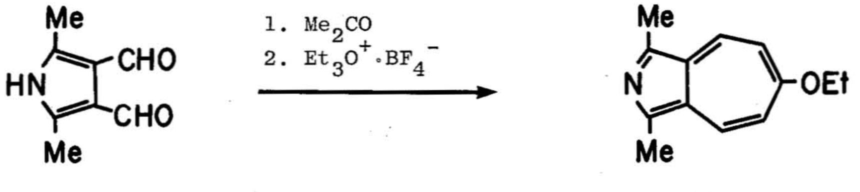
29



30

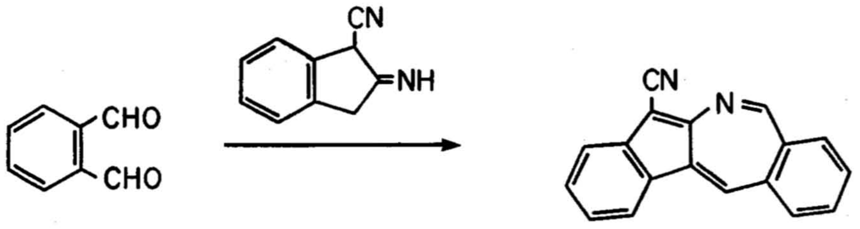
C. Syntheses Utilising Intermolecular Condensations

One-step annelation of a seven-membered ring to a five-membered one is feasible by utilising intermolecular condensations of 1,2-dialdehydes with appropriate reactants. A utility of this method is obvious from the preparations of 6-ethoxy-1,3-dimethylcyclohepta[c]pyrrole (2-azaazulene derivative) (31) [Eq. 8],[26c] benz[e]indeno[2,1-b]azepine-5-carbonitrile (32) [Eq. 9],[27] and 5,7-dimethyl-6(2H)-cycloheptapyrazolone (1,2-diazaazulan-6-one derivative) from the reaction of pyrazole-3,4-dicarboxaldehyde and diethyl ketone.[28b]



31

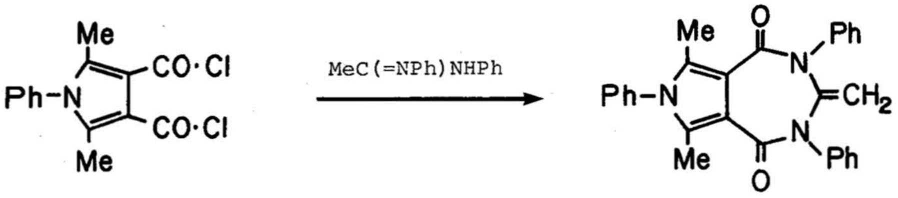
[8]



32

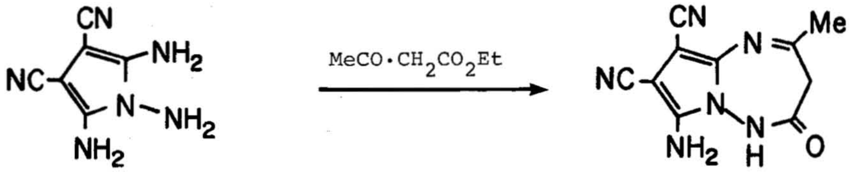
[9]

If the dialdehyde is replaced with 1,2-diacid chloride or 1,2-diamine, the hydro and oxo derivatives of polyazaazulenes may be derived, as illustrated by the preparations of 3,4-dihydro-6,8-dimethyl-3-methylene-2,4,7-triphenylpyrrolo-[3,4-e][1,3]diazepine-1,5(2H,7H)-dione (33) [Eq. 10][29] and 7-amino-4,5-dihydro-2-methyl-4-oxo-3H-pyrrolo[1,2-b][1,2,4]triazepine-8,9-dicarbonitrile (34)[Eq. 11].[30] Hydro-polyazaazulene rings were also made up from 4,5-diamino-1,2,3-[31] and 4,5-diamino-1,2,4-triazoles.[32]



33

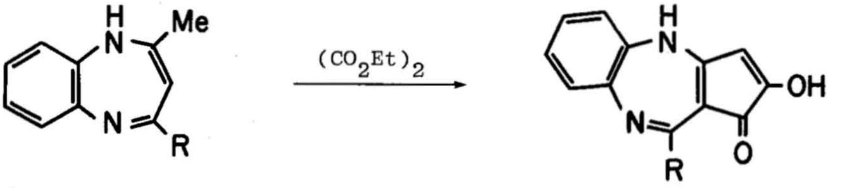
[10]



34

[11]

A polyazaazulene ring is alternatively made up from an adequate seven-membered compound utilising intermolecular condensations. Cycloheptapyrazole derivatives have been prepared by the reactions of tropones (e.g. 2,7-diaroyltropones,[33] 3-acetyltropolone,[34] 3-acetyl-2-methoxytropone,[34] and 2-acetyl-7-methoxytropone[34]) with hydrazine or methylhydrazine. Although a Claisen condensation product of 2-methyl-1H-1,5-benzodiazepine (**35**) with diethyl oxalate was wrong assigned,[35a] it has since been corrected as a benzo[b]cyclopenta[e][1,4]diazepine derivative (**36**) [Eq. 12].[35b]



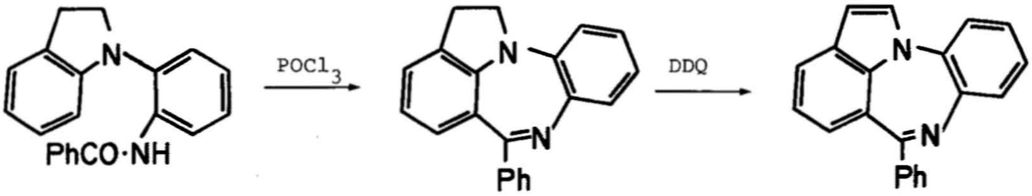
R = Me, Ph

35 **36**

[12]

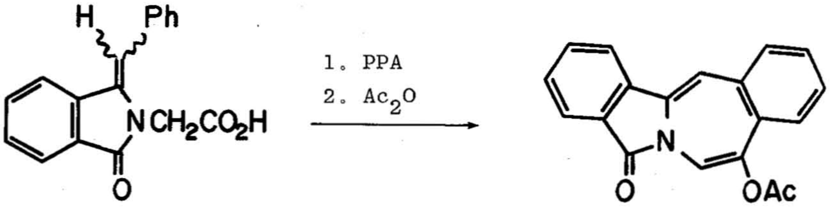
D. Syntheses Utilising Intramolecular Condensations

Intramolecular condensations of appropriately substituted esters, amides, aldehydes, and ketones are another practicalble synthetic method leading to compounds possessing a polyazaazulene ring. Thus, indolo[1,7-ab][1,5]benzodiazepine (**37**),[36] 5H-isoindolo[2,3-a][3]benzazepin-5-one (**38**),[37] 5H-pyrrolo[1,2-a]-azepin-5-one (3a-azaazulan-4-one) (**39**),[38a] 9H-pyrrolo[1,2-a]azepin-9-one (**40**),[38b] and 4H-pyrrolo[1,2-a]thieno[3,2-f][1,4]diazepin-4-one (**41**)[39] were prepared as outlined in Eqs. 13-17. The acid-catalysed cyclisation of 5-arylazo-4-ethyltropolone to **42** [Eq. 18][40a] may be regarded as one of the synthetic method of cycloheptapyrazoles. Of interest are the thermal cyclisations of 4-(1-hydroxyethyl)- and 4-(1-acetamidoethyl)-5-arylazotropolones to **42**.[40b]



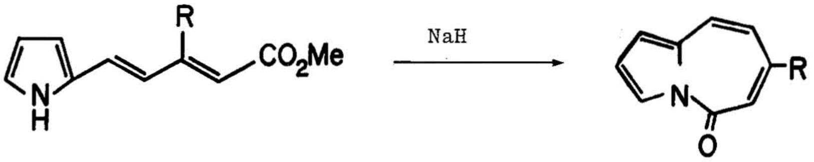
[13]

37



38

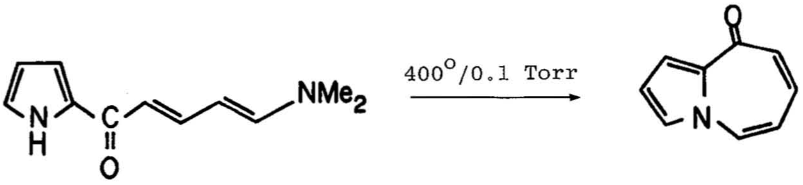
[14]



R = H, Me, Ph

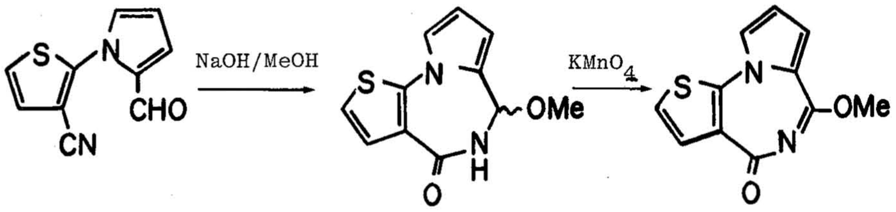
39

[15]



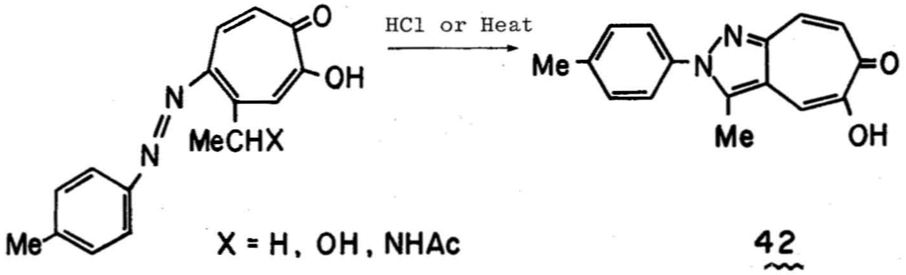
40

[16]



41

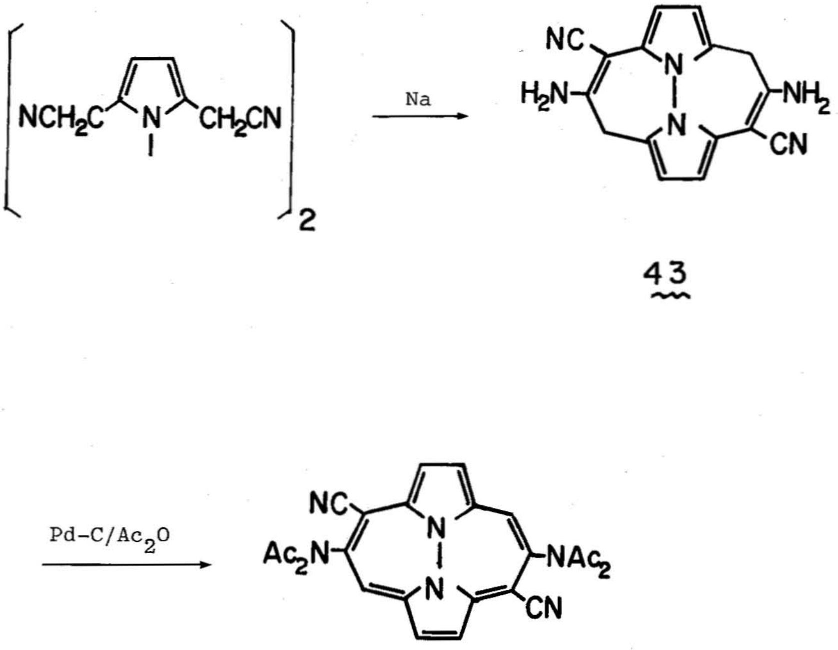
[17]



42

[18]

The 10b,10c-diazadicyclopenta[ef,kl]heptalene (44) incorporating a 3a,4-diazaazulene ring, which is a hydrazine-bridged [14]annulene, is available by the dehydrogenation of 43 obtained by Thorpe-Ziegler condensation of 2,2',5,5'-tetrakis(cyanomethyl)-1,1'-bipyrrole [Eq. 19].[41a]

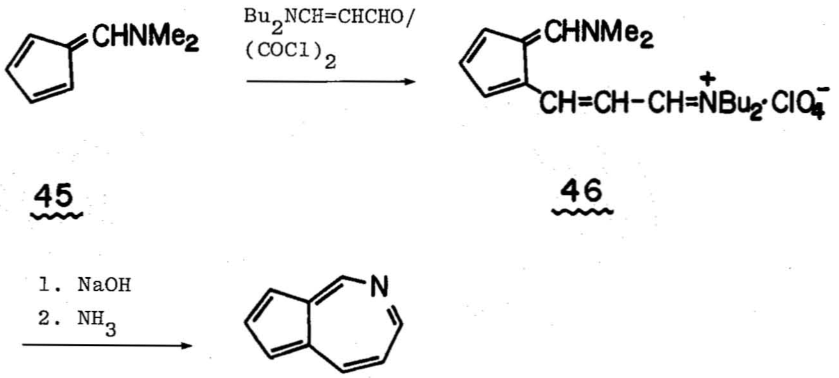


43

44

[19]

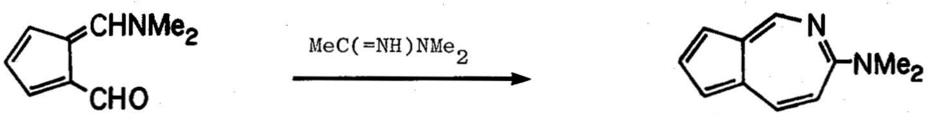
Intramolecular cyclisations of 6-(dimethylamino)fulvene derivatives provided the first syntheses of the azaazulenes possessing nitrogen atom(s) in the seven-membered ring. Thus, condensation of 6-(dimethylamino)fulvene (45) with N,N-dibutylaminopropenal in the presence of oxalyl chloride afforded the salt (46) from which cyclopent[c]azepine (5-azaazulene) (47) was formed as outlined in Eq. 20.[42] Similar approaches from 6-(dimethylamino)fulvene-2-carboxaldehyde (48) and N^1,N^1-dimethylaminoacetamidine or 1,1-dimethylguanidine furnished 3-dimethylaminocyclopent[c]azepine (49) and 3-dimethylaminocyclopenta[e][1,3]diazepine (5,7-diazaazulene derivative) (50), respectively [Eqs. 21 and 22].[1b,10] Likewise, cyclopent[d]azepines (6-azaazulene derivatives) (52) and (53) were accessible from the fulvene (51) as illustrated in Eq. 23.[10]



45 46

47

[20]



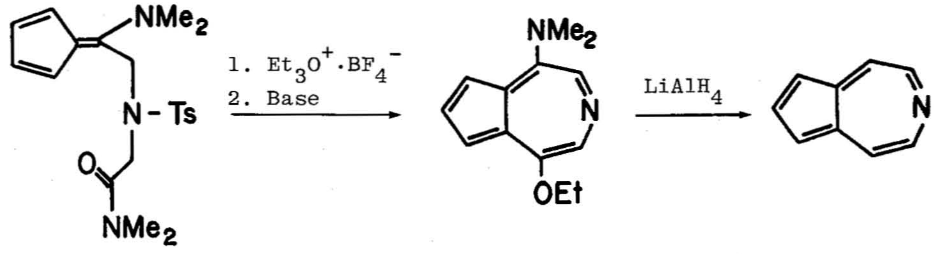
48 49

[21]

48

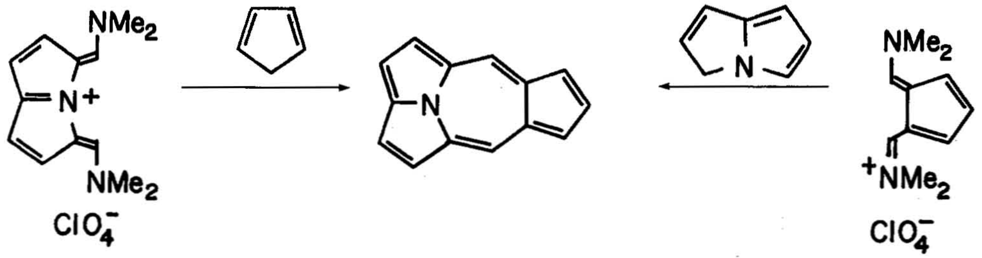
[22]

50



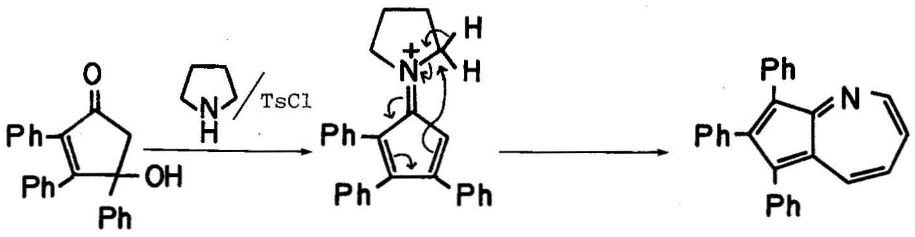
51 52 53 [23]

Cyclopent[4,5]azepino[2,1,7-cd]pyrrolizine (56)[43a] and its 2-chloro derivative[43b] were prepared utilising the condensation of cyclopentadiene with 54, or, alternatively, the reaction of the fulvene (55) with 3H-pyrrolizine [Eq. 24].



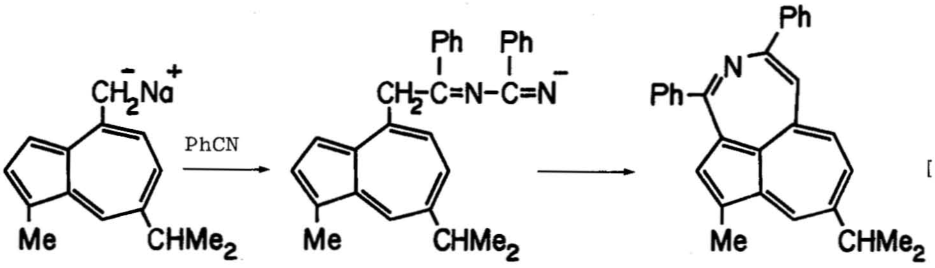
54 56 55 [24]

6,7,8-Triphenylcyclopent[b]azepine (58) appears to be the only 4-azaazulene so far prepared, which results from treatment of 4-hydroxy-2,3,4-triphenyl-2-cyclopenten-1-one with pyrrolidine; an intramolecular cyclisation of an enamine (57) and then an acid-catalysed ring enlargement of the cyclised product appear to be involved [Eq. 25].[44]



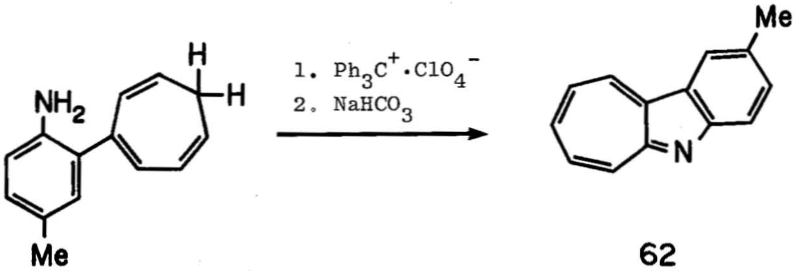
57 58 [25]

There are more examples where an azaazulene ring is made up utilising intramolecular cyclisations. The azuleno[1,8-cd]azepine (61) was synthesised by the reaction of the sodium salt of guaiazulene (59) with benzonitrile, an intramolecular cyclisation of the imine salt (60) being involved [Eq. 26].[45] Cyclohept[b]-indole (62),[46a] cyclohept[d]azuleno[6,5-b]pyrrole (63),[46b] cyclohept[d]azuleno-[5,6-b]pyrrole (64),[46b] and 2-hydroxy-3H-dicyclohepta[b,d]pyrrol-3-one,[46c] all of which are condensed 1-azaazulenes, have been prepared by the method shown in Eq. 27 or by use of a strategy closely similar to it.



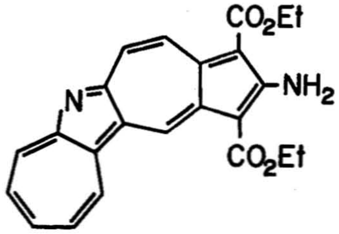
[26]

59 60 61

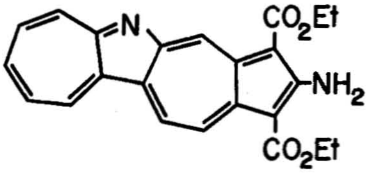


[27]

62



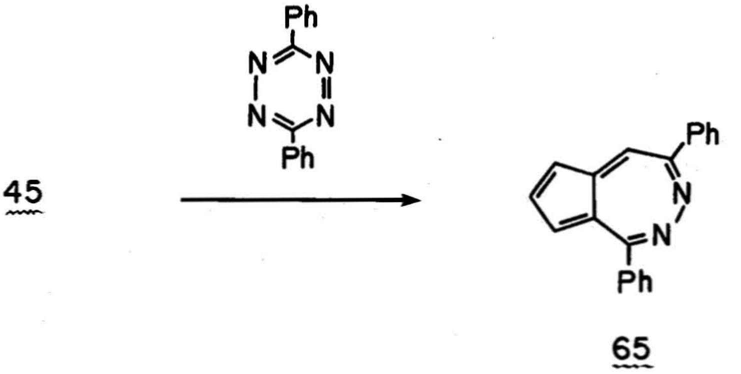
63



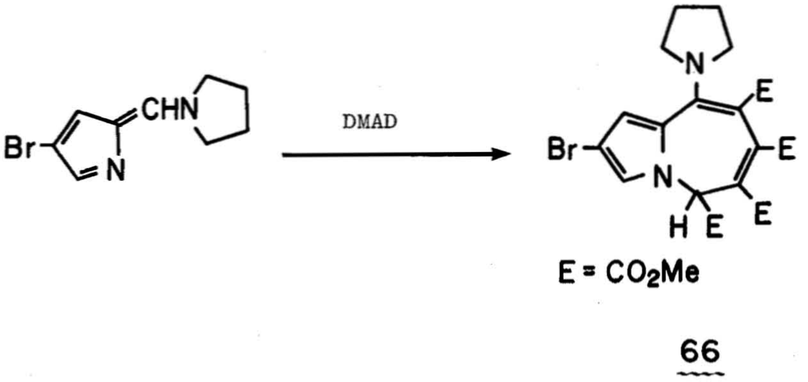
64

E. Syntheses Utilising Cycloadditions

Cycloadditions of fulvenes or pentalenes provide a useful synthetic route to azaazulenes. Thus, 1,4-diphenylcyclopenta[d][1,2]diazepine (5,6-diazaazulene derivative) (65) was obtained from a [6 + 4] cycloadduct of 45 and 3,6-diphenyl-1,2,4,5-tetrazine followed by elimination of nitrogen and dimethylamine, as shown in Eq. 28,[47] whereas the 5H-pyrrolo[1,2-a]azepine (3a-azaazulene derivative) (66) was derived by the addition of the 2-pyrrolydinylmethylenepyrrolylidene and dimethyl acetylenedicarboxylate (DMAD) as outlined in Eq. 29.[48] o-Benzoquinone-diimines also react with fulvene to afford a [6 + 4] cycloadduct possessing the cyclopenta[b][1,5]benzodiazepine structure.[49]

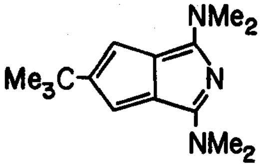


[28]

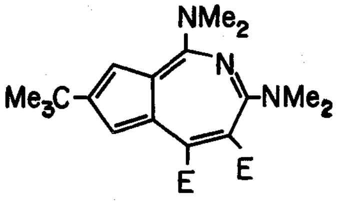


[29]

Whilst 1,3-bis(dimethylamino)cyclopenta[c]pyrrole (2-azapentalene derivative) gave only a C(5)-substituted product upon reaction with DMAD, a similar treatment of the cyclopenta[c]pyrrole (67) having a bulky substituent at C-5 was found to afford the cyclopent[c]azepine (68).[50] This reaction also involves a sequence of cycloaddition and ring enlargement of an adduct and is interesting because this provides an alternative route to simple 5-azaazulenes (see Ref. 10). It has been proposed that the reaction product of 8-methyl-5,7-dehydro-5H,7H-indazolo[1,2-a]-benzotriazole with DMAD has the triazaazulene structure (69), for which further confirmations will be required.[51] The reaction of 3H-pyrrolizine with DMAD gave a 1:2 adduct, for which the azepino[2,1,7-cd]pyrrolizine structure (70) has been assigned.[52] The compound (70) is a simple cycl[4,2,2]azine derivative and incorporates a 3a-azaazulene ring.

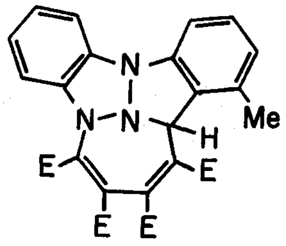


67



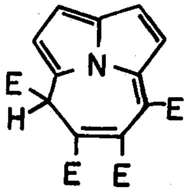
E = CO_2Me

68



E = CO_2Me

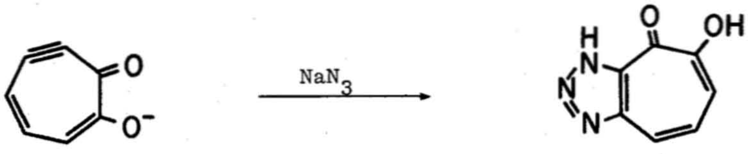
69



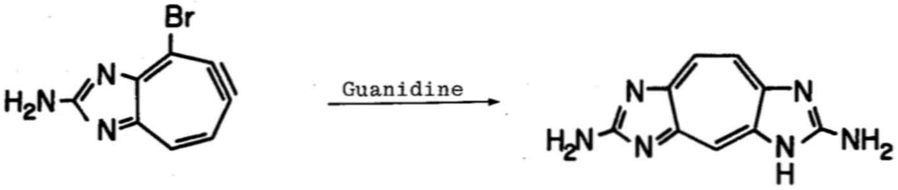
E = CO_2Me

70

Cycloaddition of 6,7-dehydrotropolone (71) with azide to form 5-hydroxy-4(3H)-cycloheptatriazolone (72) [Eq. 30][53] opened a simple synthetic route to C-demethylated parazoanthoxanthin (74) from 2-amino-4-bromo-5,6-dehydrocyclohept-imidazole (73) and guanidine [Eq. 31].[54] Its preparative value is obvious from comparison with the strategy adopted for the syntheses of natural zoanthoxanthins by Büchi, et al.[55]

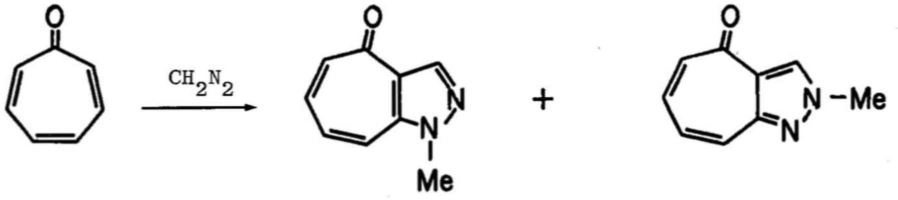


71 72 [30]

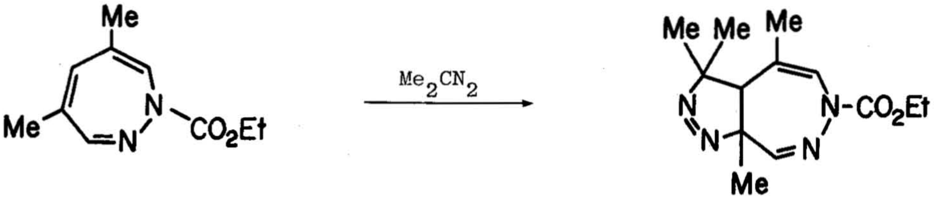


73 74 [31]

3,5,7-Tribromo-2-methoxy-[56] and 2-chloro-5-hydroxy-tropones[57] afforded halogen-substituted 1-methyl-8(1H)-cycloheptapyrazolones upon treatment with diazomethane, whereas tropone (75) gave 1-methyl-4(1H)- (76) and 2-methyl-4(2H)-cycloheptapyrazolones (77) in the ratio of *ca.* 3:1 [Eq. 32].[58] Orientation of the cycloaddition is the reverse of that of diazomethane to simple α,β-unsaturated ketones in the latter reaction. Difference in the regiochemistry of these two pericyclic reactions is very interesting. A [4 + 2] cycloadduct of 75 with diphenylnitrilimine was reported to be 6,7-dihydro-1,3-diphenylcycloheptapyrazol-8(1H)-one.[59] The reaction of the 1H-1,2-diazepine (78) with diazopropane was studied and the structure of 3,3a,6,8a-tetrahydropyrazolo[3,4-d][1,2]diazepine (1,2,6,7-tetraazaazulene derivative) (79) was assigned to the product [Eq. 33].[60] However, if there is no substituent at C-4 of the diazepine, a primary [4 + 2] cycloadduct tends to rearrange to a more conjugated isomer. Some 3,3-dialkyl-4(3H)-cycloheptapyrazolones are accessible from the pericyclic reactions of 7H-benzocyclohepten-7-one[61a] or the iron tricarbonyl complex of tropone,[61b] with diazoalkane.



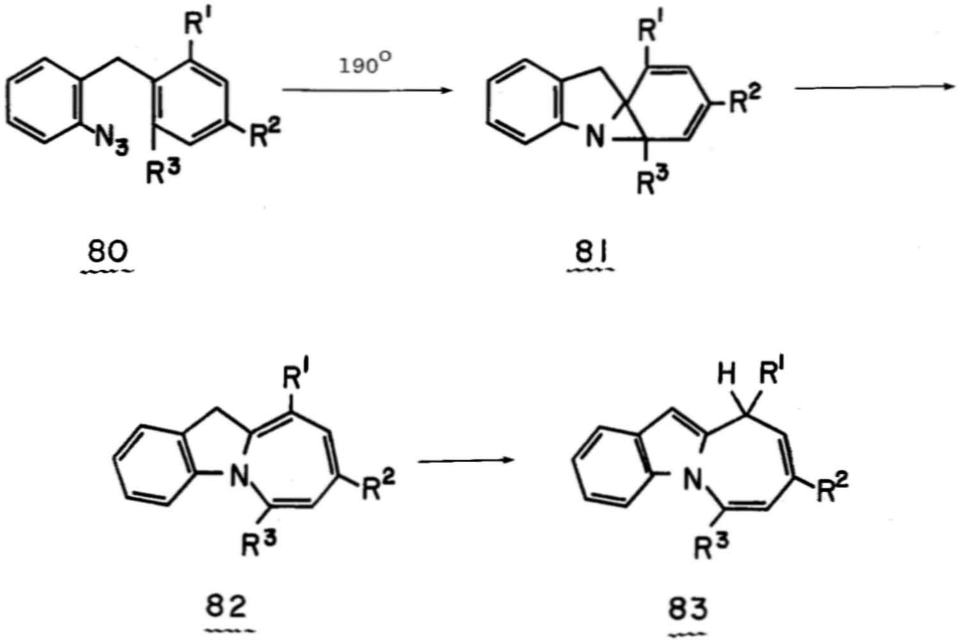
75 76 77 [32]



78 79 [33]

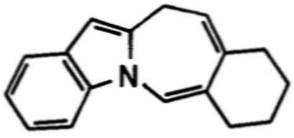
F. Syntheses *via* a Nitrene Intermediate

A thermolysis product of *o*-benzylphenyl azide (80; $R^1=R^2=R^3=H$), originally assigned as 11H-azepino[1,2-a]indole (82; $R^1=R^2=R^3=H$),[62] was corrected as its 10H-isomer (83; $R^1=R^2=R^3=H$),[63a] and the scope of the reaction was subsequently expanded.[63b-d] This reaction obviously proceeds through a nitrene intermediate [Eq. 34], but yields of 83 are generally unsatisfactory (the only exception is 8,9,10,12-tetrahydro-7H-indolo[1,2-b][2]benzazepine (84) obtained in good yield by the decomposition of 6-(2-azidobenzyl)-1,2,3,4-tetrahydronaphthalene).[63c] Not only 8H- and 6H-isomers are formed as a consequence of 1,5- and 1,7-hydrogen migrations from 82, but also substantial amounts of acridan and acridine derivatives are produced through an alternative ring-opening of an azanorcaradiene intermediate (81). The latter trend is especially remarkable for the decompositions of 2'-methoxybenzylphenyl azides[63b] and *o*-azidotriphenylmethanes,[63d] for which further clarifications will be required.



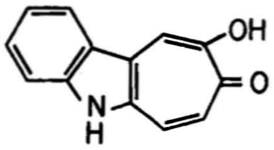
80 81 82 83

[34]

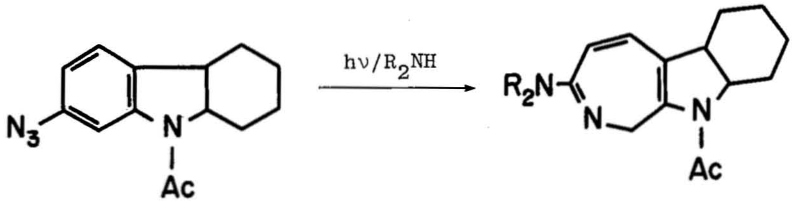


84

Thermal decomposition of 5-azido-4-phenyltropolone yielded 9-hydroxycyclohept[b]indol-8(5H)-one (85) in a moderate yield.[64] Ring-expansion of azido-indoles does not generally take place presumably because ring-expansion of an aziridine intermediate must occur with loss of aromaticity of an annelated pyrrole ring, but 9-acetyl-7-azido-1,2,3,4,4a,9a-hexahydrocarbazole (86) was found to be transformed into 5b,6,7,8,9,9a-hexahydroazepino[3,4-b]indole (87) under photolytic conditions [Eq. 35].[65]



85

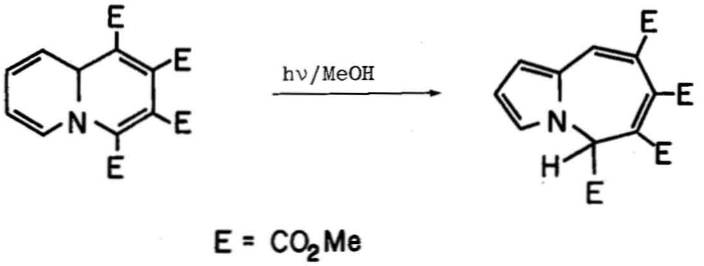


[35]

86 **87**

G. Miscellaneous Syntheses

Photo-induced valence-bond isomerisations of appropriate heterocycles may be exploited for the preparations of azaazulenes, but studies so far published suggest the reactions to be of only theoretical interest. Thus, a low yield transformation of the 9a-quinolizine (**88**) into the pyrrolo[1,2-a]azepine (**89**) was reported [Eq. 36],[66] whereas azaazulanones were detected among the photo-products of acridine 10-oxide,[67a] its 2,7-dimethyl,[67b] and 9-cyano derivatives,[67c] and benzo[a]phenazine 12-oxide.[67d] Photolysis of acridine 10-oxide with a visible light in the presence of alumina dyed with eosin afforded a low yield of cyclohept[b]indol-10(5H)-one (**28**).[68]



[36]

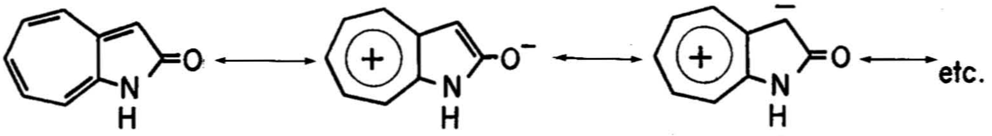
88 **89**

II. Chemical Properties of Azaazulenes

Chemical properties of relatively limited kinds of azaazulenes have been scrutinised so far in a somewhat unsystematic way. They include 1-aza-, 1,3-diaza-, 3a-aza-, 5-aza-, 5,7-diaza-, and their oxo-derivatives. Unfortunately and somewhat surprisingly, the kinetic aspect of their reactions appear to have been neglected, in comparison with the corresponding chemistry of pyridine and its related heterocycles. Difficulties attending the syntheses may be one of the reasons behind these situations.

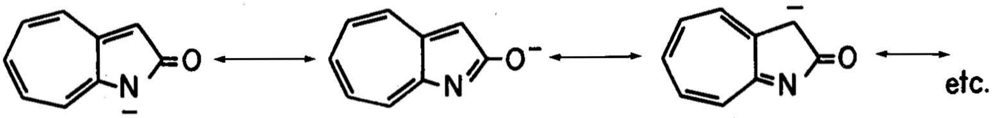
A. Reactions of Azaazulanones

Little is known on the tautomerism of azaazulanones with the exception of cyclohepta[b]pyrrol-2(1H)-one (**3**) which appears to exist predominantly as the oxo-form.[1] The same situation probably obtains in most cases, and it therefore seems appropriate to write all azaazulanones in this form. As inferred from its resonance formulas [Eq. 37], **3** would be predicted to be attacked at the seven-membered ring by nucleophiles and at C-3 by electrophiles. Furthermore, its anion (**90**) would be attacked at C- 3, N, and O-atoms by electrophiles [Eq. 38]. These predictions are in agreement with the experimental results so far published.



[37]

3 **3a** **3b**



[38]

90 **90a** **90b**

A-1. Reactions with Nucleophiles

6-Chloro derivative of 3, though inert towards potassium hydroxide, sodium methoxide, ammonia, sodium cyanide, and *p*-toluidine, was found to undergo a nucleophilic displacement at C-6 with sodium *p*-toluenethiolate.[69] A C-6 substitution also results from the reaction of cycloheptimidazol-2(1H)-one with morpholine in the presence of copper(II) acetate.[70]

A-2. Reactions with Electrophiles

High reactivity of the 3-position of cyclohepta[b]pyrrol-2(1H)-ones is evident from Vilsmeier-Haack[71a] and Mannich reactions[72] of 3, the bromination, nitration, and diazo-coupling of its 6-chloro-derivative,[69] and the displacement of 3-(cycloheptatrien-7-yl)cyclohepta[b]pyrrol-2(1H)-one with bromine to yield a 3-bromo derivative of 3.[71b]

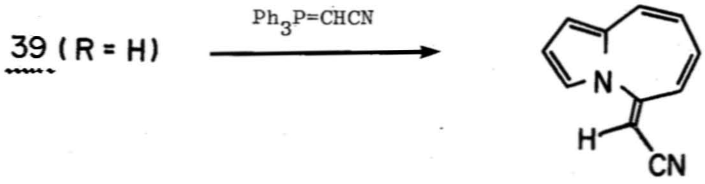
In common with other potentially tautomeric hydroxy-substituted nitrogenous heterocycles, acetylation and alkylation take place at either of the nitrogen or oxygen atoms of azaazulanones. Thus, exclusive N-acetylation was reported for a number of 6-chloro and 6-bromo derivatives of 3,[69] but orientation of alkylations appears to be directed by the nature of the reagent used. Whilst exclusive N-alkylation with alkyl halide was recorded for the anions derived from 3 and its 3-substituted derivatives[73] and cycloheptimidazol-2(1H)-one,[74] the reactions of 3 with diazomethane or dimethyl sulfate led to both N- and O-alkylations,[1] and the reaction of the sodio-salt of 3 with benzyl chloride gave C(3)- as well as N-benzyl derivatives.[74]

Formylation at C-3 resulted from Vilsmeier-Haack reaction of 7-alkyl-5H-pyrrolo[1,2-a]azepin-5-one (39).[75]

A-3. Reactivity of the Carbonyl Group of Azaazulanones

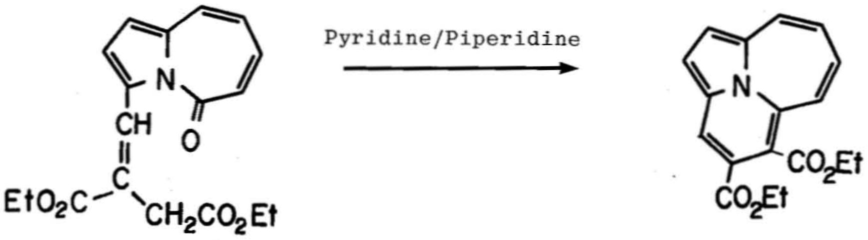
Wittig reaction of 39 yielded 91 [Eq. 39].[75a] The pyrrolo[1,2-a]azepinone possessing an appropriate substituent at C-3 (*e.g.* 92) undergoes an intramolecular cyclisation to produce the azepino[2,1,7-cd]indolidine (cycl[4,3,2]azine derivative) (93) [Eq. 40].[41,75]

Condensation of the cyclohepta[c]pyrrol-6-one (94) with 4,5-dichlorocyclopentene-1,3-dione produced 95 [Eq. 41][76] and a related reaction of the thioxo derivative (96) with diphenyl diazomethane gave 97 [Eq. 42].[77]



91

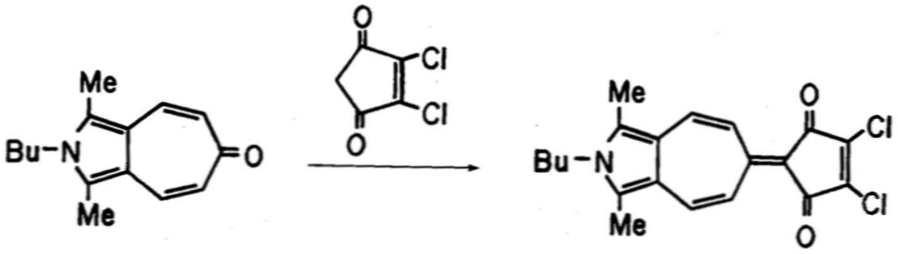
[39]



92

93

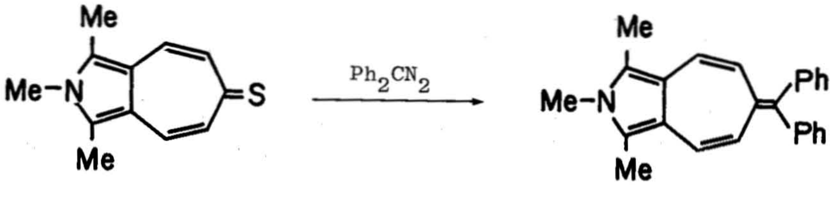
[40]



94

95

[41]



96

97

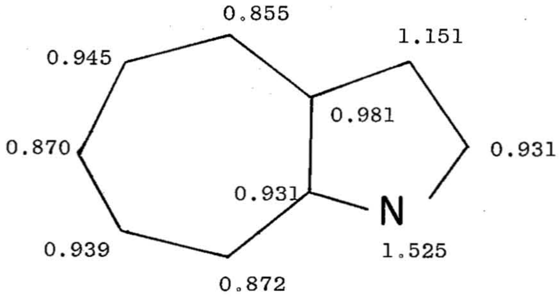
[42]

The 8(1H)-cycloheptapyrazolones are unreactive towards methylhydrazine.[34b] In passing, the hyrdazone of 3-methyl-8(1H)-cycloheptapyrazolone was prepared by a separate way[34a] and gave 3,4-dihydro-2,2a,4,5-tetraazabenzo[cd]azulenes upon reactions with aldehydes or ketones.[34a,78] A ring cleavage of azaazulanone by hydrazine was observed for 11-methylazepino[1,2-a]indol-10-one, from which 3-methyl-2-(Δ^2-pyrazolinyl)acetyl-3-methylindole was obtained.[63a]

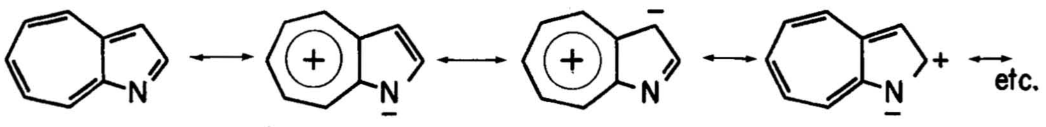
Reduction, with hydrides ($NaBH_4$ and $LiAlH_4$), of 11-methylazepino[1,2-a]indol-10-one and of the iron tricarbonyl complex derived from it has revealed that reduction of the seven-membered ring takes place as well as reduction of the carbonyl group,[63a] but the tribromopyrrolo[1,2-a]azepinone (21) led to simultaneous reduction of the seven-membered ring and removal of the bromine atoms without the reduction of the carbonyl group.[19a] However, the carbonyl group at C-6 of cyclohepta[c]pyrrole was reduced with $LiAlH_4$ to the corresponding carbinol.[26a]

B. Chemical Reactivities of Azaazulenes

The π-electron density diagram[2a,c] and resonance formulas [Eq. 43] suggest that 1-azaazulenes are susceptible to electrophilic attack at nitrogen and C-3 and to nucleophilic attack at C-2 and the seven-membered ring carbons (particularly at C-6 and C-8).



π-Electron Density of Cyclohepta[b]pyrrole (5) Calculated by H. Kon[2a]



5, 5a 5b 5c

[43]

B-1. Reactions with Electrophiles

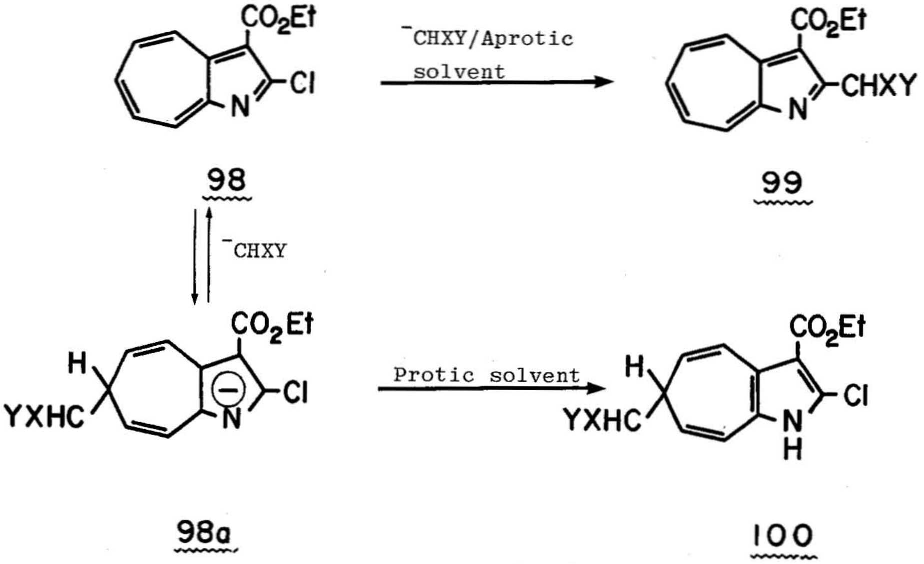
Nitration and diazo-coupling readily take place at C-3 of **5** if there is an electron-donating substituent at C-2.[1] If the position 2 is occupied with an electron-attracting group, bromination is the only reaction to occur at C-3.[69] Quarternisations of 2-chloro- and 2-methoxy-derivatives of **5** was achieved using dimethyl sulfate, but not with methyl iodide.[73] Chemical reactivities of other azaazulenes including cyclazines have not been studied in detail with the only exception of **70** reported to undergo electrophilic substitutions (deuteriation, nitration, nitrosation, acylation, bromination, and Mannich reaction) at C-6 and C-8.[43a]

B-2. Reactions with Nucleophiles

In common with other aromatic systems, halogen or a carboxymethylthio group can be displaced from azaazulenes by a nucleophile. Examples include displacement of halogen at C-2 by OR, NR_2, and SR in derivatives of **5**,[1] of halogen at C-6 by NR_2 in derivatives of benzo[5,6]cyclohept[1,2-b]indole,[23] and of SCH_2CO_2H at C-2 by $NHNH_2$ in derivatives of **8**.[80] For 2,6-[69] and 2,8-dihalo-derivatives[79] of **5** and 2,6-dihalo-,[81,82] 6-bromo-2-ethoxy-,[17a] and 2-ethoxy-6-nitro-derivatives[17a] of **8**, the substituent on the seven-membered ring is preferentially displaced by a nucleophile.

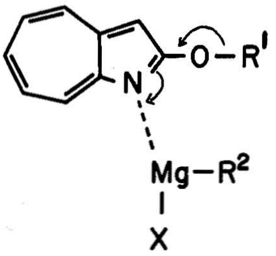
The reaction of 2-chlorocyclohepta[b]pyrrole (**98**) with the carbanion derived from active methylene compounds proceeds competitively to give either **99** or **100**.[83,84] Formations of **99** and **100** highly depend on reaction conditions (*inter alia*, the polarity of the solvent); **99** is preferentially formed in dioxane and **100** in ethanol.[84] It is conceivable that there is established an equilibrium between **98** and an anion (**98a**) and **100** is formed by protonation of **98a**, rapidly in a protic solvent, or more slowly in an aprotic solvent [Eq. 44].

For the reactions presumed to involve the coordination of a reagent with the ring nitrogen atom, nucleophilic attack at C-8 appears to be preferred. Thus, **98** reacts with Grignard reagents at C-4, C-6, and C-8, their reactivities being in the order of C-8 ≫ C-4 > C-6,[85a] and an increased formation of the C-6-alkylation product was observed if a bulky reagent was employed.[85b] Approach of a bulky reagent to the ring nitrogen must be less favourable. A similar trend has been observed for the reactions of **8** with Grignard reagents; phenylmagnesium bromide attacks C-4, whereas *t*-butylmagnesium bromide attacks C-6 more readily.[86] Fur-

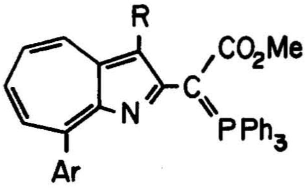


[44]

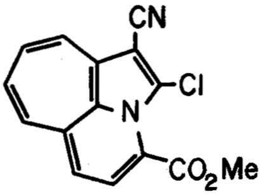
thermore, despite an efficient formation of 2-alkylazulenes from the reaction of 2-alkoxyazulenes with Grignard reagents,[87] 2-alkoxycyclohepta[b]pyrroles were found to change into cyclohepta[b]pyrrol-2(1H)-ones quantitatively.[88] Obviously, cleavage of an O-Alkyl bond must be assisted by the coordination of the reagent to the ring nitrogen atom, as shown below. When aryllithium was allowed to react with 6-bromo-2-ethoxycycloheptimidazole, exclusive formation of the corresponding 4-aryl derivative was noted.[17a]



Only a ylide (101) was produced from the transylidation of 8-aryl-2-chlorocyclohepta[b]pyrroles and methyl (triphenylphosphoranylidene)acetate, but the reaction of 2-chlorocyclohepta[b]pyrrole-3-carbonitrile produced low yields of its 8-methyl derivative and the cyclohept[hi]indolizine (102), besides a transylidation product.[89]



101

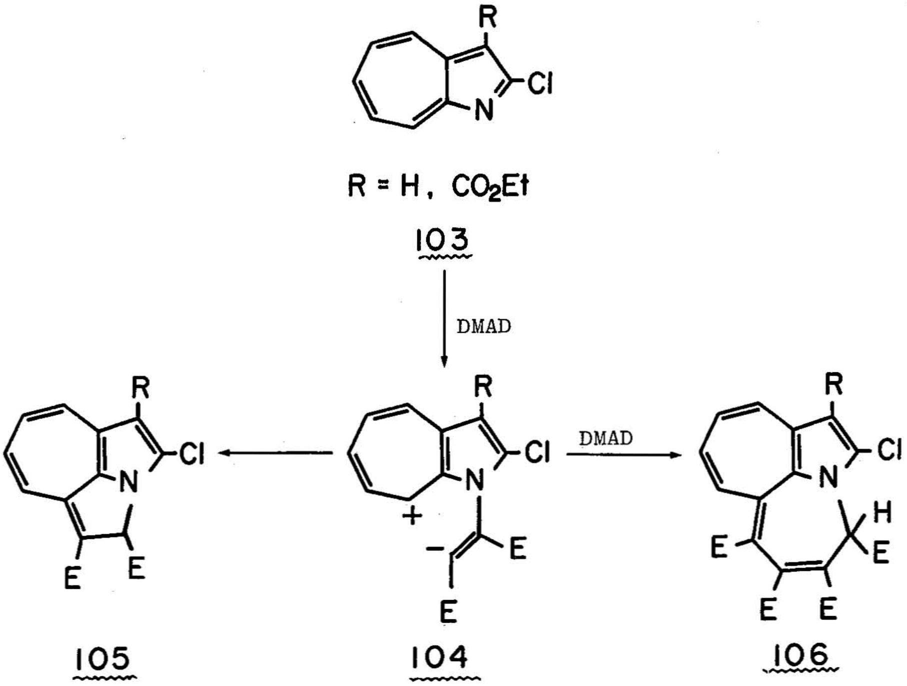


102

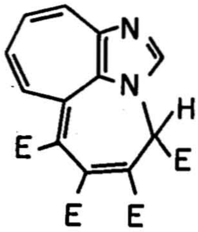
B-3. Cycloadditions

Cycloadditions of azaazulenes, first and independently studied by us and Hafner, are now providing novel features to the reaction of nitrogenous heterocycles with acetylenic esters.[90]

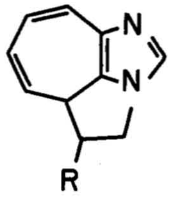
The reaction of the cyclohepta[b]pyrroles (103) with DMAD afforded the 2H-cyclohepta[gh]pyrrolizines (105) and the 3H-2a-azacyclopenta[ef]heptalenes (106), whereas that of 8 with DMAD proceeded rapidly to yield the 3H-1,2a-diazacyclopenta[ef]heptalene (107).[91] These pericyclic reactions are postulated to proceed through a dipolar intermediate [*e.g.* 104 in Eq. 45], and the regiochemistry was recently confirmed by the reactions of 8 with electron-deficient olefins to give 108.[92]



[45]



107

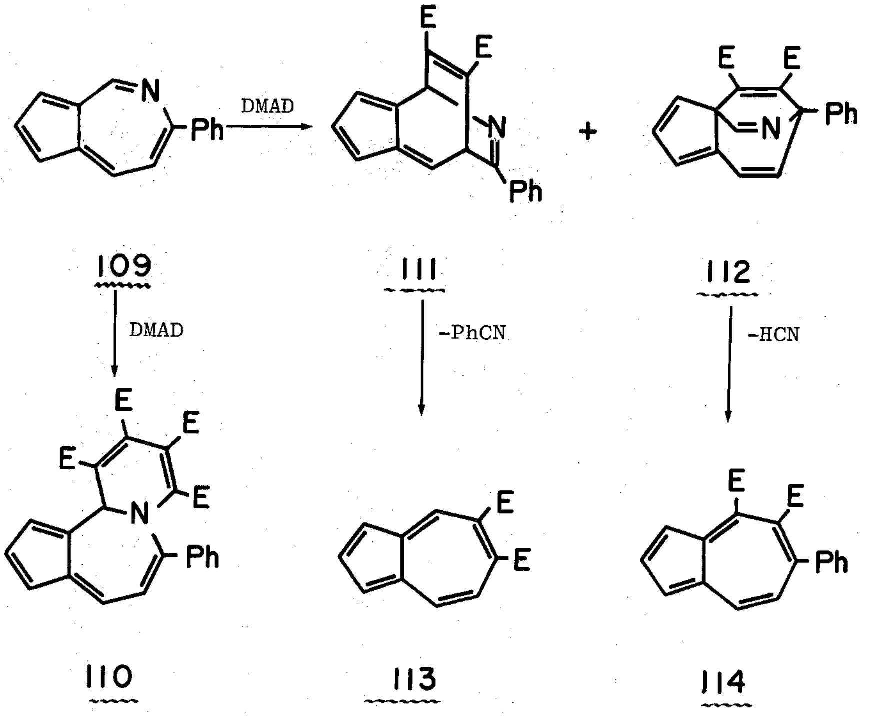


R = CN, CO_2Et

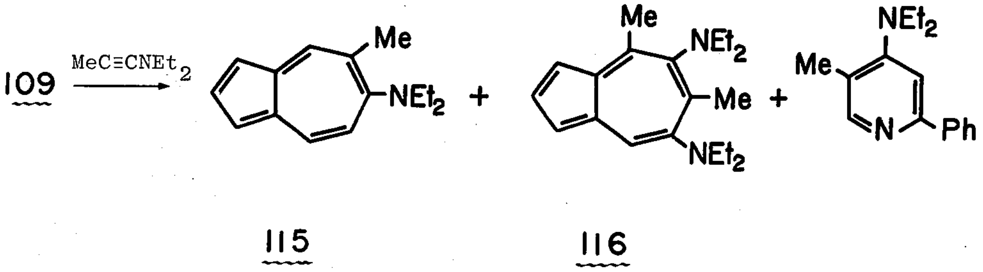
108

Periselectivity dependent on temperature was observed for the addition of cyclopent[c]azepine (109) with DMAD. Whereas the 2H-cyclopenta[c]pyrido[1,2-a]-azepine (110) was produced at 80°, two kinds of carbocyclic azulenes (113) and (114) were obtained at 160°; they must have formed by loss of a nitrile from primary adducts (111) and (112) [Eq. 46].[93,94] An intermediate like 111 was in fact isolated by heating 109 with cyclooctyne at 170° for 15 sec. and found to decompose by heating at 250° for 3 sec. into 5,6,7,8,9,10-hexahydrocyclooct[f]-azulene and 3-phenyl-5,6,7,8,9,10-hexahydrocycloocta[c]pyridine. Likewise, the azaazulenes 109 and 50 reacted with a ynamine (N,N-diethylamino-1-propyne).[10] Two aminoazulenes (115) and (116) and 4-N,N-diethylamino-5-methyl-2-phenylpyridine were obtained from 109 [Eq. 47], whereas a cycloadduct (117), the aminoazulene (116), and 4-N,N-diethylamino-2-N,N-dimethylamino-5-methylpyrimidine were formed from 50 [Eq. 48]. A satisfactory rationalisation for the formation of 116 from 109 or 50 has not yet be advanced.

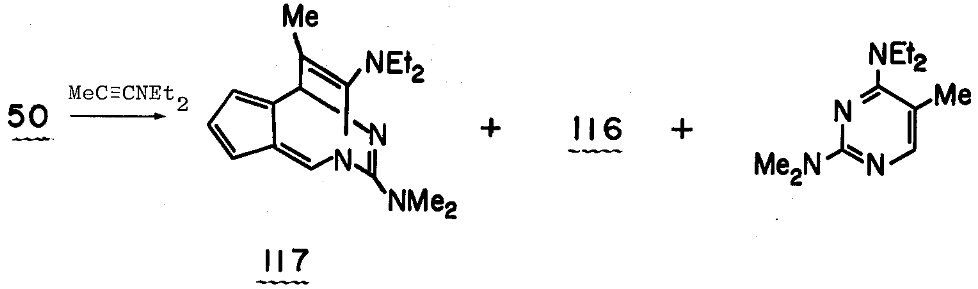
8-E-Styrylcyclohepta[b]pyrrole (118) reacted stereospecifically with DMAD giving trans-7H-6a-azacyclobuta[j]cyclopent[cd]azulene (119). This reaction is accounted for in terms of a symmetry-allowed thermal $[_{\pi}2_{s} + {}_{\pi}2_{a} + {}_{\pi}6_{a}]$ cyclo-addition as shown in 124.[95] A number of polycyclic heterocycles came to light from the ensuing reactions of 119. Thus, thermal rearrangements gave the 3H-2a-azacyclopent[cd]azulene (120), the 3H-2a-azadicyclopenta[ef,kl]heptalene (121), the 3H-2a-azadicyclopent[cd,ij]azulene (122), and an oxidation of the last is responsible for the formation of the 2aH-7,10b-methano-2a-azacyclopenta[ab]cycloundecene (123). A thermal rearrangement of 119 to 120 involves a rapid stereospecific cyclisation of the anion derived by the scission of the bond between nitrogen and benzylic-carbon atoms of 119 as depicted in Eq. 49.


109
DMAD
111
112
DMAD
-PhCN
-HCN
110
113
114
E
N
Ph

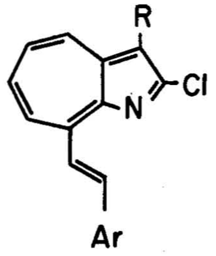
[46]


109
MeC≡CNEt2
Me
NEt2
115
116

[47]

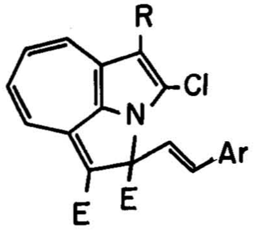

50
MeC≡CNEt2
Me
NEt2
N
NMe2
117
116
Me2N

[48]

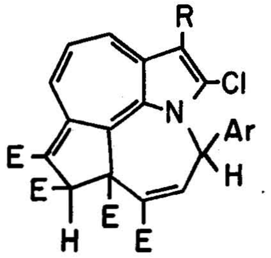


118

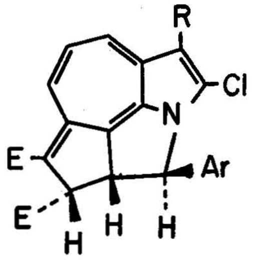
119



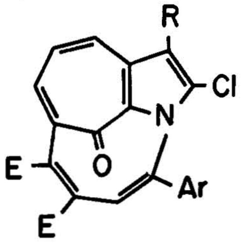
120



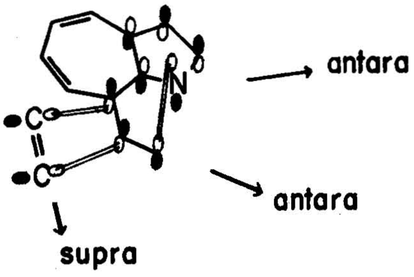
121



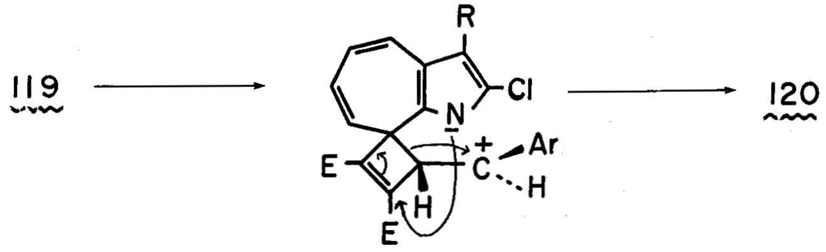
122



123

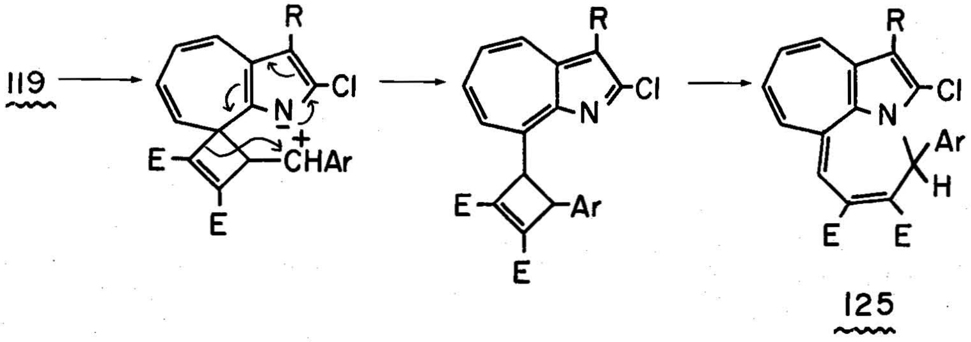


124



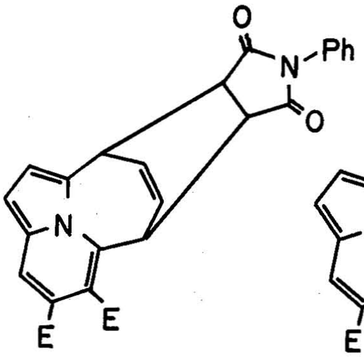
[49]

Noteworthy is the silica gel induced isomerisation[96] of 119 into the 3H-2a-azacyclopenta[ef]heptalene (125), as rationalised in Eq. 50.[97]

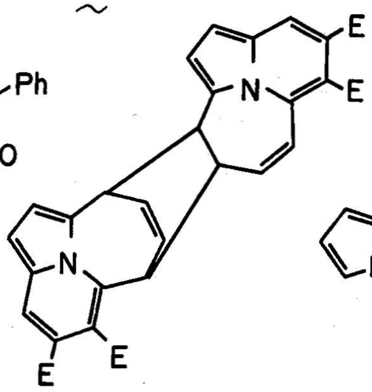


[50]

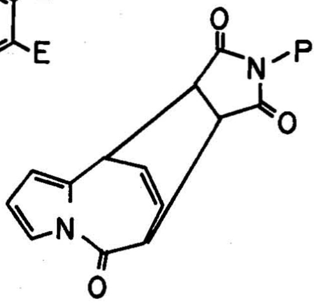
Cycloadditions of cyclazines and of azaazulanones are known. The cycl[4,3,2]-azine (93) gave [4 + 2] cycloadducts (126) and (127) upon reaction with N-phenylmaleinimide or on self-dimerisation, and the reaction of the 3a-azaazulanone (39) with N-phenylmaleinimide afforded 128.[75b]



126



127



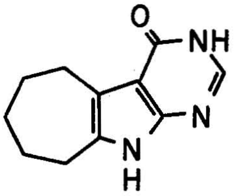
128

B-4. Miscellaneous

Methods, other than cycloadditions, to annelate rings to an azaazulene are being sought. The 2H-2a-azacylopent[cd]azulene (129) was produced by the reaction of 8-methoxy-derivative of 5 with malononitrile,[99] and the azepino[7,1,2-cd]indolizine (130)[75b] and an azepino[2,1,7-cd]pyrrolizinium salt[43b] were accessible from the reaction of 91 with oxalyl chloride or under Vilsmeier conditions. An attempt to synthesize cyclohepta[2,3]pyrrolo[5,4-d]pyrimidine from the reaction of ethyl 2-aminocyclohepta[b]pyrrole-3-carboxylic acid with an excess of formamide resulted in the unexpected reduction of the seven-membered ring to yield 131.[99]

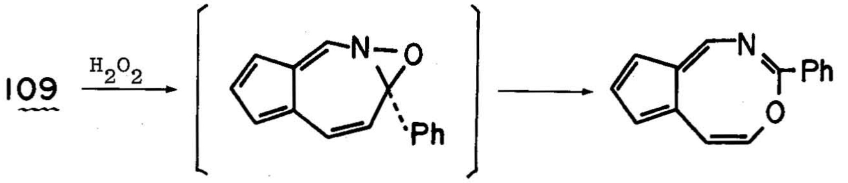
129

130



131

Ring transformation of the cyclopent[c]azepine (109) was reported, which gave a fair yield of the cyclopent[e][1,3]oxazocine (133) via an oxaziridine intermediate (132) upon treatment with hydrogen peroxide [Eq. 51].[100]



132 133 [51]

REFERENCES

1. T. Nozoe and K. Kikuchi, 'Dai Yuki Kagaku' eds. by M. Kotake, Asakura Shoten, Tokyo, 1960, vol. XIII, p. 535.
2. (a) H. Kon, *Sci. Repts. Tohoku Univ.*, Ser. I, 1954, **38**, 67; (b) U. Müller-Westerhoff and K. Hafner, *Tetrahedron Letters*, 1967, 4341; (c) R. Zahrdnik, 'Nonbenzenoid Aromatics' eds. by J. P. Snyder, Academic Press, New York, 1971, vol. II, p. 1; (d) B. A. Hess, Jr., L. J. Schaad, and C. W. Holyoke, Jr., *Tetrahedron*, 1975, **31**, 295.
3. (a) L. J. Mathias and C. G. Overberger, *J. Org. Chem.*, 1978, **43**, 3518; (b) L. J. Mathias and C. G. Overberger, *ibid.*, 1978, **43**, 3526; (c) H. Hiratsuka, Y. Tanizaki, and T. Hoshi, *Bull. Chem. Soc. Japan*, 1977, **50**, 1282.
4. L. Cariello, S. Crescenzi, G. Prota, F. Giordano, and L. Mazzarella, *J.C.S. Chem. Comm.*, 1973, 99; L. Cariello, S. Crescenzi, G. Prota, S. Capasso, F. Giordano, and L. Mazzarella, *Tetrahedron*, 1974, **30**, 3281; L. Cariello, S. Crescenzi, G. Prota, and L. Zanetti, *ibid.*, 1974, **30**, 3611; *Experientia*, 1974, **30**, 849.
5. (a) H. Nakamura, G. Koyama, Y. Iitaka, M. Ohno, N. Yagisawa, S. Kondo, K. Maeda, and H. Umezawa, *J. Amer. Chem. Soc.*, 1974, **96**, 4327; (b) P. W. K. Woo, H. W. Dion, S. M. Lange, L. F. Dahl, and L. J. Durham, *J. Heterocyclic Chem.*, 1974, **11**, 641.
6. The Merck Index, 9th Edn., 1976, NO. 3623.
7. K. Takase, *J. Synthetic Org. Chem. Japan*, 1968, **26**, 807.
8. T. Asao and Y. Kitahara, *Kagaku No Ryoiki, Zokan*, 1971, **94**, 102.
9. F. Pietra, *Chem. Rev.*, 1973, **73**, 293.
10. K. Hafner, *Lecture Heterocyclic Chem.*, 1976, **3**, 33; *Chem. Abs.*, 1976, **85**, 123677p.
11. J. Nakazawa, Y. Sato, and N. Soma, *Ann. Report Sanky Res. Lab.*, 1969, **21**, 47.
12. S. Ryu and T. Toda, *Sci. Repts. Tohoku Univ.*, Ser. I, 1968, **51**, 105.
13. (a) R. Cabrino, B. Ricciarelli, and F. Pietra, *Tetrahedron Letters*, 1974, 3069; (b) F. D. Cima, M. Cavazza, C. A. Veracini, and F. Pietra, *ibid.*, 1975, 4267; (c) M. Cavazza, R. Carbino, F. D. Cima, and F. Pietra, *J.C.S. Perkin Trans. I*, 1978, 609.
14. G. Sunagawa and H. Nakao, *Chem. and Pharm. Bull. (Japan)*, 1965, **13**, 450.
15. K. Ogura, H. Sasaki, and S. Seto, *Bull. Chem. Soc. Japan*, 1965, **38**, 306.

16. Y. Sugimura, N. Soma, and Y. Kishida, *Bull. Chem. Soc. Japan*, 1972, **45**, 3174.

17. (a) G. Sunagawa and M. Watatani, *Chem. and Pharm. Bull. (Japan)*, 1968, **16**, 1308; (b) M. Watatani, N. Soma, and G. Sunagawa, *ibid.*, 1968, **16**, 1316; (c) M. Watatani, *ibid.*, 1968, **16**, 1503; (d) M. Watatani, *ibid.*, 1968, **16**, 1513.

18. W. Treibs, *Chimia (Switz.)*, 1972, **26**, 627.

19. (a) E. W. Collington and G. Jones, *J. Chem. Soc. (C)*, 1969, 1028; (b) E. W. Collington and G. Jones, *Tetrahedron Letters*, 1968, 1935.

20. K. Yamane and K. Fujimori, *Bull. Chem. Soc. Japan*, 1972, **45**, 269.

21. K. Fujimori and K. Yamane, *Bull. Chem. Soc. Japan*, 1974, **47**, 1951.

22. T. Nozoe, Je-Kyun Shin, K. Yamane, and K. Fujimori, *Bull. Chem. Soc. Japan*, 1975, **48**, 314.

23. K. Yamane and K. Fujimori, *Bull. Chem. Soc. Japan*, 1976, **49**, 1101.

24. K. Fujimori and K. Yamane, *Bull. Chem. Soc. Japan*, 1978, **51**, 3579.

25. M. Kimura, K. Satake, and S. Morosawa, *Chem. Letters*, 1979, 807.

26. (a) A. V. El'tsov, A. A. Ginesina, and L. N. Kivokurtseva, *Tetrahedron Letters*, 1968, 735; (b) J. Duflos, D. Letouzé, G. Queguiner, and P. Pastour, *Tetrahedron Letters*, 1973, 3453; (c) R. Kreher, G. Vogt, and M.-L. Schultz, *Angew. Chem. Internat. Edn.*, 1975, **14**, 821.

27. W. Schroth and W. Treibs, *Annalen*, 1961, **642**, 108.

28. (a) C. V. Greco and M. Pesce, J. Org. Chem., 1972, **37**, 676; (b) C. V. Greco, F. C. Pellegrini, and N. A. Pesce, *J.C.S. Perkin Trans.*, 1972, 1623.

29. H. W. Heine, D. W. Ludovici, J. A. Pardoen, R. C. Weber, II, E. Bonsall, and K. R. Osterhout, *J. Org. Chem.*, 1979, **44**, 3843.

30. C. L. Dickinson, W. J. Middleton, and V. A. Engelhardt, *J. Org. Chem.*, 1962, **27**, 2470.

31. C. A. Lovelette and L. Long, Jr., *J. Org. Chem.*, 1972, **37**, 4124.

32. M. M. Kochhar, *J. Heterocyclic Chem.*, 1972, **9**, 153; R.-M. Claramunt, J.-M. Fabrega, and J. Elguero, *J. Heterocyclic Chem.*, 1974, **11**, 751.

33. M. Laćan, I. Susnik-Rybarski, and Z. Stefanac, *Croat. Chem. Acta*, 1974, **46**, 57.

34. (a) A. Yamane, M. Nagayoshi, K. Imafuku, and H. Matsumura, *Bull. Chem. Soc. Japan*, 1979, **52**, 1972; (b) A. Yamane, K. Imafuku, and H. Matsumura, *ibid.*, 1980, **53**, 1461.

35. (a) S. Veibel and S. F. Hromadko, *Chem. Ber.*, 1960, **93**, 2752; (b) S. Veibel and J. I. Nielsen, *ibid.*, 1966, **99**, 2709.

36. E. J. Glamkowski and J. M. Fortunato, *J. Heterocyclic Chem.*, 1979, **16**, 865.

37. V. Scartoni, R. Fiaschi, S. Catalano, I. Morelli, and A. Marsilli, *J.C.S. Perkin Trans*. I, 1979, 1547.

38. (a) W. Flitsch, B. Müter, and U. Wolf, *Chem. Ber*., 1973, **106**, 1993; (b) W. Flitsch, F. Kappenberg, and H. Schmitt, *ibid*., 1978, **111**, 2407.

39. S. Rault, M. Cugnon de Sèvricourt, and M. Robba, *Heterocycles*, 1979, **12**, 1009.

40. (a) T. Nozoe, K. Takase, and K. Umino, *Bull. Chem. Soc. Japan*, 1965, **38**, 358; (b) T. Nozoe, K. Takase, and K. Suzuki, *ibid*., 1965, **38**, 362.

41. (a) W. Flitsch and H. Peeters, *Chem. Ber*., 1973, **106**, 1731; (b) W. Flitsch and H. Peeters, *Tetrahedron Letters*, 1975, 1461; (c) W. Flitsch and H. Peeters, *Chem. Ber*., 1977, **110**, 273.

42. K. Hafner and M. Kreuder, *Angew. Chem*., 1961, **73**, 657.

43. (a) M. A. Jessep and D. Lever, *J. Chem. Soc. Chem. Commun*., 1970, 790. (b) W. Flitsch and E. R. Gesing, *Tetrahedron Letters*, 1979, 3405.

44. M. K. Conner and E. LeGoff, *Tetrahedron Letters*, 1970, 2687.

45. L. L. Replogle, K. Katsumoto, T. C. Morrill, and C. A. Minor, *J. Org. Chem*., 1968, **33**, 823.

46. (a) K. Takase, T. Asao, and N. Hirata, *Bull. Chem. Soc. Japan*, 1968, **41**, 3027; (b) N. Hirata, K. Otomo, N. Iwagame, M. Yasunami, and K. Takase, Abstracts of Symposium on Nonbenzenoid Aromatic Compounds, 1972, p. 207; (c) N. Hirata, M. Yasunami, and K. Takase, *Tetrahedron Letters*, 1975, 1849.

47. T. Sasaki, K. Kanematsu, and T. Kataoka, *J. Org. Chem*., 1975, **40**, 1201.

48. P. E. Sonnet, J. L. Flippen, and R. D. Gilardi, *J. Heterocyclic Chem*., 1974, **11**, 811.

49. W. Friedrichsen and H.-G. Oeser, *Tetrahedron Letters*, 1974, 4373.

50. K. Hafner, H.-G. Klas, and M. C. Bohm, *Tetrahedron Letters*, 1980, **21**, 41.

51. O. Tsuge and H. Samura, *Tetrahedron Letters*, 1973, 597.

52. D. Johnson and G. Jones, *J.C.S. Perkin Trans I.*, 1972, 844.

53. T. Yamatani, M. Yasunami, and K. Takase, *Tetrahedron Letters*, 1970, 1725.

54. M. Yasunami, Y. Sasagawa, and K. Takase, *Chem. Letters*, 1980, 205.

55. M. Braum and G. Büchi, *J. Amer. Chem. Soc*., 1976, **98**, 3049; M. Braum, G. Büchi, and D. F. Bushey, *ibid*., 1978, **100**, 4208.

56. S. Itō, K. Takase, N. Kawabe, and H. Sugiyama, *Bull. Chem. Soc. Japan*, 1966, **39**, 253.

57. T. Nozoe, T. Asao, E. Takahashi, and K. Takahashi, *Bull. Chem. Soc. Japan*, 1966, **39**, 1310.

58. L. J. Luskus and K. N. Houk, *Tetrahedron Letters*, 1972, 1925.

59. K. N. Houk and C. R. Watts, *Tetrahedron Letters*, 1970, 4025.

60. G. Taurand and J. Streith, *Tetrahedron Letters*, 1972, 3575; G. Kiehl, J. Streith, and G. Taurand, *Tetrahedron*, 1974, **30**, 2851.

61. (a) M. F.-Neumann and D. Martina, *Tetrahedron Letters*, 1975, 1755; (b) M. F.-Neumann and D. Martina, *Tetrahedron Letters*, 1975, 1759.

62. L. Krbechek and H. Takimoto, *J. Org. Chem.*, 1968, **33**, 4286.

63. (a) G. R. Cliff, E. W. Collington, and G. Jones, *J. Chem. Soc. (C)*, 1970, 1490; (b) G. R. Cliff and G. Jones, *J. Chem. Soc. (C)*, 1971, 3418; (c) R. N. Carde and G. Jones, *J.C.S. Perkin Trans. I*, 1974, 2066; (d) R. N. Carde, G. Jones, W. H. McKinley, and C. Price, *J.C.S. Perkin Trans. I*, 1978, 1211.

64. T. Nozoe, H. Horino, and T. Toda, *Tetrahedron Letters*, 1967, 5349; T. Nozoe, H. Horino, and T. Toda, *Bull. Chem. Soc. Japan*, 1972, **45**, 226.

65. E. F. V. Scriven, H. Suschitzky, D. R. Thomas, and R. F. Newton, *J.C.S. Perkin Trans. I*, 1979, 53.

66. R. M. Acheson and J. K. Stubbs, *J. Chem. Soc. (C)*, 1969, 2316.

67. (a) M. Ishikawa, C. Kaneko, and S. Yamada, *Tetrahedron Letters*, 1968, 4519; (b) S. Yamada, M. Ishikawa, and C. Kaneko, *ibid.*, 1972, 971; (c) S. Yamada, M. Ishikawa, and C. Kaneko, *J.C.S. Chem. Comm.*, 1972, 1093; (d) C. Kaneko, S. Yamada, and M. Ishikawa, *Tetrahedron Letters*, 1970, 2329.

68. N. Hata, *Chem. Letters*, 1975, 401.

69. T. Toda, S. Seto, and T. Nozoe, *Bull. Chem. Soc. Japan*, 1968, **41**, 2102.

70. K. Kikuchi, Y. Maki, and N. Saito, *Bull. Chem. Soc. Japan*, 1978, **51**, 3087.

71. (a) T. Toda, *Bull. Chem. Soc. Japan*, 1967, **40**, 590; (b) T. Toda, S. Ryu, Y. Hagiwara, and T. Nozoe, *ibid.*, 1975, **48**, 82.

72. A. Sato, S. Nozoe, T. Toda, S. Seto, and T. Nozoe, *Bull. Chem. Soc. Japan*, 1973, **46**, 3530.

73. Chi-Rhi Wu and Paw-Wang Yang, *Hua, Hsueh*, 1977, 45; *Chem. Abs.*, 1980, **92**, 94177n.

74. H. Nakao, N. Soma, Y. Sato, and G. Sunagawa, *Chem. and Pharm. Bull. (Japan)*, 1965, **13**, 473.

75. (a) W. Flitch and B. Müter, *Angew. Chem. Internat. Edn.*, 1973, **12**, 501; (b) W. Flitch, A. Gurka, and B. Müter, *Chem. Ber.*, 1975, **108**, 2969;

(c) W. Flitch and E. Mukidjam, *ibid*., 1979, **112**, 3577.

76. G. Seitz, R. A. Olsen, and H. Monninghoff, *Arch. Pharm*., 1979, **312**, 120.

77. G. Seitz, R. A. Olsen, T. Kampchen, and R. Matusch, *Chem. Ber*., 1979, **112**, 2087.

78. K. Imafuku, M. Sumio, and H. Matsumura, *Synthesis*, 1980, 261.

79. K. Yamane, K. Fujimori, Je-Kyn Shin, and T. Nozoe, *Bull. Chem. Soc. Japan*, 1977, **50**, 1184.

80. I. Murata, *Bull. Chem. Soc. Japan*, 1960, **33**, 1367.

81. T. Nozoe, T. Mukai, and T. Asao, *Bull. Chem. Soc. Japan*, 1962, **35**, 1188.

82. G. Sunagawa and M. Watatani, *Chem. and Pharm. Bull. (Japan)*, 1968, **16**, 1300.

83. S. Matsumura, *Bull. Chem. Soc. Japan*, 1961, **34**, 1361; 1962, **35**, 677.

84. N. Abe and T. Nishiwaki, *Bull. Chem. Soc. Japan*, 1978, **51**, 667.

85. (a) N. Abe, *Heterocycles*, 1976, **4**, 221; (b) N. Abe and T. Nishiwaki, unpublished work.

86. T. Mukai, H. Tsuruta, and Y. Momotari, *Bull. Chem. Soc. Japan*, 1967, **40**, 1967.

87. N. Abe and K. Takase, *Tetrahedron Letters*, 1973, 4739.

88. N. Abe and T. Nishiwaki, unpublished work.

89. T. Nishiwaki, N. Abe, K. Ishida, and K. Miura, *Bull. Chem. Soc. Japan*, 1978, **51**, 1573.

90. R. M. Acheson,and N. F. Elmore, *Adv. Heterocyclic Chem*., 1978, **23**, 263.

91. N. Abe, Y. Tanaka, and T. Nishiwaki, *J.C.S. Perkin Trans. I*, 1978, 492.

92. N. Abe and T. Nishiwaki, *Bull. Chem. Soc. Japan*, 1980, **53**, 1773.

93. K. Hafner and J. Häring, *Erdoel Kohle, Erdgas, Petrochem*., 1979, **32**, 136.

94. K. Hafner, J. Häring, and W. Jakel, *Angew. Chem. Internat. Edn*., 1970, **9**, 159.

95. N. Abe and T. Nishiwaki, *J.C.S. Chem. Comm*., 1979, 476; N. Abe and T. Nishiwaki, *Bull. Chem. Soc. Japan*, 1980, **53**, 1406.

96. A. McKillop and D. W. Young, *Synthesis*, 1979, 401; M. Hojo and R. Masuda, *J. Synthetic Org. Chem. Japan*, 1979, **37**, 537, 689.

97. N. Abe and T. Nishiwaki, *Heterocycles*, 1979, **12**, 1031.

98. N. Soma and Y. Watanabe, Japan Kokai, 1972, 41358.

99. T. Nozoe, S. Seto, and T. Toda, *Bull. Chem. Soc. Japan*, 1968, **41**, 208.

100. G. Schaden, *Chem. Ber*., 1972, **105**, 3128.

Received, 26th July, 1980