HETEROCYCLES, Vol. 9, No.12, 1978

THE CHEMISTRY OF DIAZAQUINONES

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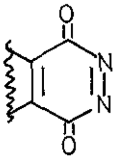
This article presents a survey of the synthesis, properties and reactions of 3,6-pyridazinedione, 1,4-phthalazinedione and related compounds.

CONTENTS

1.- INTRODUCTION

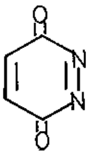
Since Clement in 1960[1] and Kealy in 1962[2] first prepared compounds of type I, for which the generic term diazaquinones was proposed, the study of the properties and reactions of these compounds has given rise to an increasing interest and has generated a good number of papers during the past few years.



I

The main significance of these compounds lies in their intense dienophilic character due to the -N=N- double bond, which allows them to undergo cycloaddition reactions that may be applied to the synthesis of heterocyclic compounds. Some of the products thus obtained are useful as plant growth regulants and control agents for noxious weeds[3]. Other such products have shown cytostatic activity[4]. The role of diazaquinones in the chemiluminiscence of some cyclic hydrazides has been reviewed[5].

In addition to the simplest diazaquinone , 3,6-pyridazinedione (II), prepared by Kealy[2], its derivatives 4,5-dihydro-3,6-pyridazinedione (III)[6], 4,5-difluoro-3,6-pyridazinedione (IV)[2] , 4-chloro-3,6-pyridazinedione (Va) and 4-bromo-3,6-pyridazinedione (Vb)[7] as well as its benzo-analog 1,4-phthalazinedione and derivatives (VI) are known.



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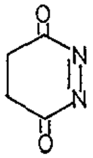

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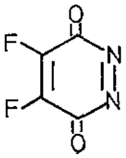

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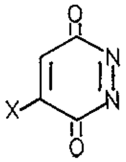
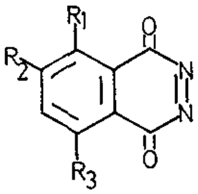


V

a; X=Cl

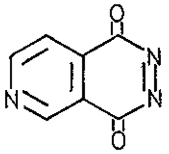
b; X=Br



VI

a: $R_1=R_2=R_3=H$ (Ref. 1)
b: $R_1=NH_2$; $R_2=R_3=H$ (Ref. 8)
c: $R_1=R_3=H$; $R_2=(CH_3-CH_2)_2N$ (Ref. 8)
d: $R_1=NO_2$; $R_2=R_3=H$ (Ref. 9)
e: $R_1=R_3=H$; $R_2=NO_2$ (Ref. 9)
f: $R_1=CH_3-CO-NH$; $R_2=R_3=H$ (Ref. 9)
g: $R_1=Cl$; $R_2=R_3=H$ (Ref. 10)
h: $R_1=OH$; $R_2=R_3=H$ (Ref. 10)
i: $R_1=R_3=Cl$; $R_2=H$ (Ref, 10)

Diazaquinones in which an heterocyclic ring is fused with the diazaquinone ring, such as VII-XI[11], XII[12] and XIII-XVI[13], as well as polycyclic diazaquinones XVII and XVIII[8] have also been described.



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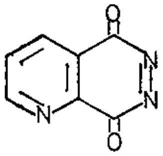

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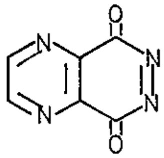

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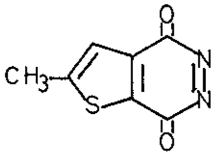
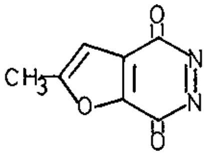


X



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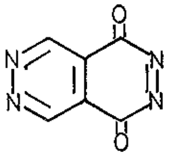
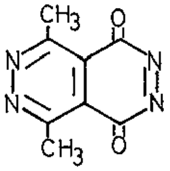
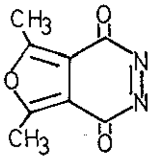


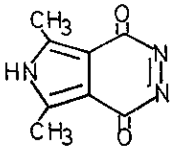
XII



XIII



XIV



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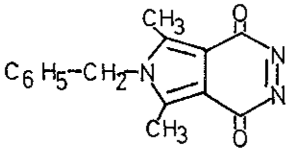
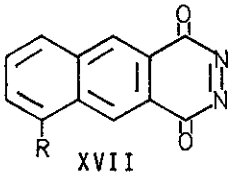
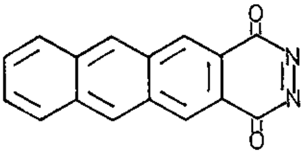


XVI



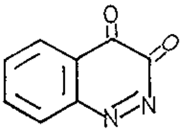
XVII

a: R=H (Ref. 14)
b: $R=NO_2$ (Ref. 10)



XVIII

The synthesis of diazaorthoquinones such as 3,4-diketocinnoline (XIX) has been unsuccessfully attempted[15,16].

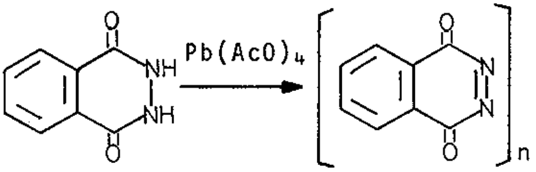

XIX

2.- SYNTHESIS AND STABILITY OF DIAZAQUINONES

2.1.- Preparation of diazaquinones

The preparation of diazaquinones is accomplished through the oxidation of cyclic hydrazides.

The first diazaquinone was prepared by Clement[1] by oxidizing phthalic hydrazide. When the oxidation with lead tetraacetate is carried out in acetonitrile, a green solution is obtained which very rapidly deposites a white, amorphous solid, formulated as a polymer ({VIa}n) of 1,4-phthalazinedione.

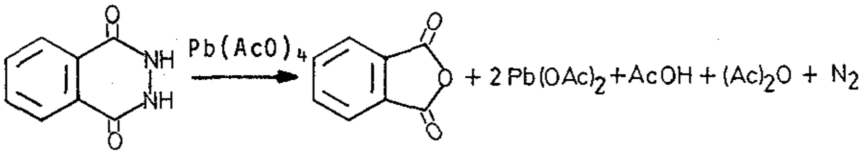


{VIa}n

The diazaquinone is the initial product of oxidation and is responsible for the colour but, due to its instability, it decomposes in short time. Clement showed the formation of 1,4-phthalazinedione (VIa) as an unstable compound by oxidizing phthalic hydrazide in the presence of butadiene.The cycloaddition reaction allows the interception of the diazaquinone as a Diels-Alder adduct.

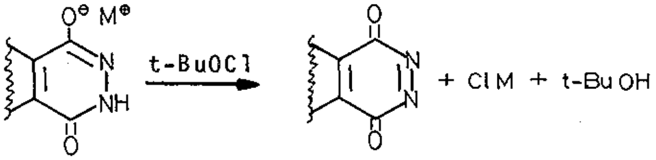
The oxidation of cyclic hydrazides to diazaquinones may also be accomplished in other solvents[6]. Acetone like acetonitrile provides reasonably stable solutions with the colour of the diazaquinone, such as 3,6-pyridazinedione (II) , 4,5-dihydro-3,6-

pyridazinedione (III) and 1,4-phthalazinedione (VIa), lasting a fairly long time. On the other hand, in methylene chloride the solutions of diazaquinones are very unstable but, in this chlorinated solvent, both the oxidation and the reaction with dienes go much quicker. The preparation of 1,4-phthalazinedione (VIa) and 3,6-pyridazinedione (II) was also achieved by employing lead tetraacetate in benzene[17]. The use of lead tetraacetate as the oxidizing agent results in undesirable side-reactions such as formation of cyclic anhydride from the hydrazide[1] as well as the previously mentioned polymerization of the diazaquinone.



Nevertheless, when the objective is the *in situ* preparation of adducts with reactive dienes, this procedure may be used with good results.

The second procedure for the synthesis of diazaquinones, reported by Kealy[2], is to oxidize the potassium or sodium salts of the cyclic hydracides (XX) with t-butyl hypochlorite in acetone solution at -77°C.



XX I

In this way 3,6-pyridazinedione (II), 4,5-difluoro-3,6-pyridazinedione (IV) and 1,4-phthalazinedione (VIa) were prepared and under these conditions may be obtained as emerald-green solutions after filtration of the inorganic salts under nitrogen at -77°C. This method of preparing diazaquinones is preferred to the Clement's method because almost no inorganic by-products are obtained and the unreacted hydrazide may be removed by the filtration at low temperature. Essentially pure solutions of diazaquinones are thus obtained and may be kept at -77°C for some hours without decomposition.

It is even possible to precipitate the diazaquinones from these solutions by means of addition of highly chlorinated solvents. However, the green solid that separates frecuently decomposes suddenly during the isolation procedures[2].

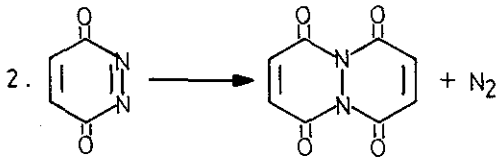
Kealy's procedure *is widely used and has been applied to the* preparation of substituted 1,4-phthalazinediones[9], diazaquinones with a fused heterocyclic ring[11] and polycyclic diazaquinones[10].

When Kealy's method fails, the oxidation of cyclic hydrazides with chlorine in 1,2-dimethoxyethane at -50°C has been successfully employed[14]. The use of nickel peroxide as the oxidant and methylene chloride as the solvent has also been reported[18].

2.2.- Stability of diazaquinones

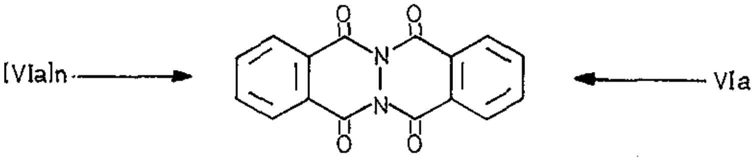
Kealy *has studied*[2] *the decomposition reactions of* diazaquinones II, IV and VIa. When the acetone solutions of diazaquinones are slowly warmed, decomposition takes place well below room temperature, as shown by the gradual fading of the green colour and the evolution of nitrogen. 3,6-Pyridazinedione (II) and 4,5-difluoro-3,6-pyridazinedione (IV) decompose quickly at -30°C. The solutions of 1,4-phthalazinedione retain their colour even up to room temperature.

The products of these decomposition reactions have been isolated and identified. 1,4,6,9-Tetraketopyridazino{1,2-a}pyridazine *(XXI) is the principal product from the decomposition of* 3,6-pyridazinedione (II) and this accounts for the observed nitrogen evolution. The solutions of 1,4-phthalazinedione (VIa)



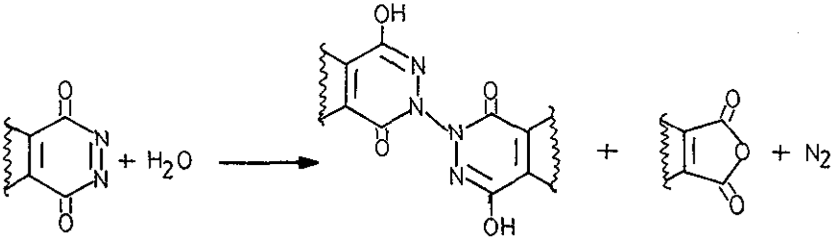
II XXI

decompose with little gas evolution and form the polymer {VIa}n, previously reported by Clement[1], which in turn looses nitrogen by thermal decomposition to yield 5,6,11,12-tetraketophthalazino-{2,3-b}-phthalazine (XXII). This compound is also obtained when the isolation of 1,4-phthalazinedione (VIa) by precipitation with chlorinated solvents is attempted.



XXII

The diazaquinones are very susceptible to attack by water giving the bishydrazides XXIII[2]. Thus, during the preparation and handling of diazaquinone solutions it is desirable to exclude atmospheric moisture. However, attack by water is only of minor importance in the decomposition of II and VIa. On the other hand the decomposition of 4,5-difluoro-3,6-pyridazinedione (IV) appears to proceed exclusively *via* attack by water, leading to a bishydrazide XXIII.



I XXIII

Some 1,4-phthalazinediones (VI) are more stable than the 1,4-phthalazinedione itself (VIa). Thus, the violet acetone solutions of VId, VIe and VIf can be kept at 5°C without decomposition[9] and

VIc can even be isolated as a deep violet crystalline solid[8].

On the other hand, the diazaquinones with a fused heterocyclic ring are very unstable. Compounds VII-XI[11] and XII[12] cannot be isolated and they decompose when their solutions are warmed. In the decomposition of VIII a bishydrazide XXIII has been isolated[11]. *The diazaquinones XIII-XVI are neither* stable in solution nor can they be isolated from their solutions. These solutions range in colour from orange (XIII), to yellow (XIV) and red (XV and XVI)[13].

Polycyclic diazaquinones are much more stable. *Compound XVIII* can be isolated as violet crystals[8] and XVIIa is isolated as maroon crystals so stable that its analysis and spectroscopic study have been carried out[14]. It show a carbonyl band at 1715 cm^{-1} in the infrared and three maxima in the UV: 425 nm (logε 3.5), 296 (4.0) and 242 (4.8).

3.- *REACTIONS OF DIAZAQUINONES*

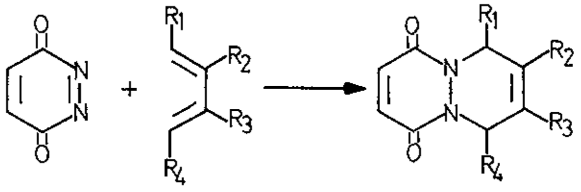
Due to instability of the diazaquinones, their reactions must be carried out, without previous isolation, in the reaction medium where they are prepared by oxidation of cyclic hydrazides , although in some instance they have been isolated prior to the reaction[19]. When Kealy's procedure[2] is employed, the diazaquinone is first prepared and then the other reactant is added to the filtered solution at -77°C. When Clement's procedure[1] is used, the oxidation of the cyclic hydrazide is performed at 0°C with the other reactant present.

3.1.- {4+2} Cycloaddition reactions

The most characteristic reactions of diazaquinones are the Diels-Alder cycloadditions. The diazaquinones are, together with 1,2,4-triazolin-3,5-diones[20-22], among the most potent dienophiles known. They undergo cycloaddition reactions even at -77°C with a great variety of dienes. Use of the diazaquinones in the Diels-Alder reaction has made some otherwise difficultly accessible ring systems readily available.

3.1.1.- Cycloadditions with open chain dienes

3,6-Pyridazinedione (II) reacts with butadiene and its derivatives to give the adducts XXIV.



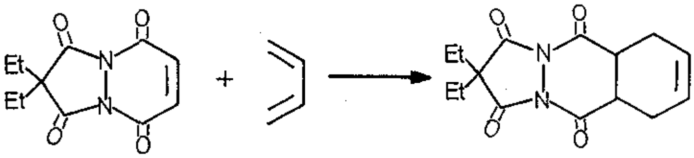
II

XXIV

a: $R_1=R_2=R_3=R_4=H$ (Ref. 2,3,6)
b: $R_1=R_3=R_4=H$; $R_2=CH_3$ (Ref. 23)
c: $R_1=R_4=H$; $R_2=R_3=CH_3$ (Ref. 2,3)
d: $R_1=R_3=R_4=H$; $R_2=Cl$ (Ref. 23)
e: $R_1=R_4=H$; $R_2=R_3=Cl$ (Ref. 23)
f: $R_1=R_4=Ph$; $R_2=R_3=H$ (Ref. 18)

4,5-Dihydro-3,6-pyridazinedione (III) and 4,5-difluoro-3,6-pyridazinedione (IV) behave in analogous fashion when they react with butadiene and its derivatives[2,6].

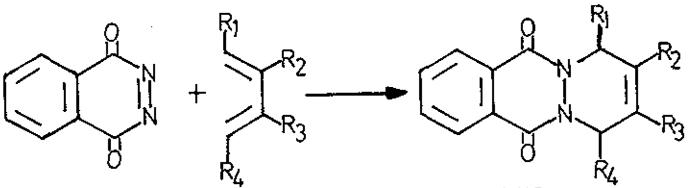
It must be pointed out that, of the two potentially dienophilic double bonds of II, only the -N=N- double bond reacts and no reactions involving the -C=C- double bond are known. Attempts to bring the -C=C- double bond into reaction by treating the adducts XXIV with excess diene have been unsuccessful[24]. However, some compounds related to II, such as XXV, form adducts (XXVI) with the -C=C- double bond[25].



XXV

XXVI

The reactions of 1,4-phthalazinedione (VIa) with butadiene and derivatives follow the same pattern as II and made it possible to obtain the adducts XXVII, representatives of the pyridazino{1,2-b}-phthalazine heterocyclic system not previously known.



VIa

XXVII

a: $R_1=R_2=R_3=R_4=H$ (Ref. 1,2)

b: $R_1=R_3=R_4=H$; $R_2=CH_3$(Ref. 18,26)

c: $R_1=R_4=H$; $R_2=R_3=CH_3$(Ref. 2,3)

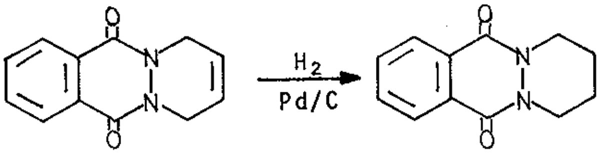
d: $R_1=R_3=CH_3$; $R_2=R_4=H$(Ref. 26)

e: $R_1=OAc$; $R_2=R_3=R_4=H$(Ref. 26)

f: $R_1=R_4=OAc$; $R_2=R_3=H$(Ref. 26)

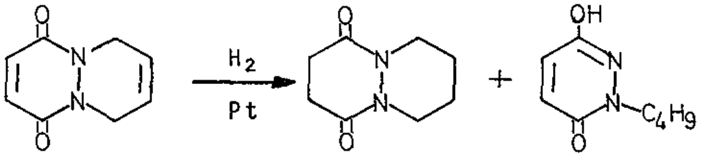
g: $R_1=R_4=Ph$; $R_2=R_3=H$ (Ref.18)

Some chemical transformations of adducts XXIV and XXVII have been studied. Hydrogenation of adduct XXVIIa affords 1,2,3,4-tetrahydropyridazino{1,2-b} phthalazine-6,11-dione (XXVIII)[1] and hydrogenation of XXIVa gives 1,2-succinoylhexahydropyridazine (XXIX) as well as 2-butyl-6-hydroxy-3(2H)-pyridazinone (XXX)[2]. Reduction of XXIV b,d,e with lithium aluminium hydride gives XXXI b,d,e[23].



XXVIIa

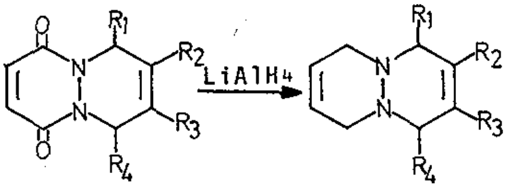
XXVIII



XXIVa

XXIX

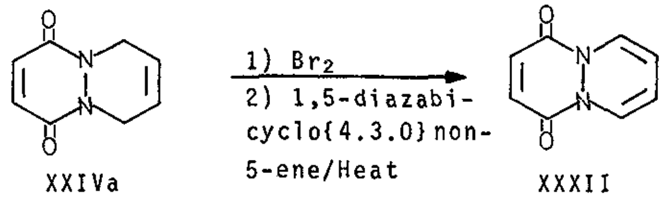
XXX



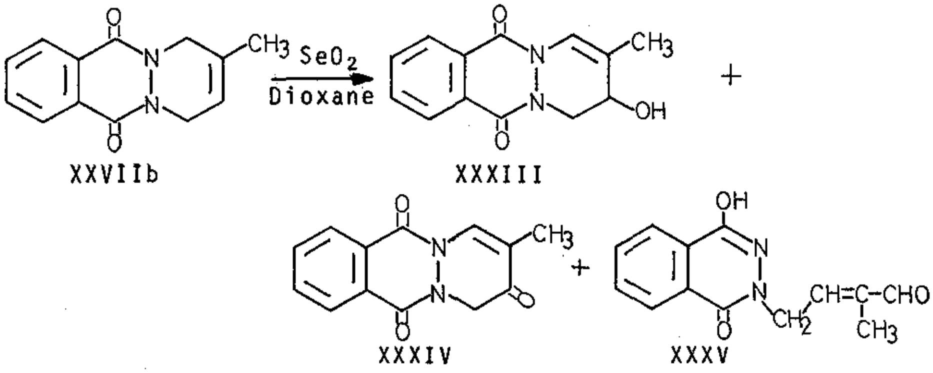
XXIVb,d,e

XXXIb,d,e

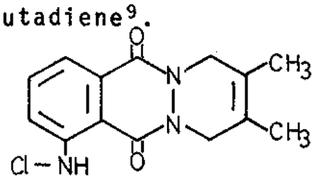
Diazanaphthoquinone XXXII, whose UV spectrum indicates the presence of the aromatic ten Π-electron ring system, was prepared by bromination of the adduct XXIVa followed by treatment with 1,5-diazabicyclo{4.3.0}non-5-ene^{27}.



The oxidation of the adducts XXIV and XXVII with selenium dioxide in dioxane leads to the hydroxy- and keto-derivatives , with rearrangement of a double bond, together with α,β-unsaturated aldehydes formed through ring opening. Thus, XXVIIb leads to XXXIII, XXXIV and XXXV^{26}.

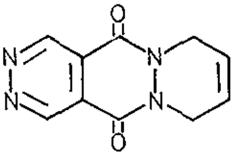


The substituted derivatives of 1,4-phthalazinedione (VI) show also a strong dienophilic character. VIc, VId and VIe form Diels-Alder adducts with butadiene, 2,3-dimetylbutadiene or 1,4-diphenylbutadiene^{9,28} and VIf, VIg, VIh and VIi behave in the same manner with 2,3-dimethylbutadiene^{9,10}. Diazaquinone VIb, when prepared by Kealy's method, affords the compound XXXVI by reaction with 2,3-dimethylbutadiene^{9}.



XXXVI

The presence of heteroatoms in the ring fused to the diazaquinone ring does not appreciably modify its dienophilic character and thus butadiene or 2,3-dimethylbutadiene undergo cycloaddition with diazaquinones VII-XI[11] and XII[12]. The adduct of XII with butadiene is of some interest since it is representative of the novel 2,3,5a,9a-tetraazaanthracene heterocyclic system.

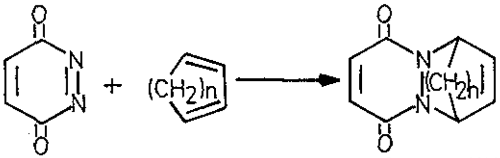


XXXVII

Butadiene, 2-methylbutadiene and 2,3-dimethylbutadiene react also with polycyclic diazaquinones XVIIa and XVIIb[10,29]. The reaction of N-bromosuccinimide with adducts obtained from XVIIa has been reported to yield different addition or substitution products depending on the solvent and the reaction conditions[29].

3.1.2.- *Cycloadditions with cyclic dienes*

3,6-Pyridazinedione (II) also forms adducts with cyclic dienes such as cyclopentadiene (XXXVIII) and cyclohexadiene (XXXIX)[2,3] and the same was observed with 1,4-phthalazinedione (VIa) and its derivatives VIb, VId and VIf, in which the substituents do not prevent the reaction[9,30].

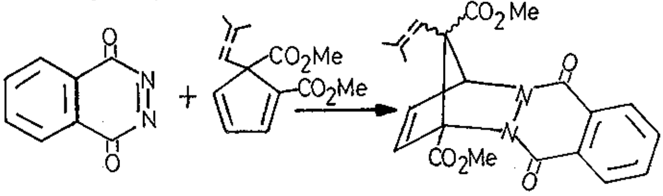


II

n=1: XXXVIII
n=2: XXXIX

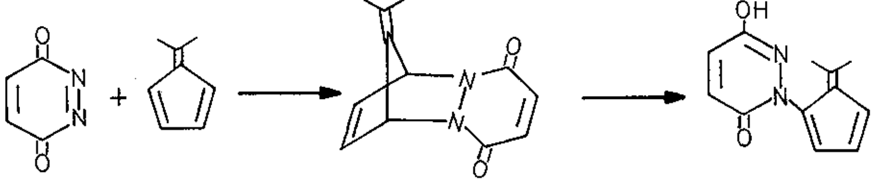
Polyheterocyclic diazaquinones VII, VIII, XIII, XIV and XVI react also with cyclopentadiene or cyclohexadiene to yield the corresponding Diels-Alder adducts[11,13], but XV fails to do so[13].

Deactivated cyclopentadiene derivatives, such as 5-(3',3'-dimethylallenyl)-1,5-bis(carbomethoxy)cyclopentadiene (XL) forms the cycloadducts XLI with 1,4-phthalazinedione (VIa)[31], but hexa chlorocyclopentadiene fails to react with diazaquinones[11].



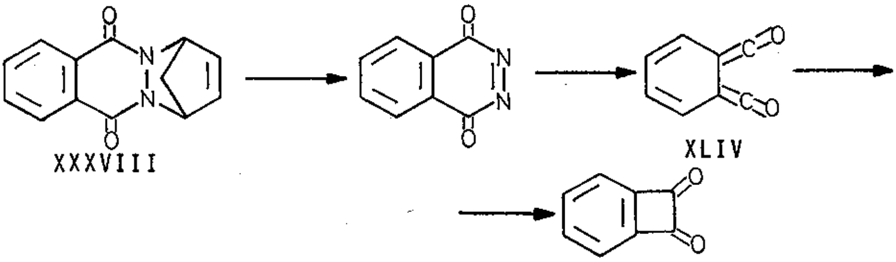
VIa XL XLI

3,6-Pyridazinedione and 6,6-dimethylfulvene give an adduct (XLII) which undergo rearrangement in the solid state to an isomeric product (XLIII) through an allylic shift of hydrogen[2].



II XLII XLIII

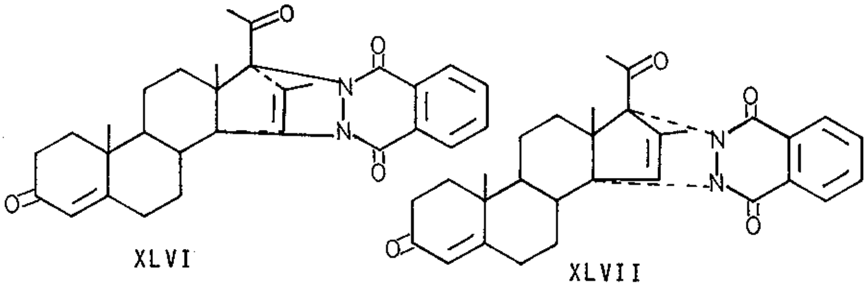
Vapour phase pyrolysis of cyclopentadiene adduct XXXVIII affords benzocyclobutenedione (XLV)[32]. This process represents a useful synthetic route to benzocyclobutenedione and can be rationalised as a retro-Diels-Alder reaction followed by nitrogen extrusion from 1,4-phthalazinedione. The bis-ketene XLIV could then close to give benzocyclobutenedione.



XXXVIII XLIV

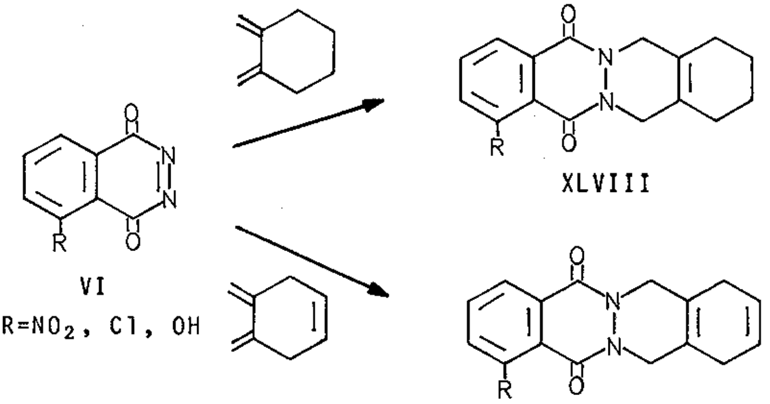
XLV

Diels-Alder cycloadditions of 3,6-pyridazinedione (II) and 1,4-phthalazinedione (VIa) to steroidal dienes have been studied[33-35]. Thus, 1,4-phthalazinedione (VIa) reacts with 16-methylpregna-4,14,16-triene-3,20-dione to give the two possible adducts XLVI and XLVII, to which the 14β,17β and 14α, 17α configurations were assigned.



XLVI XLVII

Substituted diazatetracyclic compounds referable to tetracyclines of known activity have been synthesized by Diels-Alder reaction of substituted phthalazinediones VId,g,h with 1,2-dimethylenecyclohexane (XLVIII) and 1,2-dimethylene-Δ^4-cyclohexene (IL)[10].



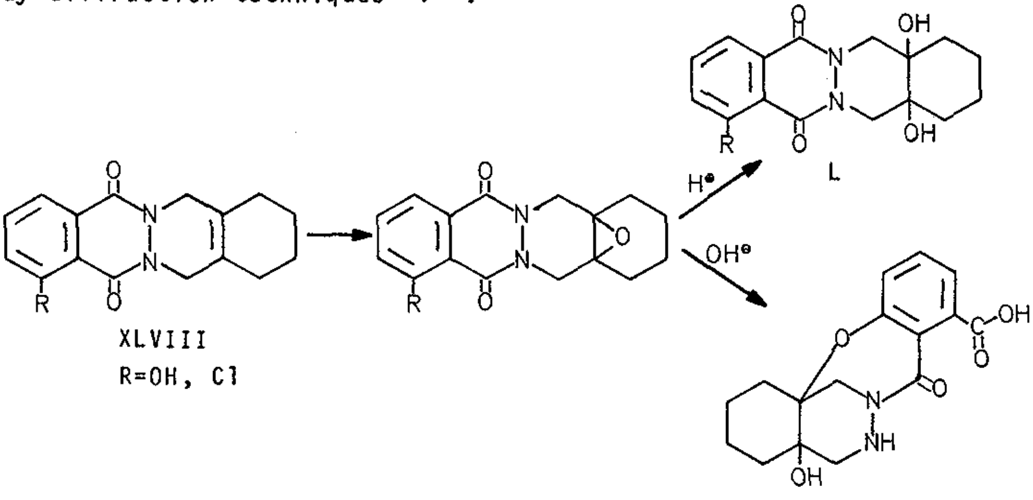
VI

$R=NO_2$, Cl, OH

XLVIII

IL

Epoxidation of adducts XLVIII from 5-hydroxy- and 5-chlorophthalazine-1,4-dione followed by solvolytic opening of the oxirane ring in acid medium has been carried out in order to modify their biological behaviour by introducing a 1,2-diol group at angular positions. Compounds L are thus obtained[36]. Attempts to obtain the diol derivatives L by solvolytic opening of the oxirane ring when R=OH in alkaline medium afford a new condensed 1,4-oxazepine derivative, namely 4-carboxy-8,8a,9,10,11,12-hexahydro-5H,12H,12bH-8a-hydroxy-5-oxophthalazine{8a,2bc}benzo{f}{1,4}oxazepine (LI), whose structure was established by single crystal X-ray diffraction techniques[37,38].

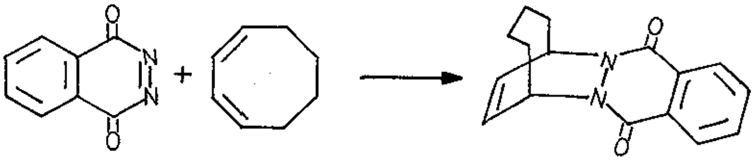


XLVIII
R=OH, Cl

L

LI

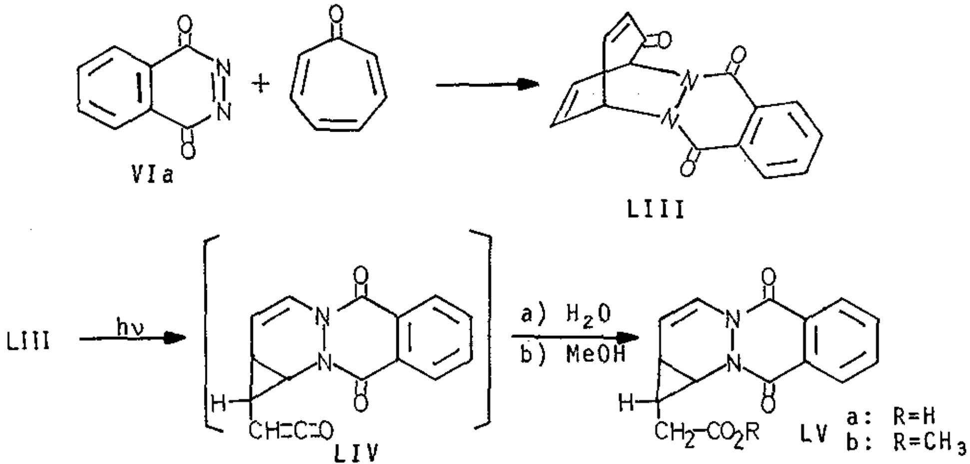
The dienophilic reactivity of diazaquinones allows them to undergo cycloaddition reactions with such unreactive dienes as 1,3-cyclooctadiene[9,18,39]. The compound LII, formed with 1,4-phthalazinedione (VIa)[39], is the first reported Diels-Alder adduct of 1,3-cyclooctadiene and its formation at low temperature emphasizes the potent dienophilic character of diazaquinones.



VIa

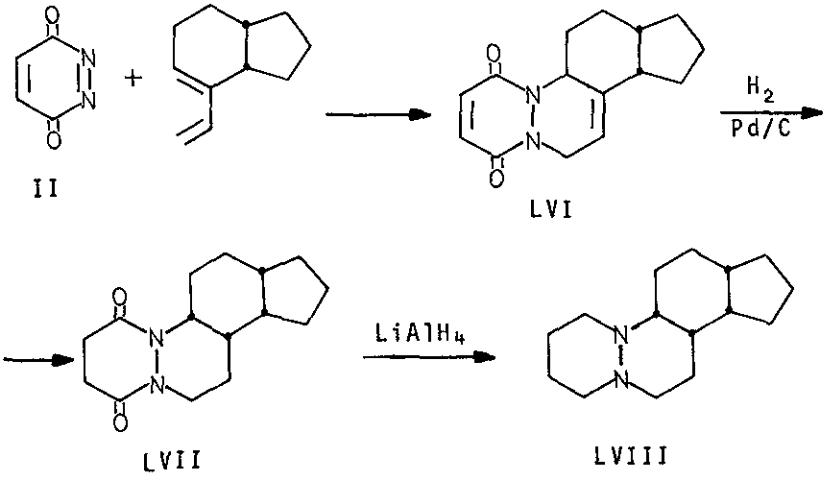
LII

Treatment of tropone with 3,6-pyridazinedione (II) does not give any product, but 1,4-phthalazinedione (VIa) forms the adduct LIII with tropone[40]. Irradiation of the compound LIII in methanol and in acetonitrile/water gave LVa and LVb respectively, formed by addition of water or methanol to the initially formed ketene LIV.



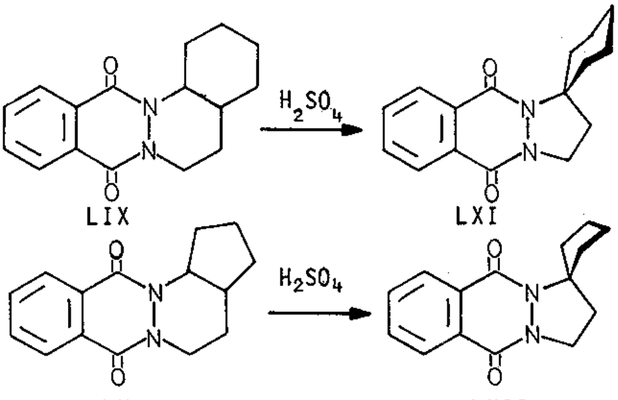
VIa LIII LIV LV

By taking advantage of the reactivity of diazaquinones towards 1-vinylcycloalkenes, the introduction of the 1,2-diazine group into the steroidal skeleton has been accomplished in a novel synthesis of *bridgehead* diazasteroids[41,42]. Thus, Diels- Alder reaction of 3,6-pyridazinedione (II) with 2,3,3a,4,5,7a-hexahydro-7-vinylindene yielded LVI, which is easily *hydrogenated* to give LVII in which the B/C ring juntion is *cis*. Reduction of LVII with lithium aluminium hydride afforded the tetrasubstituted hydrazine LVIII.



II LVI LVII LVIII

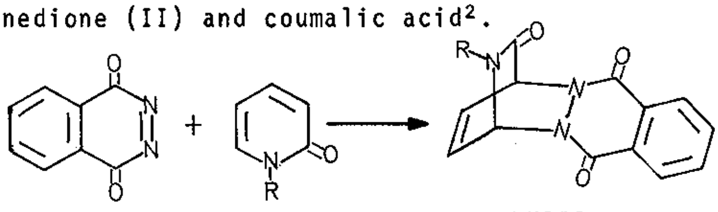
The reaction has been extended to other vinylcycloalkenes and diazaquinones[41],[42]. The hydrogenated adducts obtained from 1,4-phthalazinedione and 1-vinylcyclohexene (LIX) and 1-vinylcyclopentene (LX) were isomerized with concentrated sulfuric acid to give the spiro-compounds LXI and LXII, respectively , by ring contraction[43].

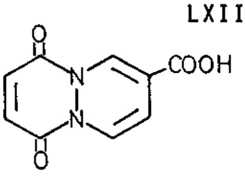


LIX LXI
LX LXII

3.1.3.- *Reactions with dienes containing heteroatoms*

Diels-Alder reactions of diazaquinones have been extended to heterocyclic dienes. Cycloaddition of 1,4-phthalazinedione (VIa) with a variety of N-substituted pyridones afforded novel azabicyclic structures LXIII[44] and adduct LXIV is obtained from 3,6-pyridazinedione (II) and coumalic acid[2].

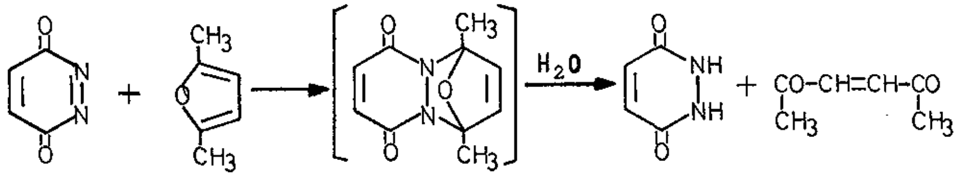

VIa LXIII


LXIV

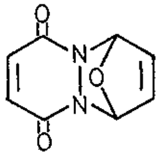
The reaction of diazaquinones with furans has been widely studied. Kealy reported[2] a rapid reaction of furan and 2,5-dimethylfuran with 3,6-pyridazinedione (II) but Diels-Alder adducts were not isolated. The product from furan precipitates from solution but decomposes exothermically on isolation. The adduct from 2,5-dimethylfuran (LXV) undergoes hydrolysis during isolation to give maleic hydrazide and 1,2-diacetylethylene. However, more recently, the isolation of the adduct LXVI from 3,6-pyridazinedione (II) and furan has been claimed[23].

Reaction of 1,4-phthalazinedione (VIa) with furan does not *lead to the Diels-Alder adduct*[45]*. The open conjugation of vinyl*furan reacts with 1,4-phthalazinedione (VIa) but the adduct is too unstable to be isolated[46].

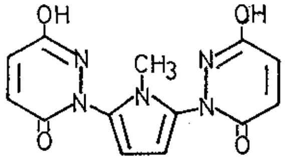
3,6-Pyridazinedione (II) has also been tested towards N-methylpyrrole[2]. The Diels-Alder adduct was not isolated but instead a compound of structure LXVII was obtained.



II LXV

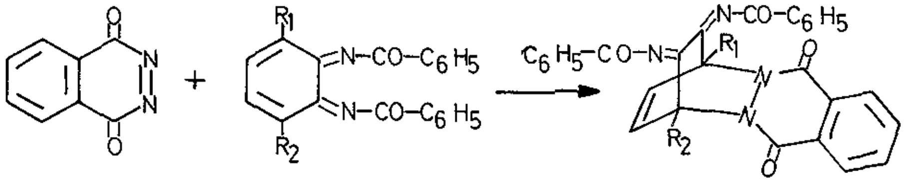


LXVI



LXVII

The reactivity of diazaquinones towards dienes containing heteroatoms in their conjugated systems was studied and the lack of reaction between 1,4-phthalazinedione (VIa) and dehydroindigo or dimethylfurazan[17], benzalazine, 2,5-dimethyl-1,3,4-oxadiazol *and cinamalaniline*[46] *nitrogenated heteroconjugations was found.* When dienes such as o-quinonedibenzimides are used, the reaction always takes place with the homoconjugation affording the adducts LXVIII, leaving the heteroconjugation unaffected[17].

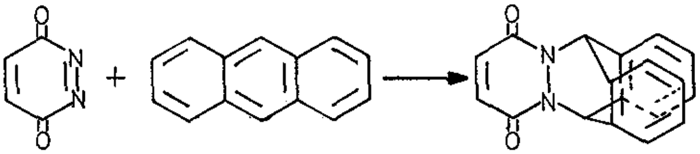


VIa LXVIII

a: $R_1=R_2=H$; b: $R_1=CH_3$, $R_2=H$; c: $R_1=R_2=CH_3$

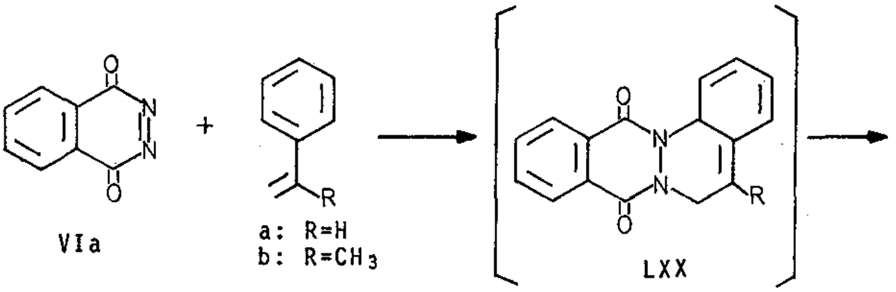
3.1.4.- Reactions with aromatic hydrocarbons

The extraordinary reactivity of diazaquinones as dienophiles allows them to react with aromatic hydrocarbons. With 3,6-pyridazinedione (II) and anthracene, the adduct LXIX is formed[6]. This normal 9,10-anthracene addition is also observed with III and VIa[6] and with polyheterocyclic diazaquinones such as XII[12].



II LXIX

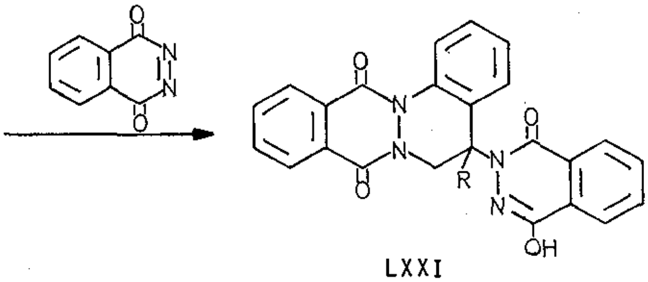
Diazaquinones react as well with vinylaromatic compounds such as styrene, anethole, isosafrole[47] and α-methyl- and β-methylstyrene[48], but great difficulties are found in the isolation of the reaction products. When adducts LXX are formed, these undergo reaction with a second molecule of diazaquinone. According to the scheme below, 1,4-phthalazinedione(VIa) leads to LXXIa and



VIa

a: R=H
b: $R=CH_3$

LXX

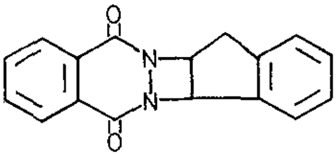


LXXI

LXXIb by reaction with styrene and α-methylstyrene respectively. β-Methylstyrene fails to give an adduct with 1,4-phthalazinedione (VIa)[48].

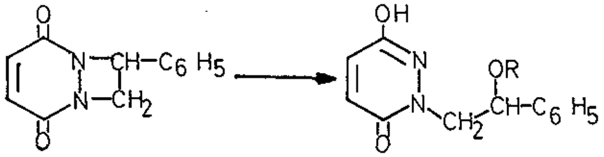
3.2.- {2+2} Cycloaddition reactions

Although diazaquinones do not easily undergo {2+2} cycloaddition reactions, some cycloadditions of this kind have been reported. This process provides a one-step synthesis of derivatives of diazacyclobutane. The first example reported was the reaction of 1,4-phthalazinedione (VIa) with indene[39], which afforded LXXII. Similarly, phenanthrene seems to give an analogous adduct by cycloadditon involving the 9,10-bond[39]. The vapour phase pyrolysis of LXXII affords benzocyclobutenedione and indene[32].



LXXII

In some reactions of diazaquinones with styrene {2+2} cycloaddition to the ethylenic double bond takes place. However, the product thus formed (LXXIII) undergoes addition of a molecule of water, t-butanol or acetic acid (originated as by-products in *the preparation of the diazaquinone). Thus, the reaction of 3,6-* pyridazinedione (II) with styrene affords the compounds LXXIVa,b, c depending upon the procedure used to generate the diazaquinone[47].

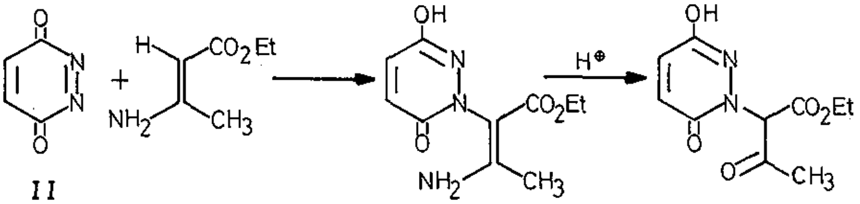


LXXIII LXXIV

a: R=H
b: R=C(CH$_3$)$_3$
c: R=COCH$_3$

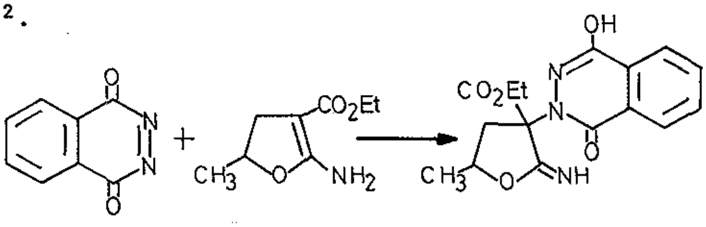
3.3.- Reactions with enamines

The addition of ethyl 3-aminocrotonate to the 3,6-pyridazinedione (II) -N=N- double bond occurs easily and compound LXXV was obtained[49]. Acid treatment of LXXV aiming to a cyclization analogous to the Nenitzescu reaction[50,51] brings about the loss of the amino group and the formation of compound LXXVI. 1,4-Phthalazinedione (VIa) behaves in the same way[49].



II LXXV LXXVI

Other enaminoesters such as LXXVII have been shown to react with 1,4-phthalazinedione (VIa) to give the iminolactone LXXVIII[52].



VIa LXXVII LXXVIII

This survey of the chemistry of diazaquinones leads to the conclusion that the cycloaddition reactions of these compounds have been widely studied and are useful for the synthesis of nitrogen heterocycles. Maybe future research on diazaquinones should focus attention on reactions other than cycloadditions.

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Received, 12th September, 1978