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DIAZAPOLYCYCLIC COMPOUNDS. IX. SUBSTITUTED DIAZAQUINONE ADDUCTS WITH DIMETHYLENECYCLOHEXANE, DIMETHYLENE-CYCLOHEXENE AND SUBSTITUTED BUTADIENES.

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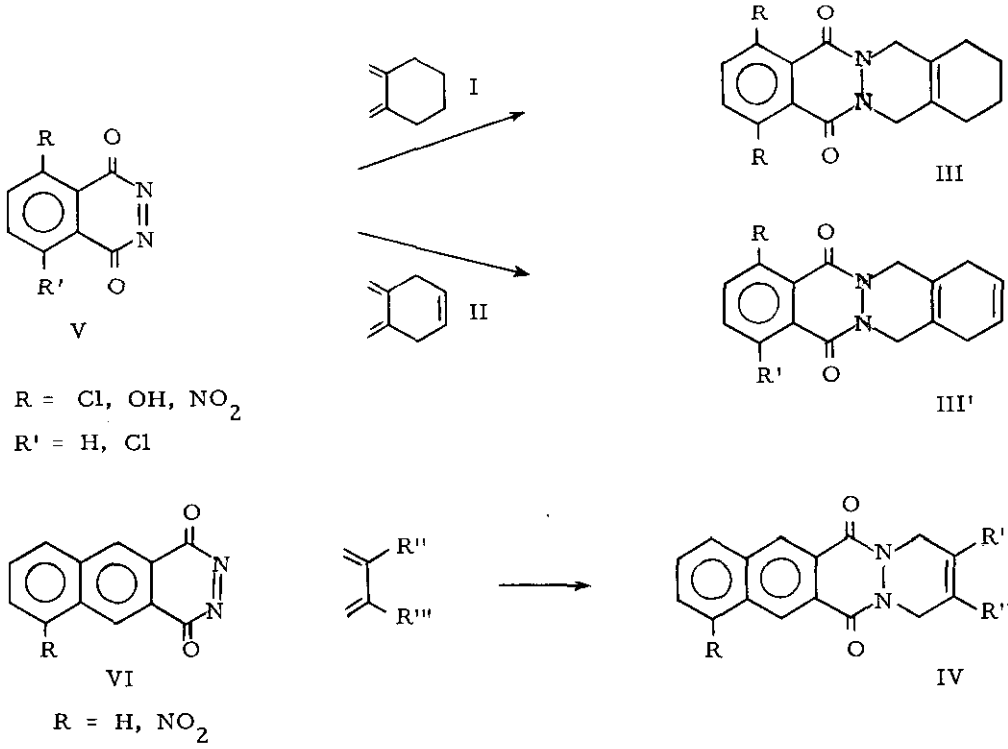
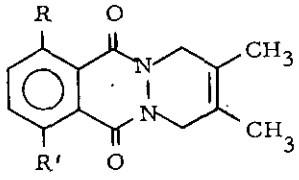
Substituted tetracyclic diaza compounds with varying positions of the nitrogen bridge have been synthesized by Diels-Alder reaction of substituted phthalazindiones with 1,2-dimethylenecyclohexane or 1,2-dimethylene-Δ^4-cyclohexene and of naphthalazindiones with substituted butadienes in order to obtain compounds referable to tetracyclines of known activity.

Substituted diazatetracyclic compounds have been synthesized by Diels-Alder reaction of diazaquinones with 1,2-dimethylenecyclohexane (I)[1], 1,2-dimethylene-Δ^4-cyclohexene (II)[2,3] and substituted 1,3-butadienes. Two types of diaza-polycyclic compounds were obtained whose skeletons differ in the position of the nitrogen bridge situated either between ring B and C (III, III') or C and D (IV), the general scheme of the synthesis beings as follows:



Oxidation of the suitable hydrazides with lead tetraacetate TAP [4] or t-butyl hypochlorite HBT [5] yields the corresponding diazaquinones V and VI in situ, which were reacted with the diene to give the 1,4-adduct. The hydrazides were prepared by usual way [6,7,8]

The phylodienic character of 5-chloro-, 5-hydroxy- and 5,8-dichloro-phthalazin-1,4-dione (V) was tested against the simple diene 2,3-dimethyl-1,3-butadiene, the adducts VIIa-c being obtained.

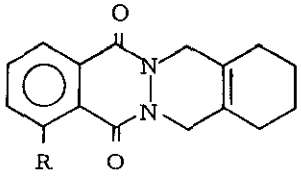


VIIa R' = Cl R = H
VIIb R' = OH R = H
VIIc R' = Cl R = Cl

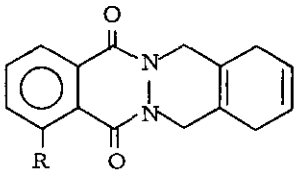
TABLE 1. NMR signals (τ) of the adducts VII

Compound	M.p. °C	Solvent	H-Ar	CH_2	CH_3
VIIa	175	CCl_4	1.4-2.6 (m)	5.62 (s)	8.15 (s)
VIIb	176	$(CD_3)_2SO$	2.0-2.9 (m)	5.60 (s)	8.25 (s)
VIIc	238 dec	CCl_3D	2.33 (s)	5.60 (s)	8.27 (s)

Reaction of the diene (I) and (II) with the diazaquinones (V) yielded the adducts VIIIa-c and IXa, b.



VIIIa R = NO_2
VIIIb R = Cl
VIIIc R = OH



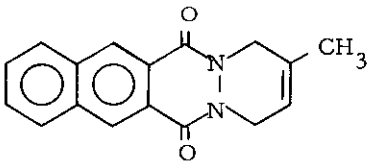
IXa R = NO_2
IXb R = Cl

TABLE 2. NMR signals (τ) of the adducts VIII and IX

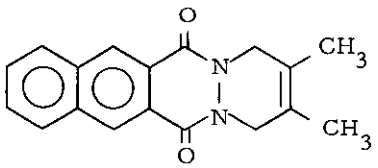
Comp.	M.p. °C	Solvent	H-Ar	CH	CH_2-N	CH_2-C	CH_2
VIIIa	132	CCl_3D	1.4-2.2 (m)		5.54 (s)	7.9 (m)	8.2 (m)
VIIIb	136 dec	S_2C	1.8-2.6 (m)		5.88 (s)	8.1 (m)	8.4 (m)
VIIIc	192	CCl_3D	2.2-3.0 (m)		5.58 (s)	7.9 (m)	8.2 (m)
IXa	286	CF_3COOH	1.1-2.0 (m)	4.1 (m)	*5.2 (m)	7.15 (m)	
IXb	148	CCl_3D	1.6-2.5 (m)	4.2 (m)	5.52 (m)	7.28 (m)	

* 4H from two AB systems.

The diazaquinones (VI) with 2-methyl-1,3-butadiene and 2,3-dimethyl-1,3-butadiene gave the adducts X and XIa, b.



X



XIa R = H

XIb R = NO_2

TABLE 3

Comp.	M.p. °C	Solvent	H-Ar	CH	CH_2	CH_3
X	180	CCl_3D	1.2-2.5 (m)	4.23 (m)	5.45 (m)	8.12 (s)
XIa	260	CCl_3D	1.1-2.5 (m)		5.43 (s)	8.13 (s)
XIb	241 dec	CF_3COOH	1.0-2.4 (m)		5.05 (s)	7.97 (s)

All the compounds described were identified by elemental analysis and ir and nmr spectroscopy (60 MHz). Compounds VIIa-c, VIIIa-c, X and XIa-b were obtained between 45 and 70%. Adducts IXa-b were obtained in 10% and 20% yields, respectively. Actually, studies are in progress in order to obtain diazatetracyclic compounds referable to tetracyclines of known activity.

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