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DIMERIZATION OF 1-METHYL PYRIDAZINIUM SALTS BY THE ACTION OF CYANIDE ION
FORMATION OF THE DIMERS WITH CYCLOBUTANE RING[1)]

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Concerning the reaction of the quaternary salts of pyridazines with cyanide, it has already been reported that pyridazine 1-oxides afforded 6-cyanopyridazines[2)], suggesting α-position to the N-oxide group is sensitive to the cyanation, and that 3,3'-bipyridazine 1,1'-dioxides gave the tetrahydro compounds[3)], which have cyano groups at the 6- and 6'-positions. As for the reaction of the pyridazines lacking the N-oxide groups with cyanide ion, only our report[3)] was published, describing the formation of 1,1'-dimethyl-4,4'-dicyano-1,1',4,4'-tetrahydro-3,3'-bipyridazines from 3,3'-bipyridazines.

This paper deals with the reaction of 1-methyl pyridazinium salts with potassium cyanide. Interestingly, as the result, two kinds of dimers having cyclobutane ring were obtained.

3-Substituted pyridazines (I) were converted into 1-methyl pyridazinium salts[4)] by the reaction with dimethyl sulfate, which were then allowed to react with 2-3 moles of KCN in water at 0-5^{o} under stirring. The reaction mixture was then extracted with CH_2Cl_2. The products thus obtained were separated by column chromatography on alumina to afford two kinds of dimers, III and IV, in 10-20% and 2-5% yields, respectively. Besides these products, two kinds of monomeric compounds*, V and VI, were obtained in the yields below 2%, respectively.

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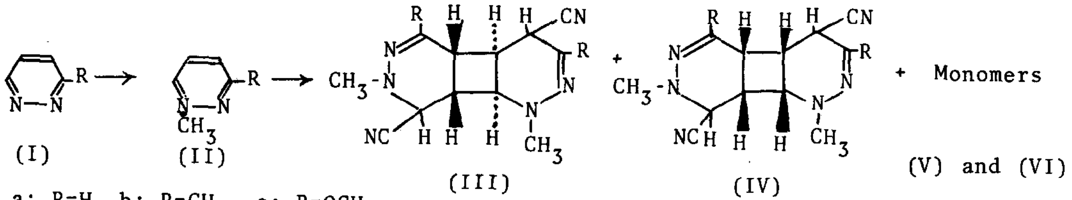
*) V; 1-methyl-6-cyano-4-pyridazinones, VI; 1-methyl-4-cyano-6-pyridazinones. 4-Methyl-, 3,6-dimethyl-, 4,5-dimethyl-, and 3-methyl-6-methoxy-pyridazines were allowed to react in a similar condition, affording no dimers, but the cyano substituted monomers, on which a paper will be published elsewhere.



a: R=H, b: $R=CH_3$, c: $R=OCH_3$

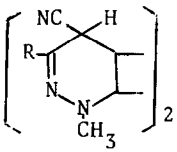
Spectral data of the dimers were shown in Table I, indicating the coupling of two molecules of the cyanated compound of (II) to form the dimer, which were inferred from the values of the elementary analyses and the molecular weight determinations. Their IR spectra exhibit common absorptions at 2240-2260 cm^{-1} due to CN, and 850-950 cm^{-1} due to the cyclobutane ring[5]. Furthermore, the spectra of NMR also suggest the structure of the dimers having the cyclobutane rings.

TABLE I. NMR Spectral Data

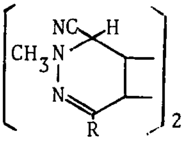
Dimers		m.p. °C	$N-CH_3$ 1 and 1'	H_6 and $H_{6'}$	H_4 and $H_{4'}$	H_5 and $H_{5'}$	miscellaneous
a	III	162-163	3.08, 2.99	3.98, 3.47	2.7-3.2	1.8-2.3	H_3 and $H_{3'}$ 6.55, 7.11
	IV	151-152	3.05, 2.92	3.89, 3.81	2.8-3.2	2.0-2.2	7.69, 7.90
b	III	174-175	2.97, 2.87	3.90, 3.60	3.0, 2.65	1.6-2.2	3- and 3'-CH_3 2.12, 1.90
	IV	155-156	3.09, 2.92	3.91, 3.52	2.9-3.2	1.6-2.4	2.55, 1.96
c	III	194-195	2.88, 2.83	3.89, 3.71	3.18, 2.45	1.6-1.8	3- and 3'-OCH_3 3.78, 3.67
	IV	175-176	2.78, 2.68	3.98, 3.98	3.05, 2.6-2.9	1.9-2.1	3.79, 3.60

If the cyano substituted dihydro compounds are allowed to dimerize at 5- and 6- or 4- and 5-positions, similar to the photo-dimerization, the structures of the dimers should be VII and VIII. In these cases, the coupling of either "head to head" or "head to tail" should result in the formation of the symmetric compounds, whose chemical shifts of the $N-CH_3$, and the two CH_3- and CH_3O- groups must be coincidental of each other. Thus, these structures (VII and VIII) are denied. When the dimerization occurs at 2- and 3-positions to form the compound (IX), there must be protons attached to the carbon-carbon double bond. So the structure (IX) should also be abandoned from the NMR spectral data.

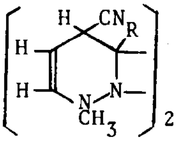
The structure (X), in which 4- and 6'-positions and 5- and 5'-positions are bonded to each other, can not be excluded from the NMR spectral data.



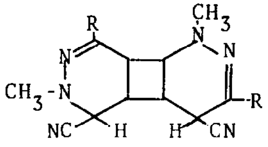
(VII)



(VIII)



(IX)

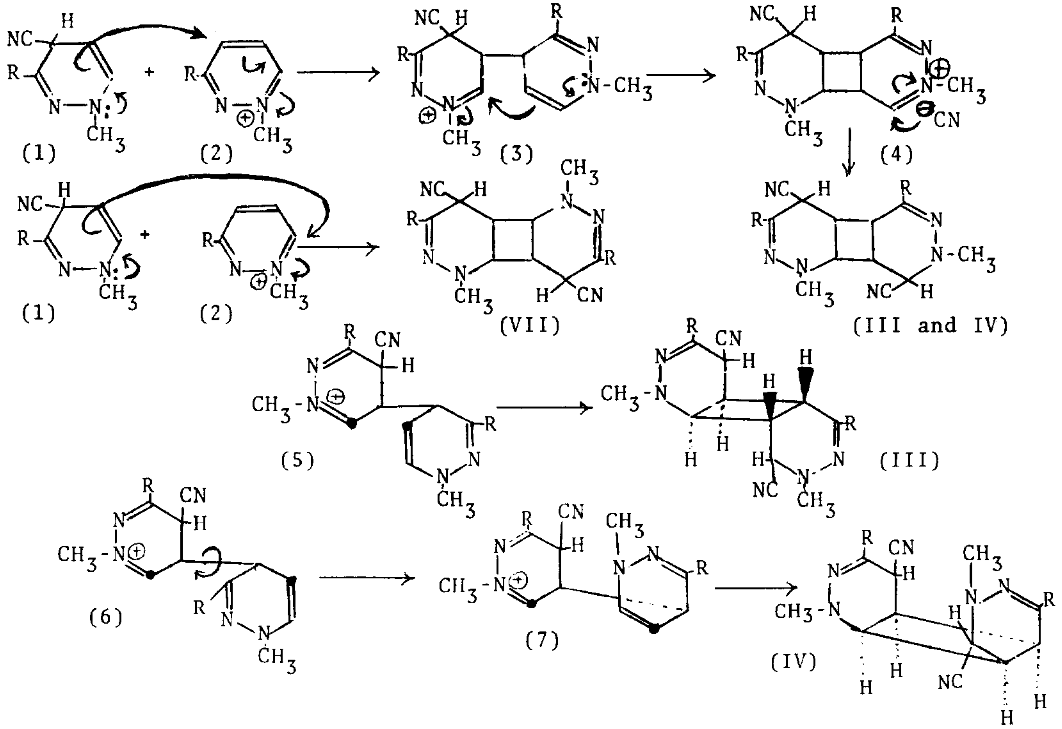


(X)

But, from the mechanistic consideration, the dimer formed by bonding 4- and 5'-positions and 5- and 6'-positions to each other, is more plausible. And the major product seems to be anti-isomer, and the minor product seems to be syn-isomer. However this isomerism is not still definite from the present data.

The signals of NMR spectra are shown in Table, and their assignments are reasonable. High field shifts of H_5- and $H_{5'}$-protons seem to be due to the effect of the cyano groups.

This reaction was also carried out in the dark room, obtaining the same results. Therefore, this dimerization is not due to the photo-sensitized reaction but rather apparently to the thermal reaction.



Concerning the formation of these dimers, the following mechanism cab be proposed as the most reasonable. 4-Cyano-dihydro compound (1) couples with the quaternary salt (2) at the 4-position to form the compound (3), followed by the formation of the cyclobutane ring (4) and the addition of the cyano anion. When (1) couples with (2) at the 6-position, the compound (VII) will be formed, but it has formerly denied.

As for the formation of the stereoisomers, the intermediate compound (3) has a possibility of being two kinds of stereoisomers, (5) and (6). The compound (5) is capable of joining directly to form the anti-dimer (III), whereas the compound (6) is able to join after rotation of the half moiety of the molecule by 180^o, forming the syn-dimer (IV). The absolute configurations of CN and N-CH_3 groups are uncertain from the present data. Accordingly, the possibility can not be excluded that two kinds of dimers are stereoisomers in regard to CN groups of the syn-dimer (IV), although it is denied from NMR spectral data to be stereoisomers of the anti-dimer (III). In order to clarify the definite structural correlation between two kinds of dimers in question, the examination by X ray are now being undertaken.

On the formation of dimers having the cyclobutane ring many reports have been published, most of which concerned the photo-sensitized dimerization. In the case of the Reissert compound of quinoline, the photochemical formation of the dimer has been reported6). And the reaction of pyridinium salts7) with cyanide afforded the dimer, 1,1'-dihydro-4,4'-bipyridyl, in which no cyano groups are added. Therefore, it is interesting that the aromatic amines afford the dimer having the cyclobutane ring by the thermal reaction, and further investigations are now underway.

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