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Studies on the Structures of Diazine N-Oxides. II.[*1] Dipole Moments of Some Alkoxy-derivatives of Pyrimidine, Pyridazine and their N-Oxides.

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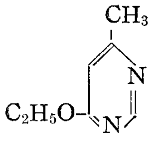
In previous paper,[*1] the authors reported on the structures of 2-substituted alkoxyquinoxaline N-oxide, in which the oxygen atom was proved to attach to the nitrogen atom distant from the alkoxyl group by the results of dipole moment measurements. Because of the fact that the observed dipole moments agreed with the calculated ones for the conformation of the alkoxyl group oriented towards the outer side of nitrogen atom in 1-position, the authors concluded that the nitrogen atom in 1-position was under the interference of the alkoxyl group, that is due to the electro-static induction between the lone pair electron of nitrogen atom in 1-position and the hydrogen of alkoxyl group.

Recently, Hayashi, *et al.*[1)] showed that the N-oxidation of monoalkoxydiazines, whose respective alkoxyl group is attached to the neighboring position of nitrogen atom, takes place always at the nitrogen atom distant from the alkoxyl group. They explained these results from the steric hindrance of the alkoxyl groups.

With the purpose of verifying this assumption, present authors attempted to determine the geometrical arrangement of substituents relating to N-oxide in diazine-ring by means of dipole moment measurements. This paper describes the structures of some diazines, such as pyrimidine, pyridazine and their N-oxides, compounds (I) to (VIII), as to whether the N-oxide group is near or distant from the substituent on the diazine nucleus, from the experimental data obtained by the measurement of the dipole moment.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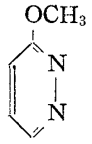
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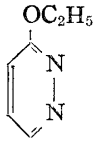
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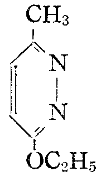
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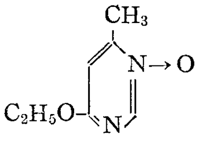
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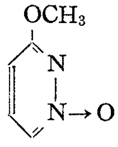
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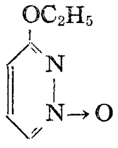
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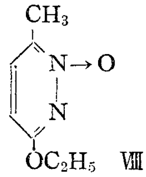
VIII

Experimental

All the measurements were carried out in benzene solution at 25° and in 40% moisture controlled under air conditioning.

The dielectric constants were measured with the apparatus by the phase compensation method[2)] described in the previous paper.[*1]

The materials used were synthesized according to the methods known on the literatures, and in purification of the same compounds the chromatographic procedures on alumina were employed. The melting or boiling points of these compounds showed good agreement with values in the literatures.

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1) E. Hayashi, T. Higashino, C. Iijima, Y. Kono, T. Doihara : Yakugaku Zasshi, 82, 584 (1962).

2) M. Ishidate, Y. Kamura, K. Nagano : *Ibid.*, **77**, 407 (1957).

4-Ethoxy-6-methylpyrimidine (I), b.p. 182~183°.[3a)] 4-Ethoxy-6-methylpyrimidine 1-oxide (II), m.p. 120~121°.[3a)] 3-Methoxypyridazine (III), b.p$_{13}$ 85~86°.[3b)] 3-Methoxypyridazine 1-oxide (IV), b.p$_{10}$ 150°.[3c)] 3-Ethoxypyridazine (V) and its 1-oxide (VI) were prepared by the same methods as for the cases of III and IV. V, b.p$_{14}$ 91~93°. *Anal.* Calcd. for $C_6H_8ON_2$: C, 58.05; H, 6.50; N, 22.57. Found: C, 58.07; H, 5.83; N, 22.52. VI, m.p. 65~67°. *Anal.* Calcd. for $C_6H_8O_2N_2$: C, 51.42; H, 5.78; N, 19.99. Found: C, 51.28; H, 4.90; N, 20.69. 3-Ethoxy-6-methylpyridazine (VII), b.p$_{20}$ 114~115°.[3d)] 3-Ethoxy-6-methylpyridazine 1-oxide (VIII), m.p. 91~92°.[3d)]

Results and Discussion

The total polarization of the solute was calculated from the dielectric constant and the specific volume of solutions according to the equation introduced by Halverstadt and Kumler.[4)] The deformation polarization of each compound was assumed to be 1.05 times as large as the molar refractions. The results obtained were listed in Table I, where the α and β denoted respectively the change of dielectric constant and density of the solutions with the weight fraction of the solute.

TABLE I. Dipole Moments of Some Alkoxy-derivatives of Pyrimidine, Pyridazine and their N-Oxides in Benzene Solution at 25°

Comp. No.	α	β	P_A+P_E (ml.)	μD
I	4.35	0.37	40.49	2.20
II	11.50	0.40	42.35	3.95
III	8.72	0.43	30.88	2.87
IV	20.20	0.35	32.75	4.80
V	9.03	0.24	35.76	3.17
VI	17.82	0.27	37.63	4.76
VII	9.85	0.41	40.64	2.86
VIII	18.81	0.31	42.51	5.11

The theoretical dipole moment of each compound was calculated assuming the next provisions. The moments of pyrimidine, pyridazine and their N-oxides are equal to the vector sums of the moments of two pyridines (2.22 D),[5)] or pyridine and its N-oxide (4.24 D).[5)] This assumption was justified through fair agreement of the calculated values, 2.22, 3.85, and 5.63 D, of pyrimidine, pyridazine and 3-methylpyridazine N-oxide with the observed values of respective 2.36,[6)] 3.94,[7)] and 5.23 D.[8)] The moments of methyl and methoxyl group were taken as equal with those of toluene, 0.37 D[7)] and anisol, 1.28 D,[9)] respectively, and as the moment of ethoxyl group was used that of anisol in place of phenetol.

As seen in Fig. 1, the vectorical moments of these compounds were devided into two axis parts, parallel (μx) and perpendiculer (μy), and each components were added up together and the calculations were made by the next equation.

$$\mu=\sqrt{\mu x^2+\mu y^2}$$

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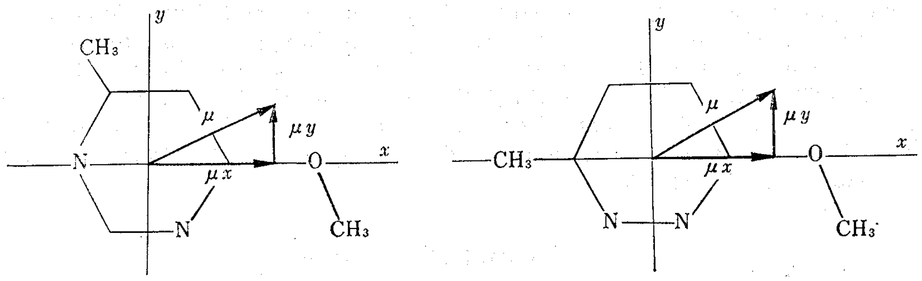

Fig. 1.

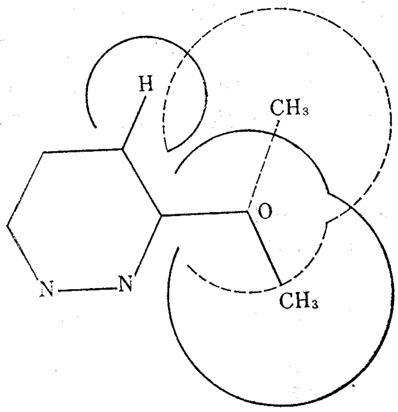

Fig. 2.

——— *cis* form
– – – *trans* form

Concerning the structure of alkoxyl group, it has been well known that the O-alkyl group is co-planer with the hetero-ring, as the oxygen atom takes a form of the sp^2 hybrid orbital, and the 2 *Pz* electrons belonging to the oxygen atom conjugate with the π electron system of the hetero-ring. Hence the direction of the moment of alkoxyl group is considered to maintain the angle of 108°[9] with x axis. The *cis* form means the conformation in which the alkyl group attached to the oxygen atom bends towards the near-by nitrogen atom. And to the contrary, the conformation of alkyl group bending far from the nitrogen atom is called *trans* form. In Fig. 2, the schematic relations of the spacial arrangements are presented by the bond lengths and the bond angles, referred to from the description of Sutton, *et al.*[10] The calculations thus obtained and observations are summarized in Table II.

In the alkoxy derivatives of diazine and their N-oxides, comparing the observed values with the calculated, the former is consistent with the moment of *cis* forms. It may be true that the forced conformation of *cis* form results from the aforementioned static relations and the repulsion between the ring-hydrogen of neighboring position and the alkoxyl group, as shown in Fig. 2. On the N-oxidation, it may therefore be explained that the reaction here is inhibited by the steric hindrance, and another nitrogen atom should be available. And in fact, it seemed to be that the dipole moments of mono N-oxides of alkoxy-diazine favor the structures of the N-oxides distant from the alkoxyl group, as shown in Table II.

On the alkoxyl derivatives of diazine and their N-oxides, appreciable discrepancy between the moment values calculated and observed is probably due to the electro-static interaction and the mesomeric moment, between the hetero or the hetero N-oxide ring and the alkoxyl group.

In addition, at the structures of diazines whose positions of two nitrogen atoms are respectively located at *p*- and *m*-positions, *i.e.* quinoxaline and pyrimidine, relatively large differences between calculated values of *cis* 1-oxide and the other *cis* N-oxide are noticed, and the determination of these N-oxide structures by means of dipole moment measurements would be justifiable. But on the pyridazine compounds in which the two nitrogen atoms at *o*-position, the calculated values of both *cis* forms of 1-oxide and 2-oxide are rather too close to be distinguished from each other with the experimental errors. In these geometrical configuration, the effective small values are incapable of deciding the correlation, and the other determination of chemical method

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10) K. B. Everard, L. E. Sutton: J. Chem. Soc., **1949**, 2312.

Table II. Comparison of the Dipole Moments calculated and observed in Some Alkoxy-diazine Compounds

Compd. No.	Conformation of alkoxyl group	Position of N-oxide	Calcd.	Found	Difference
I	*cis*		$\underline{1.67}$	2.20	0.53
	trans		3.60		−1.40
II	*cis*	1-oxide	2.79	3.95	1.16
		3-oxide	$\underline{3.49}$		0.46
	trans	1-oxide	5.12		−1.17
		3-oxide	4.71		−0.76
III	*cis*		$\underline{2.66}$	2.87	0.21
	trans		5.08		−2.21
IV	*cis*	1-oxide	$\underline{4.60}$	4.80	0.20
		2-oxide	4.42		0.38
	trans	1-oxide	6.96		−2.16
		2-oxide	6.84		−2.06
V	*cis*		$\underline{2.66}$	3.17	0.51
	trans		5.08		−1.91
VI	*cis*	1-oxide	$\underline{4.60}$	4.76	0.16
		2-oxide	4.42		0.33
	trans	1-oxide	6.96		−2.20
		2-oxide	6.84		−2.08
VII	*cis*		$\underline{2.63}$	2.86	0.23
	trans		5.06		−2.20
VIII	*cis*	1-oxide	$\underline{4.50}$	5.11	0.61
		2-oxide	4.39		0.72
	trans	1-oxide	6.89		−1.78
		2-oxide	6.72		−1.61

should be employed. But as well as in the case of other alkoxy-diazine, the *cis* form of 1-oxide structure may be supported considering the steric hindrance caused by the bending structure of alkoxyl group.

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Summary

The dipole moments of some pyrimidine, pyridazine, and their N-oxides (I to VIII) were measured in benzene solution at 25°.

In alkoxy derivatives, the moments of two forms, *cis* and *trans* were considered by the bending structure of alkoxyl group, and the respective vectorical sums were calculated.

Alkoxydiazines whose respective alkoxyl group is attached to the neighboring position of nitrogen atom showed all to exist as *cis* form. By the steric hindrance of *cis* form, in the alkoxy-diazine mono N-oxide the oxygen atom was postulated to attach to the nitrogen atom distant from the alkoxyl group.

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