Mathematical treatment of $[\phi]$ values of acetyl-cycloheximides also leads to the same conclusion as above. Moreover, this treatment shows that contribution of axial (2S)-2-methyl group is represented as $[\phi]_B-[\phi]_I$ (=2,348°), provided that the contribution of equatorial 2-methyl group is ignored.[*3,*4]

Recently, Lawes[4)] found that cycloheximide undergoes pyrolysis at about 200° to afford (2S:4R)-2,4-dimethylcyclohexanone and further, from conformational considerations and known isomerization reactions,[5)] he deduced the configuration of cycloheximide tentatively as depicted as (IV) or (VI). This is different from the conclusion reached in the present series of considerations, but his experimental observations are also well explicable from the structure assigned by the present authors.

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[*3] The contribution of axial (2S)-2-methyl group is correctly represented as $[\phi]_B-[\phi]_I-X_e$, in which X_e is the contribution of equatorial (2S)-2-methyl group.

[*4] Effect of the bulky substituent at C-2 position of equatorial orientation was treated by Prof. C. Djerassi (J. Am. Chem. Soc., 83, 3334 (1961)).

4) B.C. Lawes: Private Communication (cf. Abstracts of Papers, 139th Meeting of the American Chemical Society, 1961, p. 33N).

5) A.J. Lemin, J.H. Ford: J. Org. Chem., 25, 344 (1960).

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Reaction of Dehydroacetic Acid under a Mild Condition

It was reported in previous papers[1)] that dehydroacetic acid is very reactive with ammonia, primary amines, and some of the compounds possessing amino group, such as amino acids and sulfanilamides. The structure of the primary reaction product easily formed from them under a mild condition was deduced to be Schiff base-type compound derived from the combination of $\rangle$C=O group of 3-acyl side-chain of dehydro-acetic acid and NH_2 group in the amino compound.

Later, it became necessary to investigate the question of whether or not the reaction of dehydroacetic acid always stopped at the formation of a Schiff base in solution. Therefore, the reaction between dehydroacetic acid and amino compounds was reëxamined in view of the expectation that the primary reaction product (Schiff base) might change secondarily in solution, at least to a certain extent, even under a mild condition. For this purpose, the experiment was first carried out using ammonia and methylamine. The test solutions were prepared by adding dehydroacetic acid (1 g.) into the solution (50 cc.) of various concentrations of ammonia or methylamine, and kept in an incubator (37°). Progress of the reaction was traced periodically by paper chromatography. As was

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1) S. Iguchi, *et al.*: Yakugaku Zasshi, **77**, 1258 (1957); This Bulletin, **7**, 323 (1959); *Ibid.*, 8, 1 (1960).

expected, pyridone derivatives, which were assumed to be produced by transformation from the primary product, were clearly recognized in all the test solutions. For example, in the case of 10% ammonia, lutidone was detected after 24 hours, and it became more predominant in the solution after 48 hours, in proportion to the disappearance of unchanged dehydroacetic acid and dehydroacetic acid-imide (the primary product). A similar tendency was seen more markedly and rapidly beyond the expectation in methylamine solution. The formation of N-methyllutidone was recognized already 1 hour after the addition of dehydroacetic acid into 5% methylamine solution, and after 24 hours, unchanged dehydroacetic acid and 3-methyliminoethyl-4-hydroxy-6-methyl-2-pyrone (the primary product) could no longer be detected by paper chromatography, with formation of N-methyllutidone. Similar phenomenon was also observed in ammonium chloride solution (10%), though a far longer time was necessary in this case. This experiment has demonstrated the marked reactivity of dehydroacetic acid, especially the ease with which dehydroacetic acid was transformed even under a mild condition.

Detail of this work will be reported in the near future.

Throughout the experiment, Dragendorff reagent was used as a spraying reagent and BuOH-AcOH-H_2O (4:1:5) system as the developing solvent in paper chromatography.

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Separation and Structure of 3-Methylpyridazine 1-Oxide and 2-Oxide

Recently, N-oxidation of 3-methylpyridazine (II) with hydrogen peroxide in glacial acetic acid was reported by Kumagai,[1] who obtained a mono-N-oxide as hygroscopic crystals, $b.p_6$ 145°, but whether this mono-N-oxide is 1-oxide (IV) or 2-oxide (III), or a mixture of (IV) and (III) remained to be determined. The present writers prepared 3-methylpyridazine N-oxide according to the procedure of Kumagai. By a gas-chromatographic procedure, the product gave two distinct peaks, with no evidence of decomposition on the column. Conditions suitable for effective separation were found through the use of a Thermol-2 (Shimadzu), 3m. × 6mm., column at 180° and hydrogen flow rate of 200 cc./min. The product (2.4 g.) was dissolved in benzene, chromatographed on alumina, and the column was eluted with benzene and chloroform. The fraction eluted with benzene gave, after recrystallization from benzene, 630 mg. of (III) as colorless prisms, m.p. 83~84°; UV λ_{max}^{EtOH} mμ (log ε) : 257 (4.00), 314 (3.68). *Anal.* Calcd. for $C_5H_6ON_2$: C, 54.54; H, 5.49; N, 25.44. Found: C, 54.76; H, 5.60; N, 25.29.

The fraction eluted with chloroform gave, after recrystallization from benzene, 230 mg. of (IV) as very hygroscopic crystals, m.p. 68.5~69.5°; UV λ_{max}^{EtOH} mμ (log ε) : 262 (4.03), 312 (3.72). *Anal.* Calcd. for $C_5H_6ON_2$: C, 54.54; H, 5.49; N, 25.44. Found : C, 54.59;

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1) M. Kumagai : Nippon Kagaku Zasshi, 81, 1148 (1960).