ment solution. The detailed report concerning to the triple point procedures will be published in near future.

The extent of interference by metabolic products of the drug was assayed by a countercurrent distribution technique (Fig. 4) and ultraviolet absorption spectrum (Fig. 5), and the results indicated that the material was at least 93% pure.

The authors wish to thank Eisai Co., Ltd., for their supply of 2-methyl-3-*o*-tolyl-4(3*H*)-quinazolinone (Hyminal).

Summary

Two methods are described for the estimation of 2-methyl-3-*o*-tolyl-4(3*H*)-quinazolinone (MTQ) in biological fluids and tissues. In the first, MTQ is extracted from alkalinized biological material with hexane, the solvent is evaporated, and the residue is dissolved in dilute hydrochloric acid, and measured spectrophotometrically at 234 mμ.

The second, suitable for tissues, is the method in which normal biological blank becomes negligible by geometrical treatment of its absorbances at three wave lengths.

These procedures permit the determination of MTQ in amounts as 1 μg./cc. of final measurement solution. The methods are specific for MTQ in that they do not include any transformation products of the compound.

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14. Yasuo Makisumi and Hideo Kanō : Studies on the Azaindolizine Compounds. XII.*2 Alkyl Rearrangement of 5-Methyl-7-alkoxy-*s*-triazolo[1,5-*a*]pyrimidines.

(*Research Laboratory, Shionogi & Co., Ltd.**1)

It has been known that the lactim ethers of configuration I will undergo rearrangement to their isomeric and stable lactam form II. These transformations are irreversible and can be brought about by the application of heat or through the influence of special catalytic agents, and have been observed to take place in both acyclic and cyclic compounds.

I II

This interesting rearrangement has been illustrated by Hilbert and Johnson[1] in the pyrimidine series and this study has been extended by Chi and co-workers.[2] So, a similar rearrangement in the *s*-triazolo[1,5-*a*]pyrimidine series was investigated.

The present paper deals with the synthesis, property, and alkyl rearrangment of 5-methyl-7-alkoxy-*s*-triazolo[1,5-*a*]pyrimidines.

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*1 Fukushima-ku, Osaka (牧角徳夫, 加納日出夫).

*2 Part XI : This Bulletin, **10**, 620 (1962).

1) G. E. Hilbert, T. B. Johnson : J. Am. Chem. Soc., **52**, 2001 (1930).

2) Y. F. Chi, C. Wei, N. S. Pan : J. Am. Chem. Soc., **60**, 1719 (1938).

In the previous paper of this series,[3] the authors reported that the reaction of 5-methyl-7-chloro-*s*-triazolo[1,5-*a*]pyrimidine (III) with sodium ethoxide in ethanol gave the corresponding 7-ethoxy derivative*[3] (IVb). However, it was reported by Allen and co-workers[4] that 5-methyl-7-methoxy-*s*-triazolo[1,5-*a*]pyrimidine (IVa) could not be obtained from III and sodium methoxide in dehydrous methanol, only 5-methyl-*s*-triazolo[1,5-*a*]pyrimidin-7-ol (V) being obtained. Therefore, synthesis of IVa was examined in accordance with the Allen's report.

The product which was obtained from reaction of III with equimolar amount of sodium methoxide in dehydrous methanol at room temperature, was purified by alumina chromatography using chloroform as a developing solvent at below room temperature. One substance, $C_7H_8ON_4$ which showed the double melting points at 163~164° and 205~220°, was obtained. This compound showed one spot in the paper partition chromatography (PPC) and an absorption band of the aromatic ether group at 1015 cm^{-1} in the infrared spectrum. Therefore, the structure of this compound was established to be IVa. When IVa was recrystallized from benzene, although the resulting crystals showed the same formula as IVa in the elemental analysis, those did not show the constant melting point. Moreover, those showed two small spots in addition to that of IVa in the PPC and a weak absorption band of the carbonyl group at 1710 cm^{-1} besides that of the aromatic ether group in the infrared spectrum. Such behavior was also observed when IVa was heated without solvent. Therefore, it was supposed that the crystals which were recrystallized from benzene, would contain two isomers of IVa possessing the carbonyl group and that IVa would be partially transformed to the above mentioned isomers on heating.

On the other hand, the property of the ethoxy derivative IVb which was obtained from III and sodium ethoxide in the previous work,[3] was investigated. IVb which was recrystallized from benzene, showed the constant melting point at 149~150°, an absorption band of the aromatic ether group at 1023 cm^{-1} in the infrared spectrum, and one spot in the PPC. Therefore, it was confirmed that IVb preparing in the previous work, is the sole 5-methyl-7-ethoxy-*s*-triazolo[1,5-*a*]pyrimidine and more stable than IVa on heating.

When IVa was heated at 180° for thirty minutes, the resulting solids showed two spots which differed from that of IVa in the PPC and those were separated to two isomers (VIa and VIIa) of the starting material by alumina chromatography. The first eluted product VIa, m.p. 248~249° and the second eluted product VIIa, m.p. 260~261° both showed an absorption band of the carbonyl group at 1711 cm^{-1} in each infrared spectrum and these both products were not identical with the known C-methyl derivatives (Xa and XIa). Therefore, VIa and VIIa must be any of three N-methyl derivatives, respectively. From the results of the experiments described below, VIa and VIIa were established to be 4,5-dimethyl-*s*-triazolo[1,5-*a*]pyrimidin-7(4*H*)-one and 3,5-dimethyl-*s*-triazolo[1,5-*a*]pyrimidin-7(3*H*)-one.

Similarly, the solids which were obtained by heating of IVb at 200° for one hour, were separated to one product (IX) and two isomers (VIb and VIIb) of the starting material by alumina chromatography using chloroform as a developing solvent. The first eluted product IX could not be investigated in detail because of a very low yield. But it is clear that IX can never be any of the known C-ethyl derivatives (Xb and XIb) and N-ethyl derivatives (VIb~VIIIb), because IX showed an absorption band of the nitrile group at 2236 cm^{-1} and not that of the carbonyl group in the infrared spectrum. The

*[3] This compoud was described as 5-ethoxy-7-methyl-*s*-triazolo[4,3-*a*]pyrimidine in the previous paper,[3] but that was corrected to IVb by the authors [This Bulletin, **7**, 903 (1959)].

3) H. Kanō, Y. Makisumi : This Bulletin, **6**, 583 (1958).

4) C.F.H. Allen, G.A. Reynolds, J.F. Tinker, L.A. Williams : J. Org. Chem., **25**, 361 (1960).

other products VIb and VIIb showed an absorption band of the carbonyl group at 1699 and 1698 cm^{-1} respectively in the infrared spectrum and were non-identical with the C-ethyl derivatives (Xb and XIb). Therefore, VIb and VIIb also must be any of the three N-ethyl derivatives. From the results of the following experiments, VIb and VIIb were established to be 4-ethyl-5-methyl-*s*-triazolo[1,5-*a*]pyrimidin-7(4*H*)-one and 3-ethyl-5-methyl-*s*-triazolo[1,5-*a*]pyrimidin-7(3*H*)-one.

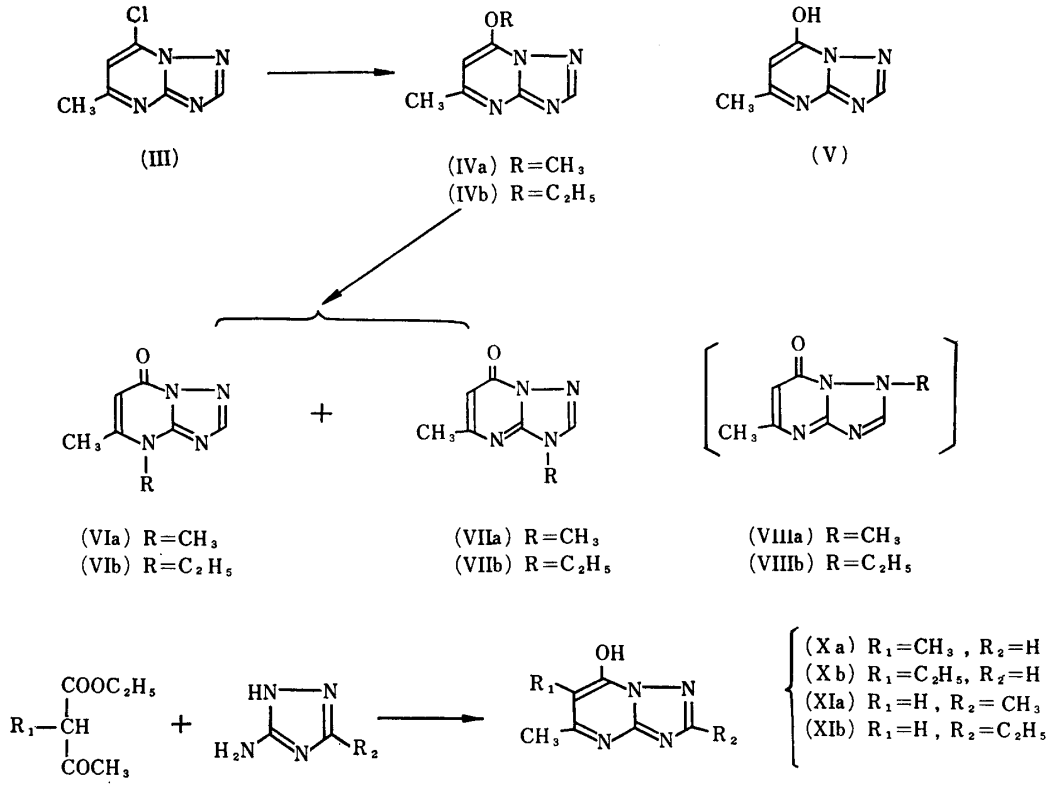

Chart 1.

Table I. Rf Value of the *s*-Triazolo[1,5-*a*]pyrimidine Derivatives

Compd.	IVa	VIa	VIIa	IVb	VIb	VIIb
Rf	0.66	0.51	0.56	0.75	0.65	0.70

In order to determine the structure of the above-mentioned products (VIa, VIIa, VIb, and VIIb), synthesis of the N-alkyl derivatives of V was investigated. As the intermediates, the N-alkyl derivatives of 5-amino-*s*-triazole were prepared by reaction of 1-alkyl-2-aminoguanidinium sulfate[5] with formic acid. Heating of 1-methyl-2-aminoguanidinium sulfate XIIa with 98~100% formic acid on a steam bath for fifteen hours gave the formylated product XIIIa, which was treated with sodium carbonate to the N-methyl derivatives (XIVa and XVa) of 5-amino-*s*-triazole. The main product XVa which was difficultly soluble in ethanol, was assigned as 4-methyl-5-amino-*s*-triazole and the by-product XIVa which was easily soluble in ethanol, was assigned as 5-methylamino-*s*-triazole from the results of elemental analysis and the diazo-coupling test. Moreover, XIVa was identified with 5-methylamino-*s*-triazole which was obtained by hydrolysis of 5,8-dimethyl-*s*-triazolo[4,3-*a*]pyrimidin-7(8*H*)-one[6] (XVIII) with aqueous potassium hydroxide. Similarly, 5-ethylamino-*s*-triazole (XIVb) and 4-ethyl-5-amino-*s*-triazole (XVb)

5) G. W. Kirsten, G. B. L. Smith : J. Am. Chem. Soc., **58**, 800 (1936).
6) K. Shirakawa : Yakugaku Zasshi, **78**, 1395 (1958).

were prepared from 1-ethyl-2-aminoguanidinium sulfate (XIIIb) and the structure of these products were proved by the results of elemental analysis and the diazo-coupling test.

Condensation of XIVa with ethyl acetoacetate in boiling glacial acetic acid gave two products isomeric to each other. The main product was determined to be 4,5-dimethyl-*s*-triazolo[1,5-*a*]pyrimidin-7(4*H*)-one by the results of elemental analysis and the spectral evidence described below and then this product was identified by mixed melting point and the infrared spectrum with VIa obtained from IVa above. The by-product was also identified by the same methods with 4,7-dimethyl-*s*-triazolo[1,5-*a*]pyrimidin-5(4*H*)-one (XVIa) which was obtained by isomerization*4 of XVIII on heating in aqueous piperidine. When this condensation reaction without solvent at 170~200° for thirty minutes was carried out, XVIa as a main product and VIa as a by-product were obtained. Similarly, condensation of XIVb with ethyl acetoacetate in glacial acetic acid afforded 4-ethyl-5-methyl-*s*-triazolo[1,5-*a*]pyrimidin-7(4*H*)-one as a main product and 4-ethyl-7-methyl-*s*-triazolo[1,5-*a*]pyrimidin-5(4*H*)-one (XVIb) as a by-product. The former was identified by mixed melting point and the infrared spectrum with VIb obtained by heating of IVb as above. When this reaction without solvent was carried out, XVIb as a main product and VIb as a by-product were obtained. The structure of these products were detected from the results of elemental analysis and spectral evidence.

On the other hand, condensation of XVa with ethyl acetoacetate in glacial acetic acid or without solvent on heating gave only the product, whose structure was determined to be 3,5-dimethyl-*s*-triazolo[1,5-*a*]pyrimidin-7(3*H*)-one by elemental analysis and the spectral evidence described below and this product was identified with VIIa obtained from IVa on heating. A similar reaction on XVb afforded only 3-ethyl-5-methyl-*s*-triazolo[1,5-*a*]-pyrimidin-7(3*H*)-one which was identified with VIIb. In these reactions, XVIIa and XVIIb were not obtained.

The absorption spectra of the six condensates which were obtained as above, were measured. All condensates showed an absorption band of the carbonyl group in the infrared spectrum. The four *s*-triazolo[1,5-*a*]pyrimidin-7-one derivatives (VIa, VIIa, VIb,

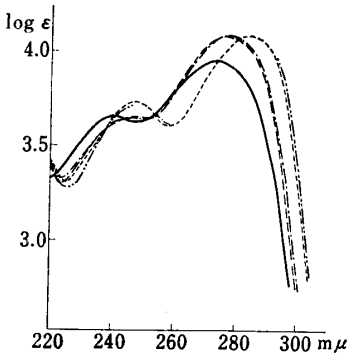

Fig. 1. Ultraviolet Absorption Spectra of the *s*-Triazolo[1,5-*a*]pyrimidin-7(3*H* or 4*H*)-one Derivatives (in EtOH)

——— XIX ------ VIb
— — — VIa —·—·— VIIb
····· VIIa

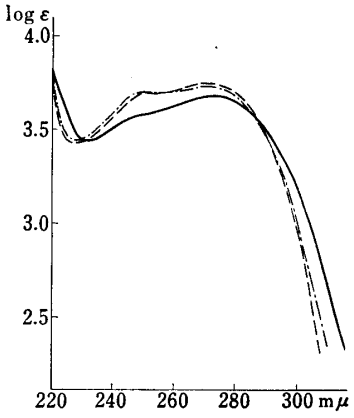

Fig. 2. Ultraviolet Absorption Spectra of the *s*-Triazolo[1,5-*a*]pyrimidin-5(3*H* or 4*H*)-one Derivatives (in EtOH)

——— XX
— — — XVIa
------ XVIb

*4 Such isomerization to *s*-triazolo[1,5-*a*]pyrimidine derivatives from *s*-triazolo[4,3-*a*]pyrimidine derivatives was discovered by K. Shirakawa.[6]

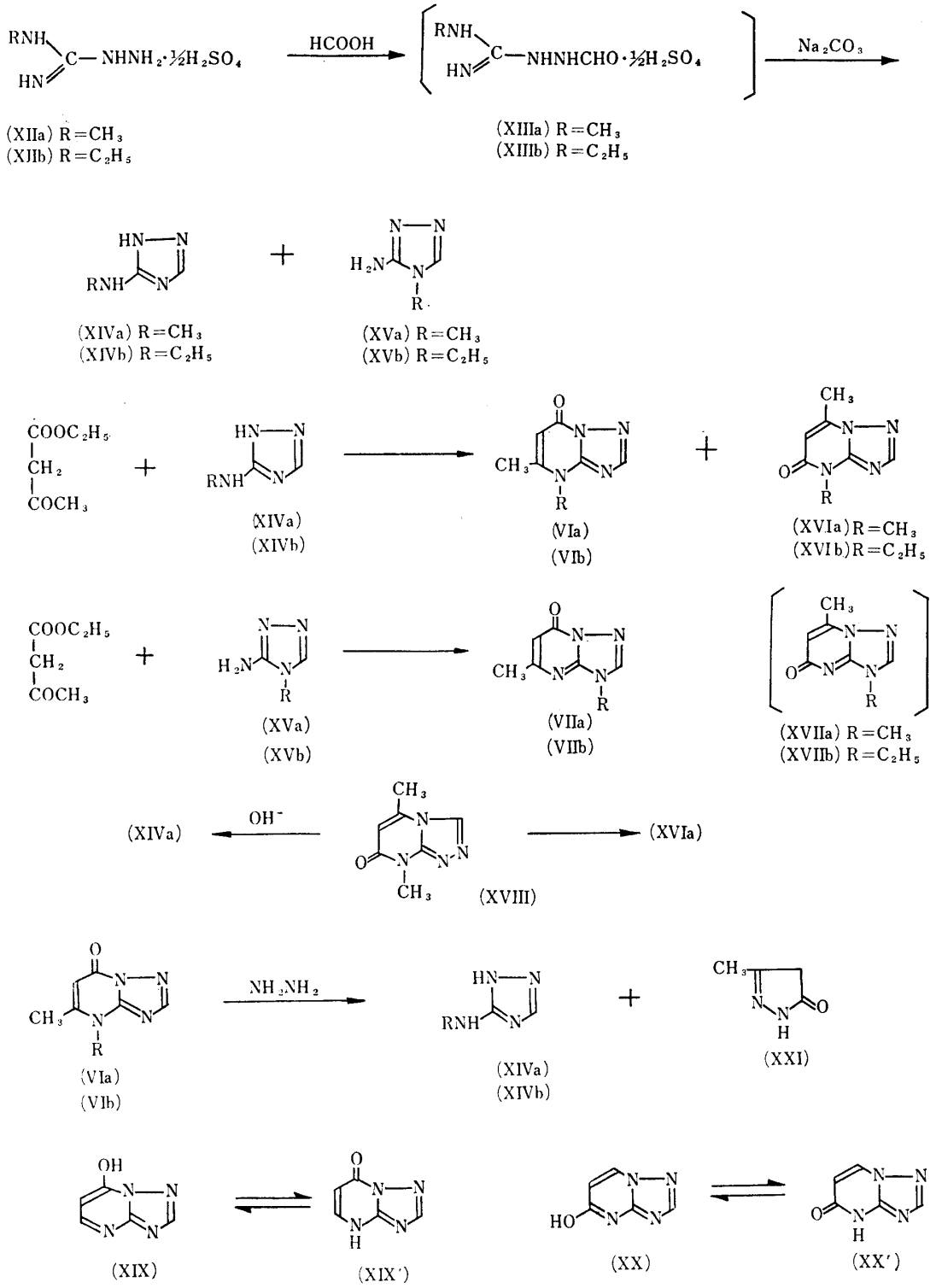

Chart 2.

and VIIb) showed the similar curve to that of *s*-triazolo[1,5-*a*]pyrimidine-7-ol[7] *5 (XIX) and the two *s*-triazolo[1,5-*a*]pyrimidin-5(4*H*)-one derivatives (XVIa and XVIb) showed the similar curve to that of *s*-triazolo[1,5-*a*]pyrimidin-5-ol[8] *5 (XX) in the ultraviolet spectrum (see Figs. 1 and 2).

*5 It is supposed that these compounds (XIX and XX) exist as the lactam forms (XIX' and XX') in the solid state or neutral medium, because XIX and XX show an absorption band of the carbonyl at 1704 and 1683 cm^{-1} in the infrared spectrum (in Nujol mull).

7) Y. Makisumi, H. Kanō: This Bulletin, **7**, 907 (1959). 8) *Idem*: *Ibid.*, **9**, 801 (1961).

Ring cleavage of 4-alkyl-5-methyl-*s*-triazolo[1,5-*a*]pyrimidin-7(4*H*)-one (VIa and VIb) was attempted. Heating of VIa with hydrazine hydrate afforded XIVa and a substance XXI, m.p. 217~218°. The latter was identified with 3-methylpyrazolone-(5) which was prepared by the reaction of ethyl acetoacetate with hydrazine hydrate. Similarly, ring cleavage of VIb with hydrazine hydrate gave XIVb and XXI. Hydrolysis of VIb with aqueous potassium hydroxide also gave XIVb.

From the results of the above-mentioned experiments, it has been clarified that the alkyl group of the 5-methyl-7-alkoxy-*s*-triazolo[1,5-*a*]pyrimidines undergoes rearrangement to the ring nitrogens at 3- and 4-positions.

Experimental*6

Paper Partition Chromatography (PPC)——Toyo Roshi No. 50 (2×40 cm) was used and compounds were all developed by the ascending procedure. The developing solvent : AcOH-BuOH-H_2O (1:4:5). After the paper was dried for 1 hr., the spot was observed under the exposure of ultraviolet ray in the dark room.

Diazo-coupling test——In order to test existence of free amino groups, the products were examined by treatment with 5% $NaNO_2$ in 5% HCl followed by addition of 5% β-naphthol in 5% NaOH.

5-Methyl-7-methoxy-*s*-triazolo[1,5-*a*]pyrimidine (IVa)——To a solution of 0.3 g. of Na in 30 cc. of dehyd. MeOH, 2.2 g. of III was added in small portions under stirring and ice-cooling and the mixture was stirred at room temperature further for 3 hr. The separated NaCl and product were collected by filtration and the filtrate was concentrated to dryness in a reduced pressure at room temperature. The resulting crystals and residue were combined, dissolved in H_2O, extracted with $CHCl_3$, and dried over $CaCl_2$. After removal of the solvent in a reduced pressure at room temperature, the residue was dissolved in $CHCl_3$ and purified by Al_2O_3 chromatography (removal of the solvent was carried out in a reduced pressure at room temperature) affording 1.9 g. of colorless needles, m.p. 163~164° in a (and 205~220°). *Anal.* Calcd. for $C_7H_8ON_4$: C, 51.21; H, 4.91; N, 34.13. Found : C, 51.09; H, 5.03; N, 34.25. IR : ν_{max}^{Nujol} 1015 cm^{-1} (C-O-C).

5-Methyl-7-ethoxy-*s*-triazolo[1,5-a]pyrimidine (IVb)——This compound was prepared by the method of the previous work*2 from III and EtONa Recrystallization from benzene gave colorless needles, m.p. 149~150°. IR : $\nu_{max}^{CHCl_3}$ 1023 cm^{-1} (C-O-C).

Reaction of 1-Methyl-2-aminoguanidinium Sulfate (XIIa) with Formic Acid——A mixture of 10 g. of XIIa and 3.6 g. of 98~100% HCOOH was heated on a steam bath for 15 hr. The resulting syrup was dissolved in 15 cc. of H_2O and treated with 3.6 g. of Na_2CO_3 at 50°. The solution was then placed in an evaporating dish, evaporated to dryness on the steam bath, and dried completely in a desiccator. The residue was extracted with 200 cc. of dehyd. EtOH under reflux, the extract was filtered, and the filtrate was concentrated to one-third of the original volume. After cooling the resulting crystals were collected by filtration and recrystallized from EtOH to yield 5.1 g. of 4-methyl-5-amino-*s*-triazole (XVa) as colorless long plates, m.p. 227~228°. *Anal.* Calcd. for $C_3H_6N_4$: C, 36.72; H, 6.16; N, 57.11. Found : C, 36.87; H, 6.43; N, 56.90. Diazo-coupling test : free amine was indicated. The filtrate (EtOH-soluble portion) was concentrated to dryness and the residue was recrystallized from Me_2CO to afford 0.5 g. of 5-methylamino-*s*-triazole (XIVa) as colorless prisms, m.p. 192~193°. *Anal.* Calcd. for $C_3H_6N_4$: C, 36.72; H, 6.16; N, 57.11. Found : C, 36.98; H, 6.28; N, 57.28. Diazo-coupling test : free amine was absent.

Reaction of 1-Ethyl-2-aminoguanidinium Sulfate (XIIb) with Formic Acid——A mixture of 19.3 g. of XIIb and 6.8 g. of 98~100% HCOOH was heated on a steam bath for 13 hr. The resulting syrup was dissolved in 27 cc. of H_2O and carefully treated with 6.8 g. of Na_2CO_3 at 50°. The solution was then placed in an evaporating dish, evaporated to dryness on the steam bath, and dried completely in a desiccator. The residue was extracted with 100 cc. of dehyd. EtOH under reflux and the extract was evaporated to dryness (13.3 g.), which was dissolved in 100 cc. of boiling benzene. The benzene-insoluble crystals were recrystallized from EtOH to yield 7.5 g. of 4-ethyl-5-amino-*s*-triazole (XVb) as colorless pillars, m.p. 200~201°. *Anal.* Calcd. for $C_4H_8N_4$: C, 42.84; H, 7.19; N, 49.97. Found : C, 43.02; H, 7.40; N, 49.79. Diazo-coupling test : free amine was positive. The benzene extract was cooled and the resulting crystals were recrystallized from benzene to give 0.53 g. of 5-ethylamino-

*6 All melting points are uncorrected. Infrared spectra were measured with the Kōken Infrared Spectrophotometer, Medel DS-301, and ultraviolet spectra were taken with the Hitachi Recording spectrophotometer, EPS-2.

s-triazole (XIVb) as white needles, m.p. 126~127°. *Anal.* Calcd. for $C_4H_8N_4$: C, 42.84; H, 7.19; N, 49.97. Found: C, 42.75; H, 6.98; N, 49.75. Diazo-coupling test: free amine was negative.

Hydrolysis of 5,8-Dimethyl-*s*-triazolo[4,3-*a*]pyrimidin-7(8*H*)-one (XVIII)——A mixture of 0.3 g. of XVIII and 10 cc. of 5% KOH was refluxed for 20 min. After cooling the reaction mixture was neutralized with dil. HCl, evaporated to dryness in a reduced pressure and then the residue was extracted with Me_2CO under reflux. The extract was evaporated to dryness and the residue was recrystallized from Me_2CO to give 0.12 g. of colorless prisms, m.p. 192~193°. *Anal.* Calcd. for $C_3H_6N_4$: C, 36.72; H, 6.16. Found: C, 36.83; H, 6.08. This showed no depression of melting point on admixture with XIVa obtained as above.

Isomerization of XVIII——To a solution of 6 cc. of piperidine and 2 cc. of H_2O, 0.3 g. of XVIII was added and the mixture was refluxed for 1.5 hr. After removal of the solvent, the residue was recrystallized from EtOH to yield 0.25 g. of 4,7-dimethyl-*s*-triazolo[1,5-*a*]pyrimidin-5(4*H*)-one (XVIa) as colorless needles, m.p. 156~157°. *Anal.* Calcd. for $C_7H_8ON_4$: C, 51.21; H, 4.91; N, 34.13. Found: C, 51.21; H, 4.98; N, 34.41. UV λ_{max}^{EtOH} mμ (log ε): 251 (3.68), 271 (3.74). IR: ν_{max}^{Nujol} 1669 cm^{-1} (lactam C=O).

Condensation of 5-Methylamino-*s*-triazole (XIVa) with Ethyl Acetoacetate——a) A mixture of 200 mg. of XIVa and 300 mg. of ethyl acetoacetate in 1.5 cc. of AcOH was refluxed for 4 hr. After removal of the solvent, the residue was dissolved in $CHCl_3$ and passed through a column of alumina. The products were eluted from the column with $CHCl_3$ and the first product was recrystallized from EtOH giving 32 mg. of colorless needles, m.p. 156~157°. *Anal.* Calcd. for $C_7H_8ON_4$: C, 51.21; H, 4.91; N, 34.13. Found: C, 51.29; H, 4.92; N, 34.25. This was identified with XVIa obtained as above by mixed melting point and the IR spectrum. The second product was recrystallized from EtOH to yield 195 mg. of 4,5-dimethyl-*s*-triazolo[1,5-*a*]pyrimidin-7(4*H*)-one (VIa) as colorless scales, m.p. 248~249°. *Anal.* Calcd. for $C_7H_8ON_4$: C, 51.21; H, 4.91; N, 34.13. Found: C, 51.35; H, 4.97; N, 34.01. UV λ_{max}^{EtOH} mμ (log ε): 247 (3.66), 277 (4.09). IR: ν_{max}^{Nujol} 1711 cm^{-1} (lactam C=O).

b) A mixture of 300 mg. of XIVa and 800 mg. of ethyl acetoacetate was heated at 180° for 15 min. and further at 210° for 15 min. After cooling the resulting solids were dissolved in $CHCl_3$, 50 mg. of the insoluble crystals XIVa were filtered off, and the filtrate was passed through a column of alumina. The products were eluted from the column with $CHCl_3$ and the first product was recrystallized from EtOH to 330 mg. of colorless needles, m.p. 156~157°, which showed no depression of melting point on admixture with XVIa obtained in (a). The second product was recrystallized from EtOH to yield 30 mg. of colorless scales, m.p. 248~249°, which showed no depression of melting point on admixture with VIa obtained in (a).

Condensation of 5-Ethylamino-*s*-triazole (XIVb) with Ethyl Acetoacetate——a) A mixture of 200 mg. of XIVb and 260 mg. of ethyl acetoacetate in 1.5 cc. of AcOH was refluxed for 4 hr. After removal of the solvent, the residue was dissolved in $CHCl_3$ and separated by alumina chromatography using $CHCl_3$ to two products. The first eluted product was recrystallized from ligroin to give 60 mg. of 4-ethyl-7-methyl-*s*-triazolo[1,5-*a*]pyrimidin-5(4*H*)-one (XVIb) as colorless pillars, m.p. 107~108°. *Anal.* Calcd. for $C_8H_{10}ON_4$: C, 53.92; H, 5.66; N, 31.45. Found: C, 53.98; H, 5.79; N, 31.22. UV λ_{max}^{EtOH} mμ (log ε): 251 (3.69), 271 (3.72). IR: ν_{max}^{Nujol} 1692 cm^{-1} (lactam C=O). The second eluted product was recrystallized from EtOH to afford 180 mg. of 4-ethyl-5-methyl-*s*-triazolo[1,5-*a*]pyrimidin-7(4*H*)-one (VIb) as colorless scales, m.p. 214~215°. *Anal.* Calcd. for $C_8H_{10}ON_4$: C, 53.92; H, 5.66; N, 31.45. Found: C, 53.81; H, 5.75; N, 31.23. UV λ_{max}^{EtOH} mμ (log ε): 247 (3.67), 278 (4.10). IR: ν_{max}^{Nujol} 1699 cm^{-1} (lactam C=O).

b) A mixture of 300 mg. of XIVb and 500 mg. of ethyl acetoacetate was heated at 170° for 15 min. and further at 200° for 15 min. After cooling the resulting solids were dissolved in benzene and separated by alumina chromatography to two products. The product eluted with benzene, was recrystallized from ligroin to give 300 mg. of colorless pillars, m.p. 107~108° which was identical with XVIb in (a). The product which was eluted with $CHCl_3$, was recrystallized from EtOH to afford 20 mg. of colorless scales, m.p. 214~215° which was identical with VIb in (a).

Condensation of 4-Methyl-5-amino-*s*-triazole (XVa) with Ethyl Acetoacetate——a) A mixture of 2 g. of XVa and 3 g. of ethyl acetoacetate in 10 cc. of AcOH was refluxed for 8 hr. After removal of the solvent in a reduced pressure, the residue was dissolved in $CHCl_3$, 0.68 g. of the insoluble crystals XVa were filtered off, and the filtrate was purified by alumina chromatography. The resulting crystals were recrystallized from EtOH to give 1.8 g. of 3,5-dimethyl-*s*-triazolo[1,5-*a*]pyrimidin-7(3*H*)-one (VIIa) as white needles, m.p. 260~261°. *Anal.* Calcd. for $C_7H_8ON_4$: C, 51.21; H, 4.91; N, 34.13. Found: C, 51.08; H, 4.83; N, 34.35. UV λ_{max}^{EtOH} mμ (log ε): 247 (3.73), 284 (4.09). IR: ν_{max}^{Nujol} 1711 cm^{-1} (lactam C=O).

b) A mixture of 0.6 g. of XVa and 1 g. of ethyl acetoacetate was heated at 170° for 15 min. and further at 200° for 15 min. After cooling the resulting solids were dissolved in $CHCl_3$, 0.21 g. of the insoluble crystals XVa were filtered off, and the filtrate was purified by alumina chromatography using $CHCl_3$ to yield 0.43 g. of white needles VIIa m.p. 260~261°.

Condensation of 4-Ethyl-5-amino-*s*-triazole (XVb) with Ethyl Acetoacetate——a) A mixture of 2.2 g. of XVb and 3 g. of ethyl acetoacetate in 10 cc. of AcOH was refluxed for 8 hr. After removal of the solvent in a reduced pressure, the residue was dissolved in $CHCl_3$ and 0.05 g. of the insoluble crystals XVb were filtered off. The filtrate was purified by alumina chromatography uisng $CHCl_3$ and the resulting crystals were recrystallized from EtOH to afford 2.2 g. of 3,5-dimethyl-*s*-triazolo-[1,5-*a*]pyrimidin-7(3*H*)-one (VIIb) as colorless needles, m.p. 199~200°. *Anal.* Calcd. for $C_8H_{10}ON_4$: C, 53.92; H, 5.66; N, 31.45. Found : C, 53.84; H, 5.67; N, 31.28. UV λ_{max}^{EtOH} mμ (log ε) : 248.5 (3.73), 284 (4.09). IR% ν_{max}^{Nujol} 1698 cm^{-1} (lactam C=O).

b) A mixture of 0.6 g. of XVb and 1 g. of ethyl acetoacetate was heated at 170° for 15 min. and further at 200° for 15 min. The resulting solids were dissolved in $CHCl_3$, 0.09 g. of the insoluble crystals XVb were filtered off, and the filtrate was purified by alumina chromatography using $CHCl_3$. The resulting crystals were recrystallized from EtOH to give 0.4 g. of colorless needles VIIb, m.p. 199~200°.

Rearrangement of IVa on Heating——1.64 g. of IVa was heated at 180° for 30 min., when the starting material was liquefied and immediately solidified. The resulting solids were dissolved in $CHCl_3$, passed through a column (30×1.5 cm.) of alumina, and the products were eluted from the column with $CHCl_3$. The first eluted product (0.815 g.) was recrystallized from EtOH to yield colorless scales, m.p. 248~249°. *Anal.* Calcd. for $C_7H_8ON_4$: C, 51.21; H, 4.91; N, 34.13. Found : C, 51.29; H, 5.01; N, 34.06. This was identified with VIa prepared as above by mixed melting point and the IR spectrum. The second eluted product (0.75 g.) was recrystallized from EtOH to white needles, m.p. 260~261°. *Anal.* Calcd. for $C_7H_8ON_4$: C, 51.21; H, 4.91; N, 34.13. Found : C, 51.35; H, 5.12; N, 34.15. This was also identified with VIIa prepared from XVa as above by mixed melting point and the IR spectrum.

Rearrangement of IVb on Heating——1.78 g. of IVb was heated at 200° for 1 hr., when the starting material was completely liquefied. After cooling the resulting solids were treated by the same method as above giving three products. The first eluted product was recrystallized from petr. benzin affording 58 mg. of white needles IX, m.p. 70°. IR : $\nu_{max}^{CHCl_3}$ 2236 cm^{-1} (C≡N). The structure of this product has not been determined yet. The second eluted product (0.68 g.) was recrystallized from EtOH to colorless scales, m.p. 214~215°. *Anal.* Calcd. for $C_8H_{10}ON_4$: C, 53.92; H, 5.66; N, 31.45. Found : C, 53.75; H, 5.73; N, 31.61. This was identified with VIb prepared from XIVb as above by mixed melting point determination and by IR spectra comparison. The third eluted product (0.745 g.) recrystallized from EtOH to colorless needles, m.p. 199~200°. *Anal.* Calcd. for $C_8H_{10}ON_4$: C, 53.92; H, 5.66; N, 31.45. Found : C, 54.05; H, 5.75; N, 31.56. This was also identified with VIIb prepared from XVb as above by mixed melting point determination and by IR spectra comparison.

Ring Cleavage of 4,5-Dimethyl-*s*-triazolo[1,5-*a*]pyrimidin-7(4*H*)-one (VI a)——A mixture of 1 g. of VIa and 20 cc. of 80% $NH_2NH_2 \cdot H_2O$ was refluxed for 4 hr. and the reaction mixture was evaporated to dryness in a reduced pressure. The residue was dissolved in H_2O and the solution was evaporated to dryness in a reduced pressure. This treatment was repeated several times to remove hydrazine completely. The resulting solids were dissolved in a small volume of H_2O, the insoluble crystals were collected by filtration, and recrystallized from Me_2CO to yield 0.35 g. of colorless prisms XXI, m.p. 217~218°. This was identified with the authentic sample of 3-methylpyrazolone-(5) by mixed melting point determination. The filtrate (H_2O-soluble portion) was concentrated to dryness in a reduced pressure and the residue was recrystallized from Me_2CO giving 0.28 g. of colorless prisms, m.p. 192~193°, which showed no depression of melting point on admixture with XIVa. *Anal.* Calcd. for $C_3H_6N_4$: C, 36.72; H, 6.16; N, 57.11. Found : C, 36.75; H, 6.25; N, 56.96.

Ring Cleavage of 4-Ethyl-5-methyl-*s*-triazolo[1,5-*a*]pyrimidin-7(8*H*)-one (VIb)——a) A mixture of 0.5 g. of VIb and 10 cc. of 80% $NH_2NH_2 \cdot H_2O$ was refluxed for 4 hr. and the reaction mixture was treated as above giving two products. H_2O-insoluble portion was recrystallized from Me_2CO to yield 0.2 g. of colorless prisms, m.p. 217~218° which was identical with XXI by mixed melting point. H_2O-soluble portion was recrystallized from benzene to yield 0.12 g. of white needles, m.p. 126~127°. *Anal.* Calcd. for $C_4H_8N_4$: C, 42.84; H, 7.19; N, 49.97. Found : C, 42.98; H, 7.14; N, 50.13. This showed no depression of melting point on admixture with XIVb.

b) A mixture of 0.3 g. of VIb and 7 cc. of 5% KOH was refluxed for 30 min. and the mixture was neutralized with dil. HCl. The resulting solution was concentrated to dryness in a reduced pressure and the residue was extracted with hot EtOH. The EtOH extract was evaporated to dryness and the residue was recrystallized from benzene to give 0.15 g. of white neeldes, m.p. 126~127°, which showed no depression of melting point on admixture with XIVb.

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Summary

5-Methyl-7-methoxy-*s*-triazolo[1,5-*a*]pyrimidine (IVa) was prepared by the reaction of the 7-chloro compound III with sodium methoxide at below room temperature. The property of the 7-alkoxy derivatives (IVa and IVb) was examined and it was discovered that the alkyl group of these derivatives undergoes rearrangement to the ring nitrogen at 3- and 4-positions. In order to determine the structure of the products being obtained by above rearrangement, the reaction of ethyl acetoacetate with 5-alkylamino-*s*-triazoles (XIVa and XIVb) and 4-alkyl-5-amino-*s*-triazoles (XVa and XVb) which were prepared from 1-alkyl-2-aminoguanidinium sulfates (XIIa and XIIb), was investigated.

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15. Toyozo Uno and Koichiro Miyajima : Determination of Surface-active Agents. V.*2 Volumetric Determination of Ethylene Oxide Content in Nonionic Surface-active Agent.*3

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Among the numerous methods for the determination of the ethylene oxide content in nonionics, the titrimetric method has been disregarded. Steele and Berger[1] reported a method using the cloud point of an aqueous solution. Karabinos[2] titrated the solution of nonionics with 5% phenol until opalescence appeared, and this method had been improved by Greenbald[3] and Lloyd.[4] Morgan[5] determined ethylene oxide condensates by cleaving the ethylene oxide bond with hydroiodic acid to ethylene iodide and ethylene.

Gravimetric methods using precipitating reagents, such as potassium ferrocyanate,[6] barium chloride and heteropolic acid,[7~10] or sodium tetraphenylborate[11~13] (STB) were also studied and reported by many workers. However, the procedures are complicated and required so much time for determination. In the preceding papers,[14~16] the volu-

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