powder (860 mg., 75.2%). *Anal.* Calcd. for $C_{44}H_{66}O_{10}Na_4P_2 \cdot 2H_2O$: C, 55.93; H, 7.47; P, 6.56. Found: C, 56.37; H, 8.02; P, 6.53.

The authors wish to express their deep gratitude to Dr. K. Tanaka, head of the second division of the research laboratories, for his kind encouragement and to Dr. Y. Sanno of this laboratory for his kind help. They are also indebted to Professor R. Sato, Institute for Protein Research, Osaka University, for his valuable advice.

Summary

1) Using the mitochondria treated with acetone, measurement was made about the activity-restoring effect of ubiquinone (35) (Ⅰ) and related compounds on the succinate oxidase system, and as the partial structure required for the effect the following points were made clear: i) the quinone nucleus is necessary, ii) the methoxyl at position of 3 may be changed to a hydroxyl but if it is converted to acetoxyl the effect is lost, iii) the length of the isoprene side chain has no influence so long as the number of the isoprene is 7~10, but when the double bonds of the side chain are saturated, the activity decreases to 1/2, and when one of the double bonds is conjugated with the quinone nucleus, the activity lowers to 1/3.

2) When added to beef-heart mitochondria, some substances in Table Ⅳ other than ubiquinone (35) (Ⅰ) and ubichromenol (35) acetate (Ⅸ) show slight inhibition of the succinate oxidase system.

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20. Akira Takamizawa and Yoshio Hamashima: Syntheses of Pyrazole Derivatives. IX.*1 Acetylation Products of 7-Aminopyrazolo[1,5-*a*]pyrimidines.

(*Shionogi Research Laboratory, Shionogi & Co., Ltd.**2)

In general, on an alkylation and acylation of aminopyrimidine derivatives, it has been known[1] that the alkylation proceeds to the ring nitrogen and the acylation to a side amino group. In a previous paper,[2] we also confirmed that the methylation of 7-amino-3,6-dimethylpyrazolo[1,5-*a*]pyrimidine (XXXII) gave 7-imino-3,4,6-trimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (XXXV). Furthermore, the structure of diacetate (XXXIV) which was prepared by an acetylation of XXXII was presumed to be 4-acetyl-7-acetylimino-3,6-dimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine. However, later the monoacetate (XXXIII) was obtained by alumina chromatography of XXIV. The ultraviolet absorption spectrum of XXXIII was similar to that of XXXIV and obviously different from XXXV. From these experimental results, we have reinvestigated the structure of diacetate and established that the diacetate was actually 7-diacetylamino-3,6-dimethylpyrazolo-[1,5-*a*]pyrimidine (XXXIV).

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*1 Part Ⅷ: A. Takamizawa, H. Sato: Yakugaku Zasshi, 85, 158 (1965).

*2 Sagisu, Fukushima-ku, Osaka (高見沢 映, 浜島好男).

1) D. J. Brown: "The Pyrimidines," (1962), John Willy and Sons Inc., New York, N. Y.
2) A. Takamizawa, S. Hayashi: Yakugaku Zasshi, 83, 313 (1963).

The acetylation of 7-amino-2,3-dimethylpyrazolo[1,5-*a*]pyrimidine (I) was attempted as a model reaction in this series under the same condition as the case of XXXII, but in this case diacetate was not obtained but only the monoacetate (III) was given and no acetylation condition could provide the expected diacetate. On the other hand, acetylation of 7-amino-2,3,6-trimethylpyrazolo[1,5-*a*]pyrimidine (II) gave the diacetate (IV) easily in fairly good yield under the common process. IV obtained is converted into monoacetate (V) on treatment with alumina chromatography or by hydrolysis under mild conditions. IV is also regenerated by the acetylation of V easily. Alkylation (methyl-, ethyl- or allylation) of I or II proceeds on the nitrogen atom at the 4-position to give 4-alkyl-4,7-dihydro derivatives (VI～XI). Moreover, on acetylation of VI and X affords 4-alkyl-7-acetylimino compounds (XII, XIII), and the structures of these XII and XIII are confirmed by the identification with authentic samples synthesized from the reactions of III and V with methyl iodide and ethyl iodide, respectively, thus providing chemical evidence for the acetyl groups of III and V at the 7-amino group. XII is hydrolyzed to give the original 7-imino compound (VI) and XIII is hydrolyzed into the 7-oxo compound (XVI) easily. XVI and other analogous 7-oxo compounds (XIV, XV) are also obtained by acid hydrolysis of 7-imino compounds (VI, IX, and X) or through the reaction of I or II with alkyl halides in the presence of sodium bicarbonate accompanied with hydrolysis. III and V are hydrogenated to give 7-ethylamino compounds (XVII, XVIII) by the lithiun aluminum hydride reduction. XVII and XVIII are apparently different from VII and X by comparison of their ultraviolet, infrared, and nuclear magnetic resonance spectra. The differences of these physical properties of XVII and XVIII from those of VII and X described above support the structures of XVII and XVIII, 7-ethylamino-2,3-dimethyl- and 7-ethylamino-2,3,6-trimethylpyrazolo[1,5-*a*]pyrimidines, respectively. Reactions of XVII and XVIII with acetic anhydride in pyridine in a sealed tube give 7-(N-ethyl-acetamido)-2,3-dimethyl- and 7-(N-ethylacetamido)-2,3,6-trimethylpyrazolo[1,5-*a*]pyrimidines (XIX, XX), respectively, of which structures are determined from the nuclear magnetic resonance and ultraviolet absorption spectra as shown in Tables I and II. An attempt to obtain 7-diethylamino compounds by the hydrogenation of XIX and XX did not succeed and only hydrolyzed compounds (XVII, XVIII) were isolated. On treatment with lithium aluminum hydride, IV looses one of two acetyl groups and gives only XVIII. On the other hand, diethyl derivatives (XXI, XXII) of I and II are obtained by ethylation of XVII and XVIII. The structures of XXI and XXII are found to be 4-ethyl-7-ethylimino-2,3-dimethyl-, and 4-ethyl-7-ethylimino-2,3,6-trimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidines not only from their ultraviolet spectra (which resembles to those of VI～XVI) but also from nuclear magnetic resonance spectral data described later.

Behaviours on acetylation of I and II mentioned above are applicable to the formylation. Namely, formylation of I with acetic formic anhydride produces monoformyl derivative (XXIII), while in contrast, mono- and diformyl compounds (XXIV, XXV) are obtained by a formylation of II. Hydrogenation of XXIII and XXIV with lithium aluminum hydride gives monomethyl compounds (XXVI, XXVII), respectively, but the hydrogenation of XXV only provides XXVII accompanied with deformylation under some reaction conditions. Methylation of XXVII gives the substituted product (XXVIII) which is assumed to be 7-methylamino-2,3,4,6-tetramethyl-4,7-dihydropyrazole[1,5-*a*]pyrimidine from its ultraviolet and nuclear magnetic resonance spectral data.

As shown in Table I, ultraviolet spectra of compounds V～XIII, XXI, XXII, and XXVIII show three maxima around 225～240, 251～270, and 314～365 mμ and these spectral correlations are analogous to those of XIV～XVI, of which the structures have been already confirmed.[2] Accordingly, the structures of these compounds are decided to be the 4,7-dihydro type, and so it is established that the alkylation of 7-aminopyrazolo[1,5-*a*]-pyrimidines in this series proceeds at 4-position. On the other hand, as the ultraviolet

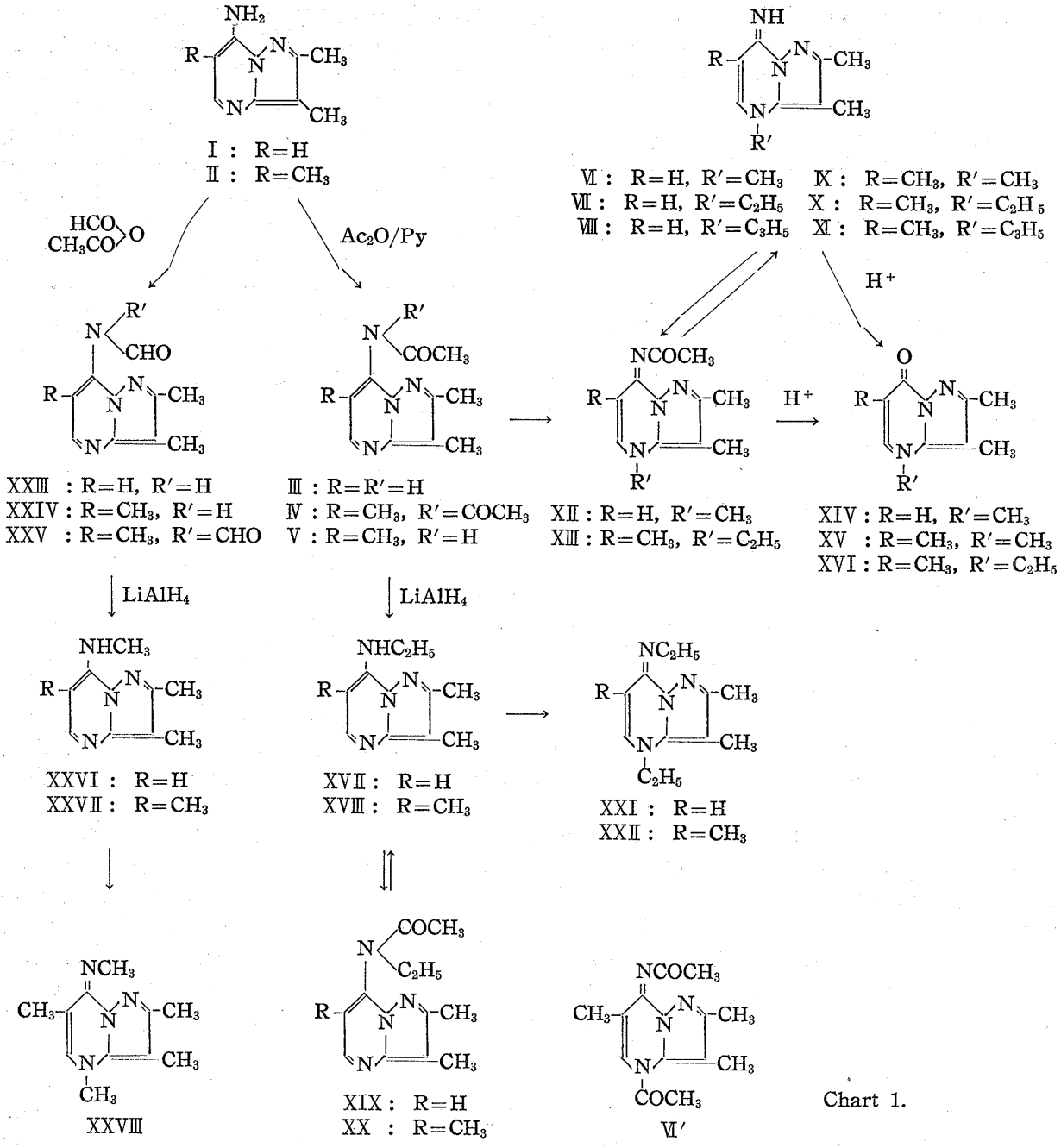


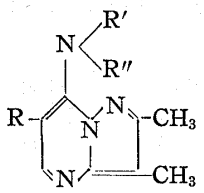
Chart 1.

spectra of both alkylamino derivatives (XVII, XVIII, XXVI, and XXVII) and acylamino compounds (III~V, XIX, XX, and XXIII~XXV) show similar curves to each other and differ from those of XIV~XVI, the structures of these groups are probably the pyrimidine type. In addition, as ultraviolet spectrum of IV is very similar to that of V, IV also should be a 7-diacetylamino structure.

Next, we discuss the nuclear magnetic resonance spectra of the compounds in this series, chemical shifts of the C-5 and acetyl protons being useful for estimating structures. Signals of the proton at the C-5 position of several C-methyl-substituted 7-aminopyrazolo[1,5-*a*]pyrimidines which we have synthesized earlier[3] appear around

3) A. Takamizawa, S. Hayashi, Y. Hamashima, R. Kido : Yakugaku Zasshi, 83, 745 (1963).

TABLE I. Ultraviolet Absorption Spectra of 7-Aminopyrazolo[1,5-*a*]pyrimidines

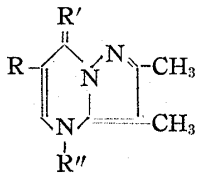


Compd. No.	R	R′	R″	λ_{max}^{EtOH} mμ (log ε)				
I	H	H	H	222 (4.58)		284.5 (3.85)		310 (3.83)
II	CH_3	〃	〃	230 (4.53)	282 (3.71 sh)	291.5 (3.79)		327 (3.72)
III	H	〃	Ac	235.5 (4.67)	280 (3.33 sh)	288 (3.39)	296.5 (3.34 sh)	343 (3.61)
IV	CH_3	Ac	〃	241 (4.66)	287 (3.16 sh)	298 (3.23)	311 (3.20)	346.5 (3.20)
V	〃	H	〃	238 (4,55)	284 (3.27 sh)	292.5 (3.32)	310 (3.24 sh)	339 (3.40)
XVII	H	〃	C_2H_5	224.5 (4.78)		290 (3.84)		321 (3.84)
XVIII	CH_3	〃	〃	232 (4.56)	285 (3.68 sh)	293 (3.75)		332 (3.83)
XIX	H	Ac	〃	239 (4.64)	285 (3.20 sh)	294.5 (3.26)	306 (3.16)	349 (3.24)
XX	CH_3	〃	〃	240.5 (4.66)	288 (3.16 sh)	298.5 (3.26)	312 (3.22)	350 (3.26)
XXIII	H	H	CHO	226.5 (4.63)	280 (3.24 sh)	289.5 (3.32)	298.5 (3.21 sh)	347 (3.53)
XXIV	CH_3	〃	〃	238.5 (4.68)	284 (3.22 sh)	294 (3.29)	311 (3.19 sh)	348 (3.43)
XXV	〃	CHO	〃	239.5 (4.67)	284 (3.18 sh)	295 (3.25)	312 (3.21)	348 (3.36)
XXVI	H	H	CH_3	235 (4.58)	280 (3.73)	289.5 (3.83)		321 (3.79)
XXVII	CH_3	〃	〃	232.5 (4.52)	284.5 (3.65)	293.5 (3.72)		335 (3.80)
XXXI	〃	CHO	Ac	239.5 (4.67)	286.5 (3.11)	297.5 (3.19)	312 (3.17)	345 (3.18)
XXIX[a)]	3-Br-6-Me-7-NH_2-			222.5 (4.80)	281 (3.66 sh)	290.5 (3.77)		327 (3.92)
XXX	3-Br-6-Me-7-$N(Ac)_2$-			238 (4.57)	282 (3.20)	291 (3.26)	302 (3.17)	345 (3.32)
XXXII	3,6-diMe-7-NH_2-			226.5 (4.62)	277 (3.75 sh)	284.5 (3.80)		319 (3.85)
XXXIII	3,6-diMe-7-NHAc-			236 (4.73)	282 (3.50 sh)	290 (3.53)	299.5 (3.42 sh)	343 (3.60)
XXXIV	3,6-diMe-7-$N(Ac)_2$			237 (4.89)	282.5 (3.43 sh)	292 (3.49)	303 (3.41)	341 (3.58)

a) Hydrochloride

TABLE I. (continued)

Ultraviolet Absorption Spectra of 7-Imino-4,7-dihydropyrazolo[1,5-*a*]pyrimidines

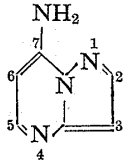


Compd. No.	R	R′	R″	λ_{max}^{EtOH} mμ (log ε)		
VI	H	NH	CH_3	229 (4.36)	265 (3.69)	322 (3.61)
VII	〃	〃	allyl	233.5 (4.42)	267 (3.79)	315 (3.77)
IX	CH_3	〃	CH_3	233.5 (4.39)	268 (3.86)	315 (3.80)
X	〃	〃	C_2H_5	234 (4.43)	265 (3.87 sh)	318 (3.76)
X[a]				234.5 (4.52)	267 (3.82 sh)	345 (3.76)
XI	CH_3	NH	allyl	234.5 (4.29)	265 (3.93 sh)	314 (3.85)
XII[b]	H	NAc	CH_3	239.5 (4.50)	257 (4.23)	365 (3.62)
XIII	CH_3	〃	C_2H_5	225.5 (4.25)	268.5 (4.03)	334 (3.93)
XIV	H	O	CH_3	216 (4.38)	267 (3.86)	313 (3.71)
XV	CH_3	〃	〃	222.5 (4.38)	269.5 (3.98)	318 (3.82)
XVI	〃	〃	C_2H_5	222.5 (4.34)	268 (3.94)	318 (3.78)
XXI	H	NC_2H_5	〃	229.5 (4.50)	253.5 (4.13)	333 (3.83)
XXII	CH_3	〃	〃	234 (4.59)	251 (4.13 sh)	348 (3.90)
XXVIII	〃	NCH_3	CH_3	236 (4.53)	255 (4.08 sh)	350 (3.83)
XXXV	3,4,6-triMe-7-NH-			231 (4.44)	272 (3.86 sh)	320 (3.85)
XXXVI	3,6-diMe-4-allyl-7-NH-			232.5 (4.28)	269 (3.88)	312.5 (3.92)
XXXVII	3,4,6-triMe-7-oxo-			221.5 (4.33)	269 (4.01)	329.5 (3.86)

a) Hydrobromide *b*) Hydroiodide

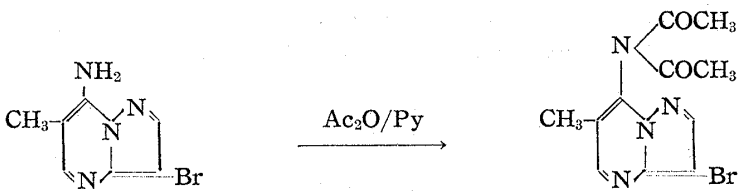
1.73～1.97 τ.*[3] The signal of the C-5 proton in III, V, and IV appear at 1.74, 1.73, and 1.67 τ, respectively. These results indicate that the influence of the acetyl group upon the C-5 proton is not significant, whereas a significant effect is exerted on the C-6

*[3] Chemical shifts of C-methyl-substituted 7-aminopyrazolo[1,5-*a*]pyrimidines in $CDCl_3$ were observed as follows[4]:



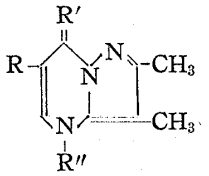
2-H: 2.00～2.16 τ 2-CH_3: 7.50～7.58 τ
3-H: 3.60～3.85 τ 3-CH_3: 7.68～7.75 τ
5-H: 1.73～1.97 τ 5-CH_3: 7.52～7.55 τ
6-H: 4.02～4.18 τ 6-CH_3: 7.80～7.87 τ
6H>3H>2H>5H

4) Unpublished data in this laboratory.



XXIX Chart 2. XXX

TABLE II. Nuclear Magnetic Resonance Data on 7-Imino-4,7-dihydropyrazolo[1,5-*a*]-pyrimidine Derivatives and their Related Compounds ($CDCl_3$, 60 Mc.p.s.).

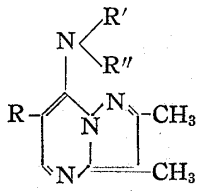


Compd. No.	R	R′	R″	Chemical shift (τ) 5-H	6-H	6-CH_3	7-NH	other H
VI	H	NH	CH_3	3.32[d] $J_{5,6}=7.0$	4.34[d]	—	4.78	6.38 (N-CH_3)
VII	〃	〃	C_2H_5	3.24[d] $J_{5,6}=8.0$	4.28[d]	—	5.25	
VIII	〃	〃	allyl	3.28[d] $J_{5,6}=7.5$	4.26[d]	—	4.00	
IX	CH_3	〃	CH_3	3.40[q] $J_{5,6}=0.6$[a)]	—	7.95[d]	5.37	6.36 (N-CH_3)
X	〃	〃	C_2H_5	3.30[q] (2.04)[b)] $J_{5,6}=1.6$[a)]	—	7.94[d] (7.61)[b)]	4.7	
XI	〃	〃	allyl	3.36[q]	—	7.94[d]	2.7	
XII	H	NAc	CH_3	2.94[d] $J_{5,6}=7.1$	3.57[d]	—	7.66 (N-Ac)	6.17 (N-CH_3)
XIII	CH_3	〃	C_2H_5	3.12[q] $J_{5,6}=1.0$[a)]	—	8.03[d]	7.68 (N-Ac)	
XIV	H	O	CH_3	2.89[d] $J_{5,6}=7.6$	4.36[d]	—	—	6.17 (N-CH_3)
XV	CH_3	〃	〃	2.95[q] $J_{5,6}=1.0$[a)]	—	7.97[d]	—	6.18 (N-CH_3)
XVI	〃	〃	C_2H_5	2.87[q] $J_{5,6}=1.1$[a)]	—	7.98[d]	—	
XXI	H	NC_2H_5	〃	3.25[d] $J_{5,6}=8.0$	4.30[d]	—		
XXVIII	CH_3	NCH_3	CH_3	3.67[q] $J_{5,6}=1.0$[a)]	—	8.13[d]	6.15 (N-CH_3) 6.51 (N-CH_3)	
XXXV	CH_3	NH	CH_3	3.39[q] $J_{5,6}=1.5$[a)]	—	7.96[d]	2.67	2.55 (2-H) 6.36 (N-CH_3)
XXXVI	〃	〃	allyl	3.34[q] $J_{5,6}=1.0$[a)]	—	7.90[d]	2.75	2.52 (2-H)
XXXVII	〃	O	〃	2.79[q]	—	7.92[d]	—	2.38 (2-H)

a) CH_3-H coupling. d: doublet; q: quartet
b) in CF_3COOH

proton as can be seen from the fact that the signal of the proton in III is shifted downfield (2.57 τ) in comparison with that in I (4.17 τ). Moreover, the signals of the two acetyl groups in IV appear as a sharp single peak as shown in Fig. 1b. Since this coincidence of the acetyl signals is shown even by using pyridine (Fig. 1c) and benzene (Fig. 1d) as a solvent, these two acetyl groups introduced are thought to be magnetically equivalent. However, it may not be concluded strictly that the chemical shifts of the

TABLE II. (continued) Nuclear Magnetic Resonance Data on 7-Aminopyrazolo-[1,5-*a*]pyrimidine Derivatives ($CDCl_3$, 60 Mc.p.s.)



Compd. No.	R	R′	R″	Chemical shift (τ) 5-H	6-H	6-CH_3	N-R′	N-R″
I	H	H	H	1.96	4.17	—	4.36 (N-H)	4.31 (N-H)
II	CH_3	〃	〃	1.95	—	7.81	4.40 (N-H)	4.40 (N-H)
III	H	〃	Ac	1.74[d] $J_{5,6}=5.0$	2.57[d]	—	0.83 (N-H)	7.65 (N-Ac)
IV	CH_3	Ac	〃	1.67[q] $J_{5,6}=0.3$[a)]	—	7.71[d]	7.69 (N-Ac)	7.69 (N-Ac)
V	〃	H	〃	1.73	—	7.72 or 7.78	−0.67 (N-H)	7.67 (N-Ac)
XVII	H	〃	C_2H_5	1.93 $J_{5,6}=6.0$	4.27	—	3.93 (N-H)	
XVIII	CH_3	〃	〃	2.06	—	7.79	3.72 (N-H)	
XIX	H	Ac	〃	1.61[d] $J_{5,6}=4.8$	3.42[d]	—	8.08 (N-Ac)	
XX	CH_3	〃	〃	1.66	—	7.68 or 7.70	8.20 (N-Ac)	
XXIII	H	H	CHO	1.66[d] $J_{5,6}=5.2$	2.56[d-d]	—	0.5 (N-H)	1.30 (N-CHO)
XXIV	CH_3	〃	〃	1.72	—	7.65 or 7.73	0.25 (N-H)	1.10 (N-CHO)
XXV	〃	CHO	〃	1.68	—	7.72 or 7.80	0.90 (N-CHO)	0.90 (N-CHO)
XXVI	H	H	CH_3	1.85[d] $J_{5,6}=5.0$	4.25[d]	—	3.64 (N-H)	6.98[d a)] ($N-CH_3$) $J=6.0$
XXVII	CH_3	〃	〃	2.08	—	7.63 or 7.78	3.69 (N-H)	6.69[d a)] ($N-CH_3$) $J=6.0$
XXXI	〃	CHO	Ac	1.66	—	7.72 or 7.79	0.50 (N-CHO)	7.96 (N-Ac)
XXIX				1.80	—	7.75	4.17 ($N-H_2$)	2.0 (2-H)
XXX				1.43[q] $J_{5,6}=0.6$[b)]	—	7.71[d]	7.70 ($N-Ac_2$)	1.91 (2-H)
XXXII				1.88	—	7.65 or 7.78	4.52 ($N-H_2$)	2.13 (2-H)
XXXIII				1.68[q] $J_{5,6}=0.8$[b)]	—	7.63[d]	0.25 (N-H)	7.67 (N-Ac) 2.17 (2-H)
XXXIV				1.61[q] $J_{5,6}=0.6$[b)]	—	7.62[d]	7.70 ($N-Ac_2$)	2.10 (2-H)

a) NH-NMe coupling. *b*) Me-H coupling

C-5 and acetyl-protons in IV result from the structure presumed above, not from its isomeric structure, 4-acetyl-7-acetylimino-2,3,6-trimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (IV′). If this compound were of the structure (IV′), the N-4 acetyl group would be fairly affected, and hence, the overlapping signals of the N-4 acetyl- and side acetyl groups would be separated by an introduction of a substituent possessing a powerful anisotropic shielding effect such as a bromine atom into the C-3 position. According to this idea, a diacetate, XXX of 7-amino-3-bromo-6-methylpyrazolo[1,5-*a*]pyrimidine (XXIX) was synthesized to observe the spectrum. Actually, the two acetyl signals of XXX also show an entire coincidence in its spectrum as shown in Fig. 1e. This fact provides us with the fine evidence that the structure is of a pyrimidine type.

Moreover, we succeeded to synthesize 7-(N-formylacetamido)-2,3,6-trimethylpyrazolo-[1,5-*a*]pyrimidine (XXXI) from two synthetic routes and ensurred the structure of XXXI chemically. Formylation of monoacetate (V) gave XXXI in good yield and this compound

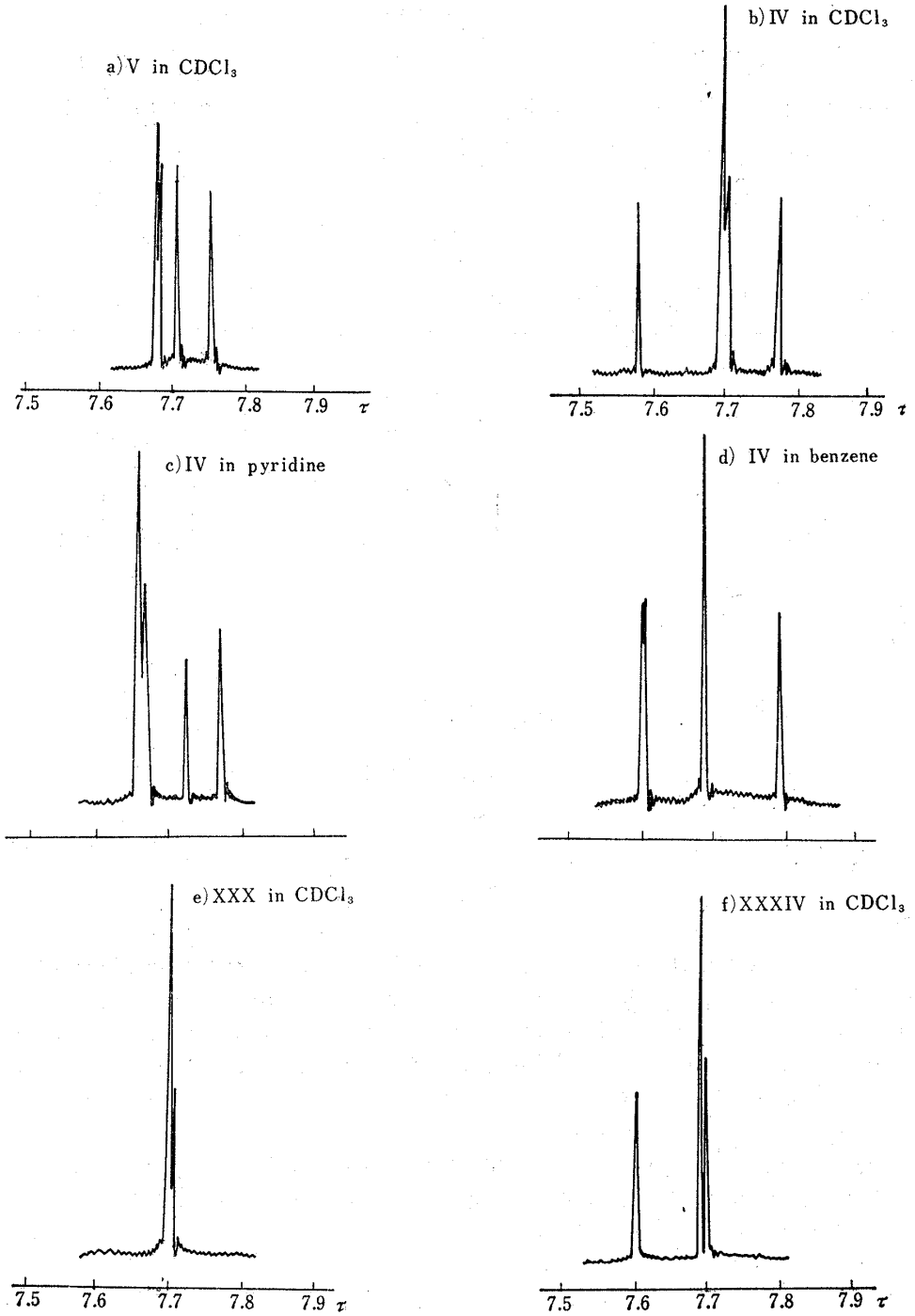


Fig. Ia~f. Proton Signals of N-Acetyl and C-Methyl Groups

was identified with the compound synthesized from an acetylation of 7-formamido compound (XXIV) by the mixture melting point determination, and infrared, ultraviolet and nuclear magnetic resonance spectral comparisons. From these results, the structure of XXXI is decided as 7-(N-formylacetamido)-2,3,6-trimethylpyrazolo[1,5-*a*]pyrimidine. The ultraviolet specutrum of XXXI resembles to those of V and XXIV. Moreover, the C-5 proton signal appears at 1.43 τ to be analogous to those of V and XXIV.

These similarities are also shown in the 7-amino-3,6-dimethylpyrazolo[1,5-*a*]pyrimidine (XXXII). On treatment of diacetate (XXXIV) with aluminum oxide chromatography, monoacetate (XXXIII) is given. which shows the likeliness to the XXXIV in its

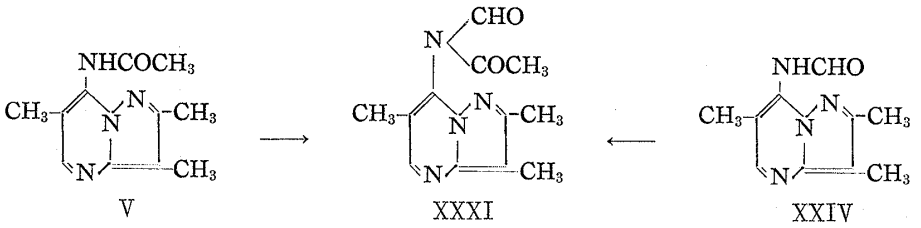


Chart 3.

ultraviolet spectrum (Table II). The proton signals of the C-5 position and acetyl groups in XXXIII and XXXIV are analogous to those of the derivatives already described.

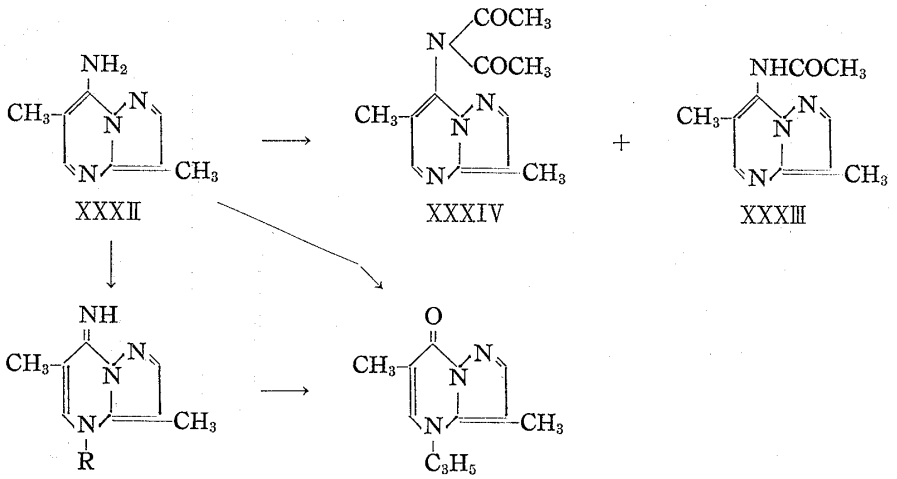


Chart 4.

From the results described it is plain enough that the acylation (formyl- and acetylation) of 7-aminopyrazolo[1,5-*a*]pyrimidines occurs at the amino group. Also it became clear that the acylation of 6-methyl derivatives afforded diacetates, in contrast, that of compounds unsubstituted at C-6 position gave monoacylates. This result will be mostly concluded depending on the stronger basicity of 7-amino group affected by the steric effect of methyl group at C-6 position.

The utility of the data and generalizations mentioned in this paper will be illustrated in a forthcoming publication describing the acylation and alkylation of a number of substituted 7-aminopyrazolo[1,5-*a*]pyrimidines.

Experimental*4

Acetylation of 7-Amino-2,3-dimethylpyrazolo[1,5-*a*]pyrimidine (I)——a) A mixture of 500 mg. of I and 3 ml. of Ac_2O in 5 ml. of pyridine was heated at 100~120° for 2 hr. The reaction mixture was concentrated and the residue was extracted with EtOAc. The EtOAc extract was washed with aq. K_2CO_3, H_2O and dried over $MgSO_4$. The residue after removal of the solvent was recrystallized from Et_2O to give colorless needles, m.p. 136°. Yield, 445 mg. *Anal.* Calcd. for $C_{10}H_{12}ON_4$: C, 58.81; H, 5.92; N, 27.44. Found: C, 58.56; H, 5.97; N, 26.89.

b) A mixture of 500 mg. of I and 3 ml. of Ac_2O in 5 ml. of pyridine was heated in a sealed tube at 120° for 18 hr. The reaction mixture was worked up in the usual manner to give only monoacetate, m.p. 136°, undepressed by admixture with an authentic sample obtained in method a). Their IR spectra were identical.

*4 All melting points are uncorrected.

Acetylation of 7-Amino-2,3,6-trimethylpyrazolo[1,5-*a*]pyrimidine (II)——A mixture of 500 mg. of II and 5 ml. of Ac_2O in 15 ml. of pyridine was heated at 100° for 6.5 hr. The reaction mixture was concentrated and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with cold 10% K_2CO_3, H_2O and dried over $MgSO_4$. The crystalline residue after removal of the solvent was recrystallized from ether to give IV as pale yellow sticks, m.p. 137~138°. Yield, 650 mg. (89.2%). *Anal.* Calcd. for $C_{13}H_{16}O_2N_4$: C, 59.98; H, 6.20; N, 21.53. Found: C, 60.41; H, 6.39; N, 21.26.

From the mother liquid were obtained colorless silky needles (50 mg.), m.p. 180~181°. Physical data of this product corresponded to the monoacetate (V). *Anal.* Calcd. for $C_{11}H_{14}ON_4 \cdot \frac{1}{2}H_2O$: C, 58.13; H, 6.66; N, 24.62. Found: C, 58.23; H, 7.06; N, 24.53.

Hydrolysis of IV——a) IV (500 mg.) was chromatographed on Al_2O_3 (*Merck.* neutral, $CHCl_3$). Elution with $CHCl_3$ afforded a product as colorless needles, m.p. 180°, which was proved to be identical with V by the mixture melting point and IR spectra determinations. Yield, 365 mg.

b) IV (100 mg.) was dissolved in 50% AcOH at room temperature and led to stand overnight. The mixture was concentrated *in vacuo*, and the colorless residue was recrystallized from acetone to give V as colorless needles, m.p. 180~181°.

7-Imino-2,3,4-trimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (VI)——To 3.0 g. of I dissolved in 50 ml. of acetone was added 2.62 g. of CH_3I. The mixture was heated at 100° in a sealed tube for 4 hr. After cooling, the precipitated crystals were collected and recrystallized from MeOH-H_2O to give colorless needles, m.p. 295° (decomp.). Yield, 5.0 g. (89%). *Anal.* Calcd. for $C_9H_{12}N_4 \cdot HI$: C, 35.54; H, 4.28; N, 18.42. Found: C, 35.63; H, 4.39; N, 18.44.

The hydroiodide was dissolved in hot H_2O and the solution was made alkaline with NaOH after being cooled to ca. 50°. The precipitated crystals were filtered and the solid was recrystallized from acetone to give colorless sticks, m.p. 164°. *Anal.* Calcd. for $C_9H_{12}N_4 \cdot \frac{1}{2}H_2O$: C, 58.35; H, 7.07; N, 30.25. Found: C, 58.24; H, 7.14; N, 29.77.

4-Ethyl-7-imino-2,3-dimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (VII)——A mixture of I (1.62 g.) and C_2H_5I (1.56 g.) in 20 ml. of acetone was treated by the ordinary method to give VII·HI as light yellow needles, m.p. 296° (decomp.). Yield, 2.4 g. (75%). *Anal.* Calcd. for $C_{10}H_{14}N_4 \cdot HI$: C, 37.78; H, 4.75; N, 17.61. Found: C, 37.23; H, 4.77; N, 17.23.

Free base in colorless plates from acetone-ether, m.p. 98~100°. *Anal.* Calcd. for $C_{10}H_{14}N_4 \cdot H_2O$: C, 57.67; H, 7.74; N, 26.90. Found: C, 57.52; H, 8.05; N, 26.81.

4-Allyl-7-imino-2,3-dimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (VIII)——A mixture of I (3.0 g.) and allyl bromide (2.24 g.) in 50 ml. of acetone was treated in a usual way. VIII·HBr as colorless sticks (EtOH), m.p. 261~262° (decomp.). Yield, 4.2 g. *Anal.* Calcd. for $C_{11}H_{14}N_4 \cdot HBr$: C, 46.65; H, 5.34; N, 19.79. Found: C, 46.56; H, 5.52; N, 19.35.

Free base in colorless rhombs. from ether, m.p. 88~91°. *Anal.* Calcd. for $C_{11}H_{14}N_4 \cdot \frac{1}{2}H_2O$: C, 62.53; H, 7.16; N, 26.55. Found: C, 62.65; H, 7.20; N, 26.47. Picrate in yellow needles from EtOH, m.p. 194°. *Anal.* Calcd. for $C_{11}H_{14}N_4 \cdot C_6H_3O_7N_3$: C, 47.33; H, 3.97; N, 22.73. Found: C, 47.37; H, 4.08; N, 22.52.

7-Imino-2,3,4,6-tetramethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (IX)——A mixture of 1.4 g. of II and 1.13 g. of CH_3I in 30 ml. of acetone was heated in a sealed tube at 100° for 8 hr. After cooling, the precipitated crystals were collected and washed. Recrystallization of the product gave IX as light yellow scales, m.p. 278° (decomp.). *Anal.* Calcd. for $C_{10}H_{14}N_4 \cdot HI$: C, 37.72; H, 4.75; N, 17.61. Found: C, 37.58; H, 4.96; N, 17.31.

Free base in colorless sands from MeOH-acetone, m.p. 154°. *Anal.* Calcd. for $C_{10}H_{14}N_4 \cdot 3/2\,H_2O$: C, 55.3; H, 7.89; N, 25.78; H_2O, 12.45. Found: C, 55.42; H, 8.19; N, 25.90; H_2O, 12.55.

4-Ethyl-7-imino-2,3,6-trimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (X)——A mixture of 2.0 g. of II, and 1.77 g. of C_2H_5I in 30 ml. of acetone was treated in a common way. Colorless needles (MeOH), m.p. 278° (decomp.). *Anal.* Calcd. for $C_{11}H_{16}N_4 \cdot HI$: C, 39.90; H, 5.16; N, 16.88. Found: C, 39.76; H, 5.16; N, 16.88. Found: C, 39.76; H, 5.23; N, 17.38.

Free base in colorless sticks from ether, m.p. 98~100°. *Anal.* Calcd. for $C_{11}H_{16}N_4$: C, 59.93; H, 8.16; N, 25.21. Found: C, 60.04; H, 8.22; N, 25.14.

4-Allyl-7-imino-2,3,6-trimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (XI)——Hydrobromide in pale yellow plates from MeOH-EtOAc, m.p. 228° (decomp.). Yield, 71%. *Anal.* Calcd. for $C_{12}H_{16}N_4 \cdot HBr$: C, 48.49; H, 5.77; N, 18.85. Found: C, 49.17, H, 5.85; N, 18.87.

Free base in colorless sticks from ether, m.p. 105~108°. *Anal.* Calcd. for $C_{12}H_{16}N_4$: C, 66.64; H, 7.46; N, 25.91. Found: C, 66.45; H, 7.61; N, 25.50.

7-Acetylimino-2,3,4-trimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (XII)——a) A mixture of 800 mg. of III and 560 mg. of CH_3I in acetone was heated in a sealed tube at 95~105° for 15 hr. After cooling, the precipitated yellow crystals were collected (1.06 g.). Recrystallization of the crystals afforded XII as yellow plates, m.p. 223° (decomp.). *Anal.* Calcd. for $C_{11}H_{14}ON_4 \cdot HI$: C, 38.16; H, 4.37; N, 16.18; I, 36.66. Found: C, 38.28; H, 4.67; N, 15.73; I, 37.03.

Hydroiodide was dissolved in small amount of H_2O and neutralized with K_2CO_3 under ice-water cooling. The precipitated solids were filtered and washed. The solids were recrystallized from acetone to give pale yellow sticks, m.p. 145°. *Anal.* Calcd. for $C_{11}H_{14}ON_4 \cdot H_2O$: C, 55.91; H, 6.83; N, 23.72; H_2O, 7.62. Found : C, 56.06; H, 7.08; N, 23.33; H_2O, 7.53.

Free base was redissolved in acetone and acidified with conc. HI, the mixture was concentrated to give yellow plates, m.p. 220° (decomp.), which was identified with the sample mentioned above.

Hydrochloride in yellow rhombs, from MeOH-acetone, m.p. >275°. *Anal.* Calcd. for $C_{11}H_{14}ON_4 \cdot HCl \cdot 3/2\,H_2O$: C, 46.89; H, 6.44; N, 19.88; Cl, 12.58. Found : C, 46.49; H, 6.74; N, 20.06; Cl, 13.02.

b) Ⅵ (500 mg.) was dissolved in 5 ml. of pyridine. To the solution was added 3 ml. of Ac_2O. The mixture was heated at 100° for 5 hr. and concentrated. The brown residues were extracted with ether and the ether extract was concentrated to leave crystals (80 mg.). The crystals were recrystallized from acetone to give pale yellow sticks, m.p. 142°, undepressed by admixture with a sample obtained in a), and their IR spectra were identical.

7-Acetylimino-4-ethyl-2,3,6-trimethylpyrazolo[1,5-*a*]pyrimidine (XIII)——a) To a solution of X (500 mg.) in pyridine (8 ml.) was added 5 ml. of Ac_2O under cooling. The mixture was led to stand at room temperatures for 2 days. The brown reaction mixture was concentrated *in vacuo*. The residue was recrystallized from acetone-ether to give colorless scales of m.p. 155~157°. *Anal.* Calcd. for $C_{13}H_{18}ON_4$: C, 63.39; H, 7.37; N, 22.75. Found : C, 63.21; H, 7.44; N, 22.71.

b) A mixture of 1.0 g. of Ⅴ and 0.86 g. of C_2H_5I in acetone was heated in a sealed tube at 110~120° for 15 hr. After being evaporated, the residue was extracted with small amount of H_2O (the residue being Ⅴ, 0.62 g.) and the yellow H_2O extract was neutralized with K_2CO_3 under cooling, the separated oil was extracted with $CHCl_3$ and the $CHCl_3$ extract was dried over $MgSO_4$. The residue after removal of the solvent was recrystallized from ether to give XIII as colorless scales (36 mg.), m.p. 154°. This product was shown to be identical with the compound obtained in a) by a comparison of the IR spectra.

Hydrolysis of XII——XII (50 mg.) was dissolved in 3 ml. of 10% HCl, the solution was heated at 80° for 30 min. under stirring. The reaction mixture was concentrated *in vacuo* to leave crystalline residue, which was redissolved in H_2O and the solution was neutralized with K_2CO_3. The precipitated solid was filtered and recrystallized from acetone to give colorless needles (15 mg.) of m.p. 154°, which was identified as Ⅵ by the mixture melting point determination and a comparison of IR spectra.

Hydrolysis of XIII——XIII (100 mg.) was dissolved in acetone. The solution was chromatographed on Al_2O_3 (*Merck.* standardized) and the eluate fraction with acetone was recrystallized from acetone to give colorless needles, m.p. 225~227°, which was identified as XVI by the direct comparison of their IR spectra.

2,3,4-Trimethylpyrazolo[1,5-*a*]pyrimidine-7(4*H*)-one (XIV)——Colorless rhombs. (from acetone-ether), m.p. 235~236°. *Anal.* Calcd. for $C_9H_{11}ON_3$: C, 61.00; H, 6.26; N, 23.72. Found : C, 60.29; H, 6.48; N, 23.39.

Acid Hydrolysis of IX——X (200 mg.) was dissolved in 20 ml. of 20% HCl. The mixture was heated in a sealed tube at 130° for 17 hr. After cooling, the reaction mixture was concentrated and redissolved in H_2O, the solution then was neutralized with K_2CO_3 and concentrated. The residue was extracted with acetone to give 151 mg. (76%) of XVI as colorless needles, m.p. 228~230°. *Anal.* Calcd. for $C_{11}H_{15}ON_3$: C, 64.36; H, 7.37; O, 7.80. Found : C, 64.88; H, 7.91; O, 7.81.

2,3,4,6-Tetramethylpyrazolo[1,5-*a*]pyrimidine-7(4*H*)-one (XV)——A suspension of 2 g. of Ⅱ, 1.0 g. of $NaHCO_3$ and 1.7 g. of CH_3I in 20 ml. of acetone was heated in a sealed tube at 150° for 8 hr. After being cooled, the brown reaction mixture was concentrated. The residue was mixed with small amount of H_2O and extracted with EtOAc (recovering of the starting material, 210 mg.) and the aqueous layer was neutralized with K_2CO_3 to precipitate the crystals. Recrystallization of the crystals from MeOH-EtOAc afforded XVI as colorless sticks, m.p. 273°. Yield, 760 mg. (43%). *Anal.* Calcd. for $C_{10}H_{15}ON_3$: C, 62.80; H, 6.85; N, 21.98; O, 8.37. Found : C, 63.11; H, 7.14; N, 21.57; O, 8.66.

Hydrogenation of III with Lithium Aluminum Hydride——$LiAlH_4$ (120 mg.) was dissolved in THF. To the solution was added dropwise Ⅲ (500 mg.) dissolved in THF under ice-water cooling and stirring. The mixture was stirred at 65° for 3 hr. After then the reaction mixture was decomposed with 20% NaOH. Green colored organic solution was decanted and concentrated. The oily residue was extracted with $CHCl_3$ and dried. The extract was concentrated and submitted to Al_2O_3 chromatography using ether. The eluted crystals were recrystallized from ether to give XVII as colorless needles, m.p. 93~94°. Yield. 86%. *Anal.* Calcd. for $C_{10}H_{14}N_4$: C, 63.13; H, 7.42; N, 29.45. Found : C, 63.16; H, 7.55; N, 29.44.

7-Ethylamino-2,3,6-trimethylpyrazolo[1,5-*a*]pyrimidine (XVIII)——Colorless sticks (from hexane), m.p. 93~94°. Yield, 14.5%. *Anal.* Calcd. for $C_{11}H_{16}N_4$: C, 64.67; H, 7.90; N, 27.43. Found : C, 64.74; H, 7.95; N, 27.28.

7-(N-Ethylacetamido)-2,3-dimethylpyrazolo[1,5-*a*]pyrimidine (XIX)——To a solution of XVII (1.0 g.) in 20 ml. of pyridine was added 10 ml. of Ac_2O. The mixture was heated (in a sealed tube) at 140~145° for 15 hr. The brown residues after being concentrated were extracted with EtOAc and the organic solution was washed with K_2CO_3, H_2O and dried over $MgSO_4$. The brown residue after removal of the sol-

vent was chromatographed on Al_2O_3. A fraction eluted with ether was evaporated and the product was recrystallized from hexane to give light yellow long sticks, m.p. 86°. Yield, 170 mg. (14%). *Anal.* Calcd. for $C_{12}H_{16}ON_4$: C, 62.05; H, 6.94; N, 24.12. Found : C, 62.25; H, 7.06; N, 24.29. From the 2nd eluate fraction was recovered 155 mg. of the starting material.

7-(N-Ethylacetamido)-2,3,6-trimethylpyrazolo[1,5-*a*]pyrimidine (XX)——XVIII (600 mg.) was treated by the above described method. Light green scales (from hexane), m.p. 72~73°. Yield, 73 mg. (11%). *Anal.* Calcd. for $C_{13}H_{18}ON_4$: C, 63.39; H, 7.37; N, 22.75. Found : C, 63.27; H, 7.38; N, 22.96.

Hydrogenation of XIX with Lithium Aluminum Hydride——To a solution of THF containing 100 mg. of $LiAlH_4$ was added dropwise 120 mg. of XIX under ice-water cooling. The mixture was warmed on a steam bath at 55° for 4 hr. Decomposed the excess $LiAlH_4$ with 20% NaOH. The organic solution was decanted and evaporated. The residue was dissolved in $CHCl_3$ and the organic solution was washed with 10% NaOH, H_2O and dried over $MgSO_4$. Evaporation of the solvent gave colorless needles, m.p. 93°, which was identified as XVII by the direct comparison of their IR spectra.

Hydrogenation of XX with Lithium Aluminum Hydride——Hydrogenation of XX was treated by the above method to give colorless sticks, m.p. 92°, undepressed by admixture with an authentic sample of XVIII.

Hydrogenation of IV with Lithium Aluminum Hydride——To a solution of THF containing 350 mg. of $LiAlH_4$ was added dropwise 500 mg. of IV in 20 ml. of THF under ice-water cooling and stirring. The mixture was then heated at 60~70° for 6 hr. After cooling, the reaction mixture was decomposed with 10% NaOH, the organic solution was separated and concentrated. The light green oily residue was extracted with $CHCl_3$ and $CHCl_3$ extract was washed with 10% NaOH, H_2O and dried. The oily residue after removal of the solvent was chromatographed on Al_2O_3. From the eluate fraction with acetone were obtained 124 mg. (31.5%) of colorless sticks, m.p. 94°, undepressed by admixture with an authentic sample of XVIII.

4-Ethyl-7-ethylimino-2,3-dimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (XXI)——A mixture of 250 mg. of XVII and 250 mg. of C_2H_5I in acetone was heated (in a sealed tube) at 100° for 15 hr. After being cooled, the precipitated crystals were collected and washed with acetone. The crystals were recrystallized from acetone to give XXI as colorless rhombs, m.p. 210° (decomp.). Yield, 430 mg. *Anal.* Calcd. for $C_{12}H_{18}N_4 \cdot HI$: C, 41.63; H, 5.53; N, 16.18. Found : C, 41.45; H, 5.61; N, 16.12.

Free base in colorless sticks from ether, m.p. 121~122°. *Anal.* Calcd. for $C_{12}H_{18}N_4 \cdot 1\frac{1}{2}H_2O$: C, 58.74; H, 8.59; N, 22.90; O, 9.80. Found : C, 58.32; H, 8.72; N, 22.71; O, 10.60.

4-Ethyl-7-ethylimino-2,3,6-trimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (XXII)——A mixture of XVIII (250 mg.) and C_2H_5I (250 mg.) in acetone (10 ml.) was heated in a sealed tube at 110° for 15 hr. After being cooled, the precipitated crystals were filtered. Recrystallization of the crystals from MeOH-acetone afforded XXII as colorless sticks, m.p. 202° (decomp.). Yield, 250 mg. *Anal.* Calcd. for $C_{13}H_{20}N_4 \cdot HI$: C, 43.40; H, 5.86; N, 15.52. Found : C, 43.23; H, 5.89; N, 15.41.

Formylation of I——Acetic formic anhydride (5.0 g.) was added to 1.0 g. of I under cooling. Exothermic reaction occurred and the mixture became yellow clear solution. After being stood at room temperatures for 1.5 days, the reaction mixture was concentrated *in vacuo*. Recrystallization of the re-sidue from acetone afforded XXIII as light green needles, m.p. 189~190° (decomp.). Yield, 88%. IR $\lambda_{max}^{CHCl_3}$ cm^{-1} : 3320 (ν_{NH}), 1720 ($\nu_{C=O}$). *Anal.* Calcd. for $C_9H_{10}ON_4$: C, 56.83; H, 5.30; N, 29.46. Found : C, 56.95; H, 5.38; N, 29.11.

Formylation of II——a) Acetic formic anhydride (10 g.) was added to 2.0 g. of II under cooling. The reaction took place together with continuous evolution of gas and resulted to become a yellow clear solution. After being stood at room temperatures for a day, the solution was concentrated under reduced pressure. Recrystallization of the residue from acetone gave light green needles, m.p. 183° (decomp.). Yield, 1.6 g. (74%). IR $\lambda_{max}^{CHCl_3}$ mμ : 3355 (ν_{NH}), 1718 ($\nu_{C=O}$). *Anal.* Calcd. for $C_{10}H_{12}ON_4$: C, 58.81; H, 5.92; N, 27.44. Found : C, 58.79; H, 6.10; N, 27.53.

b) Acetic formic anhydride (20 ml.) was added to 2.0 g. of II under cooling. After being stood at room temperatures for a day, the solution was evaporated to dryness under reduced pressure. The residue was dissolved in $CHCl_3$ and washed with cold K_2CO_3, H_2O and dried over $MgSO_4$. Recrystallization of the residue after removal of the solvent from acetone (quick treatment being neccessary) afforded diformylate (XXV) as yellow plates, m.p. 163° (decomp.). Yield, 2.26 g. IR : $\lambda_{max}^{CHCl_3}$ 1716 cm^{-1} ($\nu_{C=O}$). *Anal.* Calcd. for $C_{11}H_{12}O_2N_4$: C, 56.89; H, 5.21; N, 24.13. Found : C, 57.21; H, 5.40; N, 24.18.

Hydrogenation of XXIII with Lithium Aluminum Hydride——$LiAlH_4$ (0.7 g.) was dissolved in 60 ml. of THF. To this solution was added 1.0 g. of XXIII in THF under cooling and the mixture was stirred at 70° for 5 hr. The reaction mixture was decomposed with 10% NaOH, and the organic solution was separated and evaporated. The residue was extracted with $CHCl_3$ and $CHCl_3$ extract was washed with 5% NaOH, H_2O and dried. Recrystallization of the residue after removal of the solvent gave XXVI as colorless plates, m.p. 146°. Yield, 0.83 g. *Anal.* Calcd. for $C_9H_{12}N_4$: C, 61.34; H, 6.86; N, 31.80. Found: C, 61.50; H, 7.01; H, 31.80.

Hydrochloride in colorless needles from MeOH-acetone, m.p. 243~244°. *Anal.* Calcd. for $C_9H_{12}N_4 \cdot HCl \cdot H_2O$: C, 46.85; H, 6.55; N, 24.26. Found : C, 47.09; H, 6.82; N, 24.27.

Hydrogenation of XXIV with Lithium Aluminum Hydride——To a THF containing 200 mg. of $LiAlH_4$ was added 250 mg. of XXIV in THF under cooling and stirring. The mixture was then stirred at 60～65° for 3 hr. After being cooled, the reaction mixture was decomposed with 10% NaOH and the organic solution was separated and evaporated. The residue was extracted with $CHCl_3$ and $CHCl_3$ extract was washed with 5% NaOH, H_2O and dried. Recrystallization of the residue after removal of the solvent from acetone afforded XXVII as colorless rhombs, m.p. 157°. Yield, 205 mg. (91.5%). *Anal.* Calcd. for $C_{10}H_{14}N_4$: C, 63.13; H, 7.42; N, 29.25. Found: C, 63.24; H, 7.42; N, 29.16.

Hydrochloride in light green sticks from MeOH-acetone, m.p. 261° (decomp.). *Anal.* Calcd. for $C_{10}H_{14}N_4 \cdot HCl$: C, 53.00; H, 6.66; N, 24.72. Found: C, 52.69; H, 6.88; N, 24.83.

Hydrogenation of XXV with Lithium Aluminum Hydride——$LiAlH_4$ (0.8 g.) was dissolved in THF (80 ml.). To the solution was added dropwise 1.0 g. of XXV in 10 ml. of THF under ice cooling and stirring. The mixture was heated to gentle reflux for 5 hr. under stirring. The reaction mixture was decomposed with 10% NaOH under ice-water cooling, the organic layer was separated and evaporated. The residue was extracted with $CHCl_3$ and the $CHCl_3$ extract was washed with 5% NaOH, H_2O and dried over anhydrous $MgSO_4$. The residue after removal of the solvent was recrystallized from Me_2CO to give colorless rhombs., m.p. 156°, which was proved to be identical with XXVII by the mixture melting point determination and a comparison of their IR spectra. No other product was detected.

7-Methylimino-2,3,4-trimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (XXVIII)——A mixture of 300 mg. of XXVII and 240 mg. of CH_3I in acetone was heated in a sealed tube at 100～110° for 15 hr. After cooling, the precipitated solids were filtered. The solids were recrystallized from MeOH to give XXVIII as light green needles, m.p. 269～270° (decomp.). *Anal.* Calcd. for $C_{11}H_{16}N_4 \cdot HI$: C, 39.78; H, 5.17; N, 16.85. Found: C, 39.91; H, 5.33; N, 16.97.

Free base in colorless plates from ether, m.p. 132°. *Anal.* Calcd. for $C_{11}H_{16}N_4$: C, 64.67; H, 7.90; N, 27.43. Found: C, 65.08; H, 8.13; N, 27.45.

Acetylation of 3-Bromo-6-methyl-7-aminopyrazolo[1,5-*a*]pyrimidine (XXIX)——XXIX (600 mg.) was dissolved in 10 ml. of pyridine. To the solution was added 5 ml. of Ac_2O under cooling, the mixture was then heated at 115° for 5.5 hr. The reaction mixture was concentrated to leave brown residue. The residue was extracted with EtOAc and the organic solution was washed with cold 5% Na_2CO_3, H_2O and dried. The residue after removal of the solvent was recrystallized from ether to give colorless needles, m.p. 160～161°. Yield, 730 mg. (88%). *Anal.* Calcd. for $C_{11}H_{11}O_2N_4Br$: C, 42.44; H, 3.57; N, 18.00. Found: C, 42.64; H, 3.73; N, 17.98.

7-(N-Formylacetamido)-2,3,6-trimethylpyrazolo[1,5-*a*]pyrimidine (XXXI)——a) Acetylation of XXIV: XXIV (200 mg.) was dissolved in 6 ml. of pyridine. To this solution was added 3 ml. of Ac_2O under cooling, the mixture was led to stand at room temperatures for 48 hr. The reaction mixture was concentrated under reduced pressure (below 30°) to leave yellow oil (170 mg.). The oil was led to place in a refrigerator covered with small amount of ether. The precipitated crystals were collected and recrystallized from ether to give yellow sticks, m.p. 113°. IR λ_{max}^{Nujol} cm^{-1}: 1730, 1721, 1623, 1232. *Anal.* Calcd. for $C_{12}H_{14}O_2N_4$: C, 58.52; H, 5.73; N, 22.75. Found: C, 58.82; H, 6.11; N, 22.49.

b) Formylation of V: To 700 mg. of V was added 16 ml. of acetic formic anhydride under cooling, the mixture was stood for a week at room temperatures. The yellow reaction mixture was concentrated below 40° to leave yellow viscous oil. The oil was covered with ether to give yellow crystallines, which were recrystallized from ether to give pale yellow sticks, m.p. 113° (210 mg.), undepressed by admixture with the sample obtained in a). They also gave identical IR spectra. *Anal.* Calcd. for $C_{12}H_{14}O_2N_4$: C, C, 58.52; H, 5.73; N, 22.75. Found: C, 58.54; H, 5.80; N, 22.78.

Acetylation of 7-Amino-3,6-dimethylpyrazolo[1,5-*a*]pyrimidine (XXXII)——a) XXXII (500 mg.) was dissolved in 6 ml. of Ac_2O, the solution was heated at 120～125° for 4 hr. and evaporated. The residue was extracted with EtOAc and the organic solution was washed with cold 5% K_2CO_3, H_2O and dried over anhydrous $MgSO_4$. The residue after removal of the solvent was recrystallized from ether to give XXXIV as pale yellow rhombs. (320 mg.), m.p. 119°. *Anal.* Calcd. for $C_{12}H_{14}O_2N_4$: C, 58.52; H, 5.73; N, 22.75. Found: C, 58.84; H, 5.83; N, 22.44.

Mother liquid was concentrated and the residue was chromatographed on Al_2O_3. A first eluate fraction with acetone was evaporated and the residue was recrystallized from ether to give 15 mg. of XXXII. A second eluate fraction with the same solvent was concentrated and the crystalline residue was recrystallized from ether to give XXXIII as colorless needles, m.p. 180～181°. Yield, 150 mg. *Anal.* Calcd. for $C_{10}H_{12}ON_4$: C, 58.81; H, 5.92; N, 27.44. Found: C, 58.75; H, 6.26; N, 27.08.

b) XXXIII (50 mg.) was dissolved in 2 ml. of pyridine. To the solution was added 1 ml. of Ac_2O and the mixture was heated at 100° for 8 hr. The reaction mixture was concentrated and the residue was recrystallized to give XXXIV as pale yellow plates. Yield, 50 mg.

7-Imino-3,4,6-trimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (XXXV)——A mixture of 500 mg. of XXXII and 440 mg. of CH_3I in 15 ml. of acetone was heated in a sealed tube at 100° for 5 hr. After cooling, the precipitated crystalline was collected and recrystallized from hot H_2O to give pale yellow sticks,

m.p. 292° (decomp.). Yield, 808 mg. (86.2%). *Anal.* Calcd. for $C_9H_{12}N_4 \cdot HI$: C, 35.54; H, 4.28; N, 18.42. Found : C, 35.36; H, 4.47; N, 18.42.

Free base in colorless sticks from acetone, m.p. 170°. *Anal.* Calcd. for $C_9H_{12}N_4$: C, 61.34; H, 6.86; N, 31.80. Found : C, 61.36; H, 6.94; N, 31.12. Monohydrate in colorless rhombs., m.p. 163°. *Anal.* Calcd. for $C_9H_{12}N_4 \cdot H_2O$: C, 55.65; H, 7.27; N, 28.85. Found : C, 55.32; H, 7.46; N, 28.40.

4-Allyl-7-imino-3,6-dimethyl-4,7-dihydropyrazolo[1,5-*a*]pyrimidine (XXXVI)——Hydrobromide in colorless needles from MeOH-EtOAc, m.p. 233~234° (decomp.). Yield, 66.2%. *Anal.* Calcd. for $C_{11}H_{14}N_4 \cdot HBr$: C, 46.65; H, 5.34; N, 19.79. Found : C, 46.61; H, 5.42; N, 19.78.

Free base in colorless needles from ether, m.p. 99°. *Anal.* Calcd. for $C_{11}H_{14}N_4$: C, 65.32; H, 6.98; N, 27.70. Found : C, 64.94; H, 6.87; N, 27.90.

4-Allyl-3,6-dimethylpyrazolo[1,5-*a*]pyrimidin-7(4*H*)-one (XXXVII)——a) A mixture of 3.0 g. of XXXII, 2.24 g. of allyl bromide and 1.85 g. of $NaHCO_3$ in 30 ml. of acetone was heated in a sealed tube at 160~165° for 13 hr., the brown reaction mixture was concentrated and the residue was dissolved in H_2O, neutralized with K_2CO_3 and evaporated. Extraction with EtOH gave brown solids which were chromatographed on Al_2O_3 (*Merck*, neutral). A first eluate fraction with acetone gave crystals which were recrystallized from benzene to give XXXVII as colorless plates, m.p. 160~162°. Yield, 70 mg. *Anal.* Calcd. for $C_{11}H_{13}ON_3$: C, 65,00; H, 6.45; N, 20.68; O, 7.87. Found : C, 65.24; H, 6.55; N, 20.40; O, 8.11.

A second eluate fraction with acetone was concentrated to recover the starting material (320 mg.).

b) XXXVI (50 mg.) dissolved in 20% HCl was heated in a sealed tube at 140° for 15 hr. The reaction mixture was concentrated and redissolved in H_2O, the solution was neutrallized with K_2CO_3 and evaporated to dryness. The residue was extracted with acetone and chromatographed on Al_2O_3 to leave XXXVII as colorless plates, which were identified with the authentic sample by the mixture melting point determination and a comparison of the IR spectra.

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Summary

The behaviours of 7-amino-2,3-dimethyl- and 7-amino-2,3,6-trimethylpyrazolo[1,5-*a*]-pyrimidines (I, II) against acylation and alkylation were investigated. Mono- and diacylates were obtained from II but only monoacylate from I, of which reason was considered due to the steric effect of the methyl group at the 6-position. The substitution position of acyl groups was confirmed to be at 7-amino group but alkyl groups at N-4 position, respectively, from their chemical and physical evidences. Their nuclear magnetic resonance and ultraviolet spectra were also discussed briefly.

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