Communications to the Editor

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Intramolecular Cyclization of 4-Amino-5-(2,2-dicyanovinyl)-amino-1,3-dimethyluracil

A convenient synthesis of two 9-deazapurines (pyrrolo[3,2-*d*]pyrimidines) are described. A mechanism which consists of ring opening, followed by recyclization of 4-amino-5-(2,2-dicyanovinyl)amino-1,3-dimethyluracil is also proposed.

In connection with a previous report which concerned with intramolecular cyclization of *o*-(2-substituted-2-cyanovinyl)aminoaniline hydrochloride,[1] we have examined a cyclization of 4-amino-5-(2-substituted-2-cyanovinyl)amino-1,3-dimethyluracil (**1a**) and (**1b**).

Stahl and coworkers[2] failed to obtain 1,3-dimethylxanthine (**2**) but instead obtained 2-[[(6-amino-1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxo-5-pyrimidinyl)amino]methylene]-3-(methylimino)-butyronitrile (**3**) by refluxing 4-amino-5-(2,2-dicyanovinyl)amino-1,3-dimethyluracil (**1a**) in dimethylformamide. Our attempts to cyclize the cyano group with the amino group in the molecule of **1a** also failed. The reason for these results was thought to be due to the decreased basicity of 4-amino of **1a** by the -M effect of a conjugated carbonyl group at 6-position. In these experiments, however, we found a new route to 9-deazapurine derivatives by acidic hydrolysis of **1a** and **1b**.

Iminoesterification of **1a** by the Pinner method,[3] followed by hydrolysis gave crystals, $C_{10}H_{11}N_3O_4$, mp 266—267° (recrystallization from EtOH+CH_2Cl_2) in 48% yield. There was no absorption band in the region of a nitrile group in the infrared (IR) spectrum of the compound. Though we expected two N-methyl proton signals in its nuclear magnetic resonance (NMR) spectra, there was only one, [in dimethylsulfoxide *d*-6, δ ppm from tetramethylsilane (TMS), 1.30 (3H, triplet, J=7 Hz, $C\underline{H}_3CH_2$–), 3.25 (3H, singlet, CH_3–N), 4.28 (2H, quartet, J=7 Hz, $CH_3C\underline{H}_2$–), 7.70 (1H, singlet, olefinic proton), 10.33 (1H, broad, D_2O exchangeable) and 12.50 (1H, broad, D_2O exchangeable)].[4] These phenomena seem to be significant changes in comparison with those of the starting material. Moreover, the ultraviolet (UV) spectral data of the product were a very similar to those of ethyl 2,3,4,5-tetrahydro-3,6-dimethyl-2,4-dioxo-1H-pyrrolo[3,2-*d*]pyrimidine-7-carboxylate reported by Murata and Ukawa[5] (Table I). From these analytical data, we elucidated the structure of the compound as a 9-deazapurine derivative, ethyl 2,3,4,5-tetrahydro-3-methyl-2,4-dioxo-1H-pyrrolo[3,2-*d*]pyrimidine-7-carboxylate (**7b**).

Compound (**7b**) was also obtained from **1b** by the same method. It is worth noting that when heated in 15% hydrochloric acid the compounds (**1a**) and (**1b**) were easily converted to 2,3,4,5-tetrahydro-3-methyl-2,4-dioxo-1H-pyrrolo[3,2-*d*]pyrimidine-7-carbonitrile (**7a**) [mp> 300°; NMR[4] in dimethylsulfoxide *d*-6, δ ppm from TMS, 3.27 (3H, singlet, CH_3–N), 7.98 (1H, singlet, olefinic proton), 11.90 (1H, broad, D_2O exchageable) and 13.00 (1H, broad, D_2O exchan-

1) Y. Okamoto and T. Ueda, *J. Chem. Soc., Chem. Comm.*, **1973**, 367.
2) P.H. Stahl, R. Barchet, and K.W. Merz, *Arzneim.-Forsch.*, **18**, 1214 (1968).
3) A. Pinner and F. Klein, *Ber.*, **10**, 1889 (1877).
4) Though there lies obscurity in the assignment of NH protons, we think that the signal at lower field might be due to pyrrole ring NH proton. These assignments were based on the effect of electronwithdrawing group at 6 position and data on pyrrolo[3,2-*d*]pyrimidine systems, where a chemical shift of pyrrole ring NH proton was observed at the same or lower field than that of pyrimidine NH proton [K. Imai, *Chem. Pharm. Bull.* (Tokyo), **12**, 1030 (1964)].
5) T. Murata and K. Ukawa, *Chem. Pharm. Bull.* (Tokyo), **22**, 240 (1974).
6) K. Klemm and W. Prüsse, *Liebig's Ann. Chem.*, **1974**, 1882.

geable); IR cm^{-1} $\nu_{C\equiv N}$ 2225 (KBr); UV λ_{max}^{EtOH} nm (log ε), 221 (4.43), 269 (3.91)] in 69% yield and **7b** in 57% yield, respectively, with evolution of carbon dioxide.

We propose a mechanism where the ring opening of the starting material by hydrolytic N(3)–C(4) bond fission, followed by recyclization of the carbonyl group with the exocyclic amino group might give a new pyrimidine ring **5a** or **5b**. The enamine system in **5a** or **5b** might react with another carbonyl group to form the pyrrole ring system. No reaction was found to occur when 4-amino-5-(2,2-dicyanovinyl)amino-1-methyluracil (**8**) was treated with 15% hydrochloric acid. Therefore, it can be pointed out that the carbonyl group involved in the formation of the pyrrole ring might be at 4-position of **5a** or **5b** (Chart 1).

Although Klemm and Prüsse[6] have recently reported the ring conversion of 4-amino-1,3-dimethyl-5-nitrosouracil to 4,5-diimino-1,3-dimethyl-2-imidazolidinone, we believe that this kind of recyclization might be the first example for 1,3-dimethyluracil ring systems.

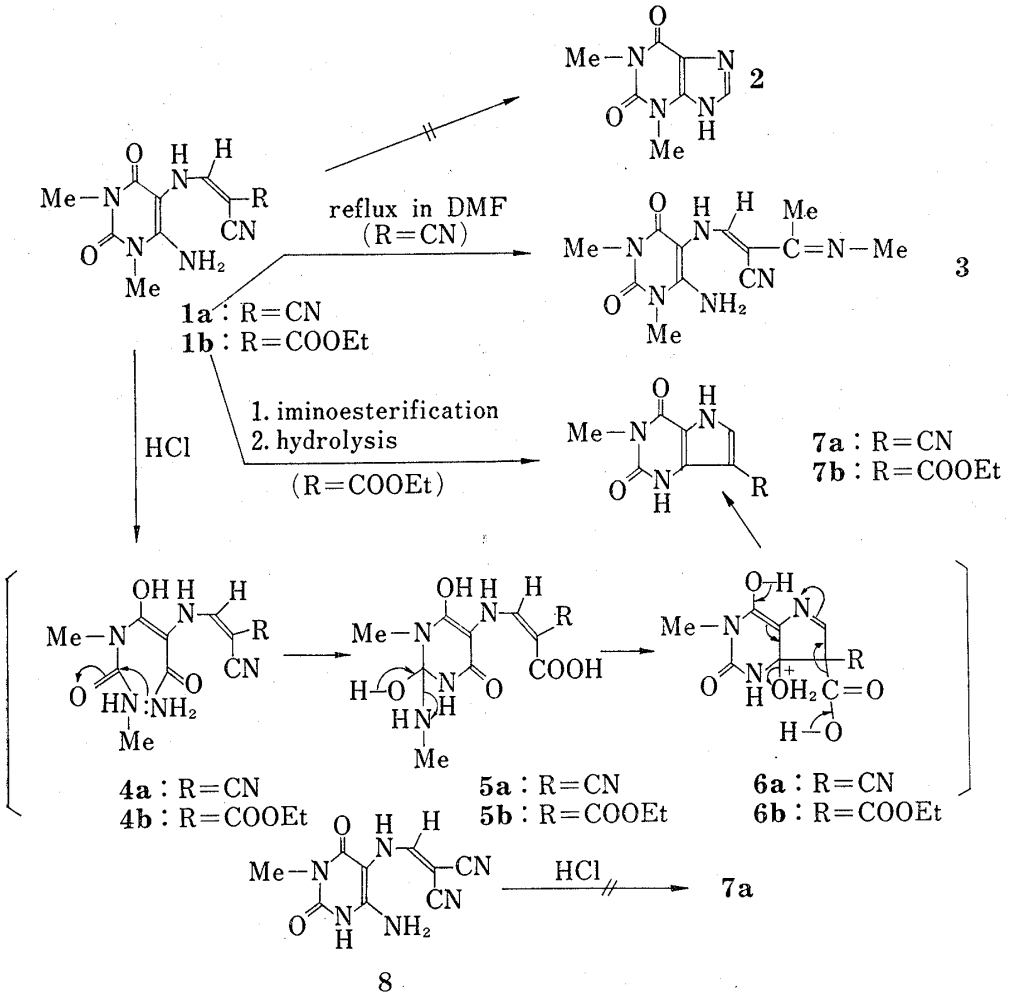
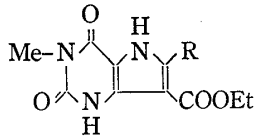


Chart 1

Table I. UV Absorption Data of **7b** and Its 6-Methyl Derivative

	R	λ_{max}^{EtOH}	nm (log ε)
	H	228.5 (4.35)	269 (3.92)
	CH_3	229.5 (4.48)	270 (4.00)

Compound (**7a**) might be a useful starting material for synthesis of its derivatives and the study is now being in progress.

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Chemische Untersuchungen der Inhaltsstoffe von *Pteris dispar* KUNZE[1)]

Im Zusammenfang mit der chemotaxonomischen Untersuchungen der Gattung *Pteris* und der verwandten Gattungen wurden aus den oberirdischen Teilen von *Pteris dispar* KUNZE neben der schon bekannten ent-11α-Hydroxy-15-oxo-Kaur-16-en-19-carbonsäure (III) vier neue ent-Kaurantyp-Diterpene, nämlich ent-11α-Hydroxy-15-oxo-16*S*-Kauran-19-carbonsäure (I), ent-11α-Hydroxy-15-oxo-16*R*-Kauran-19-carbonsäure (II), ent-7α,9-Dihydroxy-15-oxo-Kaur-16-en-19,6β-olid (IV) und ent-7α,9-Dihydroxy-15-oxo-16*S*-Kauran-19,6β-olid (V), isoliert.

In Fortsetzung unserer chemischen und chemotaxonomischen Untersuchungen der Gattung *Pteris* und der verwandten Gattungen wurde *Pteris dispar* KUNZE (jap. Name: Amakusashida, Fundort: Kagoshima, Sammelzeit: August, 1975) auf die Inhaltsstoffe untersucht. Die oberirdischen Teile dieser Pflanzen wurden mit heissem Methanol extrahiert und der konzentrierte Extrakt mit Aktivkohle behandelt. Der Rückstand des Extrakts wurde durch Säulen- und präparative Dünnschichtchromatographie fraktioniert und fünf ent-Kaurantyp-Diterpene A, B, C, D und E wurden kristallin isoliert. Unter denen konnte C als ent-11α-Hydroxy-15-oxo-Kaur-16-en-19-carbonsäure(III) identifiziert werden, die Tanaka und Miarbb. durch Hydrolyse eines aus den Blättern von *Stevia paniculata* isolierten Glykosids bekommen haben.[2)]

Wie die Massenspektroskopischen Daten von A und B zeigen, handelt es sich offensichtlich bei A und B ein Isomerenpaar, das die Summenformel $C_{20}H_{30}O_4$ besitzt. In den kernmagnetischen Resonanz (NMR)-Spektren von A und B erscheint ein Methyldublett (J=6 Hz) jeweils bei 1.23 und 1.00 ppm, an Stelle von Methylensignale, die in dem von C beobachtet werden, sonst ähneln sie dem von C gleichen. Dies lässt vermuten, dass bei A und B eine hydrierte Struktur von C vorliegt. Durch katalytische Hydrierung von C mit PtO_2 bekommt man A und weiter durch sechs stündiges Erhitzen von A mit 2% NaOH in MeOH ein Gleichgewichtsgemisch aus A und B (im Mengenverhältnis von 1:3). Das CD-Spektrum von A zeigt einen negativen Cotton-Effekt n—π^* bei 309 nm ($[\theta]_{309}$—1730°, MeOH), während das von B einen positiven Cotton-Effekt bei 301 nm ($[\theta]_{301}$+1510°, MeOH).[3)] Diese Ergebnisse

1) Chemische und chemotaxonomische Untersuchungen der Gattung *Pteris* und der verwandten Gattungen (Pteridaceae) XI. Mitteil., X. Mitteil.: T. Murakami, K. Aoyama, N. Tanaka, und Chiu-Ming Chen, *Chem. Pharm. Bull.* (Tokyo), **24**, 173 (1976).
2) H. Kohda, O. Tanaka, und K. Nishi, *Chem. Pharm. Bull.* (Tokyo), in Druck.
3) J. MacMillan und E.R.H. Walker, *J. Chem. Soc.* Perkin I, 986 (1972).