oxidative insertion of palladium into the carbon–iodine bond of the iodopurine followed by coupling of the derived Pd(II) complex with the tin enolate of acetone (formed in situ from isopropenyl acetate and tri-*n*-butyltin methoxide), trans–cis isomerization, and reductive elimination to give the product with concomitant regeneration of the Pd(0) catalyst.[19] It is the first example of the use of an organotin reagent in a palladium-catalyzed cross-coupling reaction involving nucleosides. Other methods attempted, such as the photoinduced $S_{RN}1$ reaction,[5,20] the Eschenmoser sulfide contraction,[21] and Meerwein-type reactions[22] were all unsuccessful.

The aforementioned protected acetonylated nucleoside **6** was converted to the target molecule **7** in two steps by reaction first with trimethylsilyl iodide (64%) and subsequently with tetraethylammonium fluoride (93%). The overall yield of **7** starting from guanosine was 18%. Masking of the amide carbonyl oxygen at the 6-position as a methoxy group is an effective way of protecting the inosine system as this group is relatively stable and can be easily removed at the conclusion of a reaction sequence. Compound **7** (a solid, mp 114–116 °C) was purified by reversed-phase HPLC on Amberlite XAD-4 resin and was characterized by UV, FTIR, and high field NMR spectroscopy. Only the keto tautomer of the compound was present, this form being stabilized by intramolecular hydrogen bonding. The 2-acetonyl compound **6** could be reduced readily by sodium borohydride to give, after deprotection, the diastereoisomeric alcohols **8**.

The scope of this palladium-catalyzed cross-coupling reaction can be extended to include other activated organostannanes. For example, reaction of **5** with tri-*n*-butyl(cyanomethyl)stannane[23] under palladium catalysis resulted in the formation of the 2-cyanomethylinosine in 55% yield. 2-Vinylinosine **10** (or **9**), potentially a key precursor for the synthesis of a variety of functionalized alkylated purine nucleosides, is also readily available with use of the aforementioned methodology. Thus, the thermal reaction of **5** with tri-*n*-butyl(vinyl)stannane in the presence of palladium chloride afforded **9** in excellent yields (>90%). Compound **11** (the partially deprotected form of **9**), can be hydroxylated with osmium tetroxide (65%) and then deprotected to give the highly hydroxylated compound **12**. Additionally, reaction of the vinyl compound **9** with 9-BBN followed by oxidative workup resulted in the regiospecific formation (52% yield, 65% conversion) of the terminal alcohol which was deprotected to afford **13**. Hydroboration reactions have rarely been used previously to elaborate structures in purine nucleoside chemistry.

In summary, palladium-catalyzed cross-coupling reaction of 2-iodinated purines with organostannanes is a highly efficient approach to the synthesis of new and rare functionalized purine nucleosides. This approach may find wide application in purine and related heterocyclic chemistry. Biological studies assessing the antiviral activities of the target molecules against RNA viruses are currently under investigation.[24]

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Supplementary Material Available: NMR (^1H and ^{13}C), UV, FTIR, and FAB (HRMS) spectral data for target molecules (5 pages). Ordering information is given on any current masthead page.

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(24) One of the target molecules, 2-acetonylinosine, shows very high activity against some RNA viruses.

Albomitomycin A and Isomitomycin A: Products of Novel Intramolecular Rearrangement of Mitomycin A

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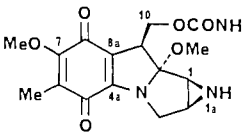
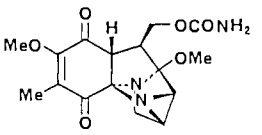
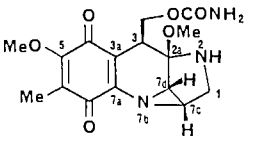
Mitomycins are potent antitumor antibiotics,[1] and considerable research efforts have been made to rationalize the mechanism of action of mitomycins.[2] As part of our approach, we have been screening the minor constituents from the fermentation broth of mitomycins[3] since 1977. Fortuitously, we found two novel isomers of mitomycin A (**1**), designated as albomitomycin A (**2**) and isomitomycin A (**3**), from *streptomyces caespitosus*, and their tripartite interconversion (**1** and **3** via **2**), refered to as mitomycin rearrangement. We herein report the structure elucidation of **2** and **3** and their unique intramolecular reactions in Michael and retro-Michael modes.



1



2



3

Albomitomycin A (**2**), isolated as colorless plates from $CHCl_3$[4] ($[\alpha]^{23}_D$ − 2.7° (*c* 0.50, $CHCl_3$)), decomposed at a temperature over 130 °C, converting, in part, to **1** and **3**. Its molecular formula, $C_{16}H_{19}N_3O_6$, was determined on the basis of elemental analysis and high resolution EI–MS.[5] The mass fragments[6] were completely the same as those of **1**, suggesting that **2** was changed to **1** in the ionization process. Furthermore, **2** was changed, in part, to **1** on TLC silica gel accompanied by a change in hue to **1**'s characteristic reddish purple color in several hours. In the electronic spectrum[7] of **2**, an important characteristic was its colorless state; it did not show any R absorption band of a quinone

(1) *Mitomycin C; Current Status and New Developments*; Carter, S. K., Crooke, S. T., Eds.; Academic Press: New York, 1979.
(2) Tomasz, M.; Lipman, R.; Chowdary, D.; Pawlak, J.; Verdine, G. L.; Nakanishi, K. *Science (Washington D.C.)* **1987**, *235*, 1204 and references therein.
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(4) The procedures of chromatographic separations for **2** and **3** are given in the Supplementary Material.
(5) Anal. Calcd for $C_{16}H_{19}N_3O_6$: C, 55.01; H, 5.48; N, 12.03. Found: C, 54.93; H, 5.43; N, 12.01. HRMS calcd for $C_{16}H_{19}N_3O_6$ *m/z* 349.1274, found *m/z* 349.1276.
(6) Mass fragments of **1** and **2**: *m/z* 349 (M^+), 317, 302, 288, 273, and 257.
(7) The electronic spectrum of **2**: λ_{max}^{EtOH} 288 nm, ε 10000, 215 nm, ε 6300.

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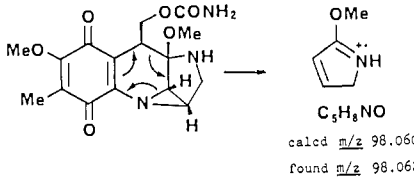
moiety, but **1** showed the R band of 525 nm (in MeOH).[8] In contrast with the complex carbonyl stretching region of **1**'s IR (KBr) the simplified carbonyl absorptions[9] of **2** also implied the transformation of the quinone skeleton.

The inspection of ^1H and ^{13}C NMR spectra of **2** revealed that the skeleton was extremely close to **1** except for the fact that the quinone of **1** was converted to 2-hexene-1,4-dione moiety in **2**. The relative configuration between the appeared methine proton at C-8a and the carbamoyloxymethyl was determined to be cis by the presence of significant NOE.[10] The C-4a (δ 87.5 in $CDCl_3$) was suggestive of the dihetero-atom-substituted sp^3 carbon in view of the chemical shift. Thus the full structure was led by the reasonable connection between the C-4a with the nitrogen of the aziridine considering the molecular formula.[11]

The discovery of **2** prompted us to search for a new tetracyclic isomer of **1**, because intramolecular retro-Michael reactions of **2** may afford both **1** and **3**. Our efforts were directed toward investigating the culture broth, and we succeeded in isolating the expected **3**.[4]

Isomitomycin A (**3**), obtained as yellowish orange needles from $CHCl_3$ (mp 78–80 °C, $[\alpha]^{23}_D$ −273 °C (*c* 0.17, $CHCl_3$), on TLC silica gel was converted, in part, to **1** and **2** in several hours. The molecular formula, $C_{16}H_{19}N_3O_6$, was determined in the same way as **2**.[13] The mass spectrum of **3**[14] was partly different from that of **1** and showed the characteristic fragment, *m/z* 98 (base peak; described later), which was not found in **1**. The electronic spectrum[15] showed the presence of a quinone. IR (KBr)[16] showed a band ascribable to a carbamoyl carbonyl (1721 cm^{-1}).

The analysis of ^1H and ^{13}C NMR spectra[10] verified the partial structure resembling C-4a through C-10 in **1** and another right wing skeletal connection consisting of a secondary amine, a methylene, and an aziridine. The plane structure of **3** was led by connecting N-7b with C-7a and C-2a with C-3 and N-2, respectively, on the basis of LSPD experiments.[17] This novel tetracyclic ring system was also supported by the fragment ion (*m/z* 98) in EI–MS, which could be interpreted as an intermediate generated by the retro-Diels–Alder reaction in **3**. The stereochemistry was unambiguously determined by the chemical property; **3** was able to be easily transformed to **1** via **2**.



In the study of structure elucidation of **3** it became of interest to examine whether **1** in itself could be transformed to **2** or **3** in a solution or not. In practice, both transformations of **1** to **2** and **1** to **3** via **2** were confirmed by HPLC in a protic solvent. Thus the absolute structures of both **2** and **3** were uniquely determined to have a relationship with that of **1**.[18] They were equilibrated in MeOH at room temperature within 3 days, and the equilibrium trended to **1**.[19] In an aprotic solvent, they were stable in several days. However, we found some Lewis acids, e.g., triisopropoxyaluminum, accelerated the rearrangement reaction even in an aprotic solvent.

A remarkable structural feature of **2** is the unprecedented pentacyclic ring system. Another conspicuous characteristic of **2** is that this new ring system would be exchangeable to the mitomycin skeleton and the novel 2,7b-diazabenzo[*f*]cyclopropa[*cd*]indene-4,7-dione skeleton of **3** through an intramolecular retro-Michael reaction. The structures of **2** and **3** present a new and promising pathway for the total syntheses of mitomycins[20] and mitomycin analogues which would be clinically more valuable than mitomycin C.[1] The study of a new analogue by the use of **2** and **3** is under way.

Acknowledgment. We are grateful to Dr. M. Kasai for his help in the preparation of this paper.

Supplementary Material Available: The procedures of chromatographic separations for **2** and **3**; listing of ^1H and ^{13}C NMR data for **1**, **2**, and **3**; and listing of the equilibrium ratio of **1**, **2**, and **3** in various solvents (5 pages). Ordering information is given on any current masthead page.

(8) Uzu, K.; Harada, U.; Wakaki, S. *Agr. Biol. Chem.* **1964**, *28*, 388.
(9) IR spectra (KBr): **1** (1500–1800 cm^{-1}) 1727, 1701, 1665, 1641, 1627, 1584, 1568 cm^{-1}; **2** 3500, 3370, 2970, 2940, 1737, 1696, 1658, 1598, 1333, 1303, 1235, 1134, 1063, 1045, 955 cm^{-1}.
(10) ^1H and ^{13}C NMR data for **2** and **3** are given in the Supplementary Material.
(11) Due to the absence of certain results in LSPD experiments in $CDCl_3$ and Py-d_5 we were unable to connect C-4a with the nitrogen of the aziridine at the beginning. The answer for this problem was given by the concurrent of X-ray crystallography for the relative configuration.[12] Later the C-4a was proven to be located in the neighborhood of H-1 by LSPD in DMSO-d_6.[10]
(12) This study was made independently. Hirayama, N.; Shirahata, K., *Acta Crystallogr., Sect. B*, to be published.
(13) Anal. Calcd for $C_{16}H_{19}H_3O_6$: C, 55.01; H, 5.48; N, 12.03. Found: C, 55.16; H, 5.55; N, 11.74. HRMS calcd for $C_{16}H_{19}N_3O_6$ *m/z* 349.1274, found *m/z* 349.1237.
(14) Mass fragments of **3**: *m/z* 349 (M^+), 288, 275, 259, and 98.
(15) The electronic spectrum of **3**: λ_{max}^{MeOH} 294 nm, ϵ 5200, 410 nm, ϵ 340. Strong end absorption was observed to 240 nm.
(16) IR spectrum (KBr): **3** 3500, 3440, 3360, 2950, 2860, 1721, 1701, 1694, 1642, 1595, 1334, 1307, 1228, 1216, 1081.
(17) The LSPD experiment in $CDCl_3$ provided unambiguous connectivity for the C-7a with the nitrogen of the aziridine; that is, an irradiation at H-7d (δ 3.17) or H-7c (δ 3.57) made the spectral wave form change more markedly on C-7a (δ 148.6) than that at H-1 (δ 3.33). The connection between the C-2a and the C-7d was supported by the LSPD experiment in $CDCl_3$; that is, an irradiation at H-7d (δ 3.17) enhanced the resonance at C-2a (δ 92.4).
(18) (a) Shirahata, K.; Hirayama, N. *J. Am. Chem. Soc.* **1983**, *105*, 1799. (b) Hirayama, N. *Acta Crystallogr. Sect. A*: Found *Crystallogr.* **1984**, *A40*, C-70. (c) This conclusion was independently verified on the basis of circular dichroic measurements. Verdine, G. L.; Nakanishi, K. *J. Chem. Soc., Chem. Commun.* **1985**, 1093.
(19) The table of the equilibrium ratio in some solvents is given in the Supplementary Material.
(20) During the processing of this manuscript, Fukuyama reported synthetic approaches toward mitomycins via isomitomycin A (**3**). Fukuyama T.; Yang, L. *Tetrahedron Lett.* **1986**, *27*, 6299.

Temperature-Dependent Geometric Isomerization Versus Fragmentation of 1,2-Dideuteriocyclobutane

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Fresh insights on the 1,4-diradical tetramethylene[1–4] generated thermally from tetrahydropyridazine (TP) and from cyclobutane (CB) have been gained through studies of stereospecifically deuteriated substrates.[5–9] At 380–420 °C, tetramethylene fragments to ethene about twice as fast as it closes to form CB; the two ends of the diradical appear to be stereochemically independent, with rotations about C–C bonds much more rapid than

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(3) Schaumann, E.; Ketcham, R. *Angew. Chem.* **1982**, *21*, 225–314.
(4) Dervan, P. B.; Dougherty, D. A. In *Diradicals*; Borden, W. T., Ed.; Academic Press: New York, 1982; pp 107–149.

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