Synthesis of 9-*epi*-Mitomycin B: The First Inversion of the C-9 Stereochemistry in Mitomycin B

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9-*epi*-Mitomycin B (**2b**) with the same C-9 stereochemistry as mitomycin C (**1**) was synthesized from mitomycin B (**2a**) through inversion at the C-9 position. 10-*O*-Decarbamoylmitomycin D (**8a**), derived from **2a** in two steps, was employed as the substrate for the epimerization. The 10-hydroxymethyl group in **8a** was epimerized on treatment with diazabicyclo[5.4.0]undec-7-ene to afford **8b**. Successive transformations performed on the functional groups of **8b** gave the desired **2b** in four steps. The stereochemistry in **2b** was confirmed by conversion of **2b** to the known mitomycin F (**4**).

Mitomycin C (**1**) is one of the most potent antitumor antibiotics known, especially against solid tumors, and it has been widely used in clinical chemotherapy.[1] For the purposes of identifying additional potent mitomycin analogues, our research efforts have been directed toward the naturally occurring mitomycins since 1977. We have found several mitomycin congeners[2,3] in the fermentation broth of mitomycins. The discovery of such analogues has led us to undertake the synthesis of compounds considered to be "missing links" in the mitomycin family. In our previous account,[4] we described the synthesis of 10-decarbamoyloxy-9-dehydromitomycins A and C, i.e., 1a-demethylmitomycins K and G. From the viewpoint of antitumor activity, hitherto unknown mitomycins with a β configuration at C-9 (such as **1**) also attracted our attention. In this article, we report the synthesis of 9-*epi*-mitomycins B[5] (**2b**) and D (**3b**) via the first example of inversion at the C-9 of mitomycins (Figure 1).

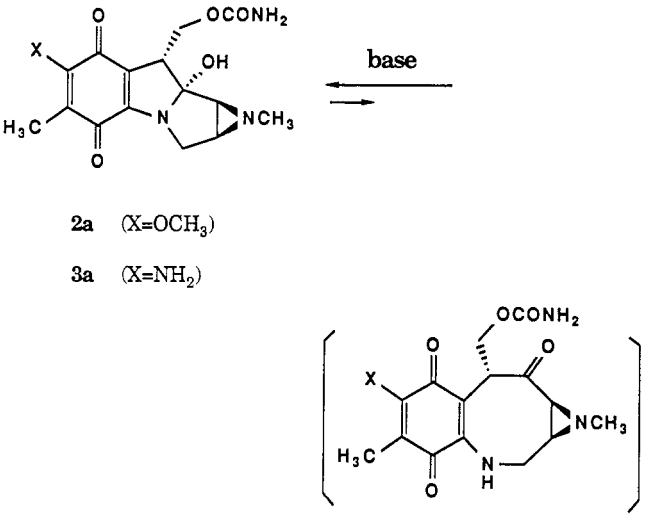
For all mitomycins with a hydroxy group in the 9a position, such as **2a** and **3a** (Scheme I), the alternative, ketone contributors **5a** and **6a** would be kinetically accessible and would exhibit increased acidity at H-9. However, in such systems, deprotonation by base would induce elimination of the C-9 carbamoyloxy residue.[6] Our synthetic plan to promote C-9 epimerization, therefore, was to exchange the carbamate at C-10 for an alcohol, which would exhibit less leaving ability.

Initially, we attempted to obtain the alcohol **8a** (Scheme II) using the known method,[7] reasoning that the compound with the 7-amino group might be more stable than **7a** under the basic conditions of epimerization.[8] However, the yield of the direct decarbamoylation from **3a** to **8a** was very poor.[9] It was therefore preferable to obtain this compound from **7a**. Thus the compound **2a** was converted to **7a** (MeONa/MeOH–benzene),[7] and amination (NH_3/MeOH)[10] of **7a** yielded **8a** (42% from **2a**).

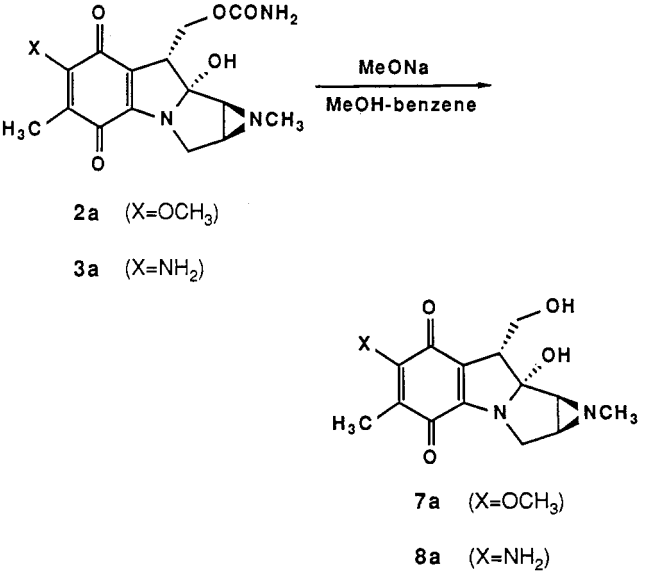
Next, we examined the conditions for epimerization using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the base. We found that prolonged reaction time caused an increase in the production of 9a-*O*-demethylmitomycin G (**9**). Consequently, the reaction was quenched when approximately a 1:1 mixture of **8b** and **8a** was generated. Thus, in refluxing tetrahydrofuran[11] for 43 h, **8b** was obtained in a yield of 37%, accompanied by 4% of **9** and 37% of recovered **8a** (Scheme III). The 9β-alcohol **8b** was purified on preparative silica gel TLC for structure elucidation ($CHCl_3$:MeOH = 9:1, developed two times, R_f(**8b**) = 0.49, R_f(**8a**) = 0.52).

The EI MS of **8b** showed fragments at m/z 291 (M^+), 273, 243, 228, and 70, which were the same as those from **8a**; however, it also showed m/z 261 ($M^+ - CH_2O$) and 258, which were not observed from **8a**. Comparison of ^1H NMR chemical shifts and coupling constants for H-1, H-2, and methylene-10 of **8b** with those of 10-*O*-decarbamoylporfiromycin (**10**)[12] showed excellent agreement. A comparison of the same features between **8b** and **8a** were not

Scheme I



Scheme II



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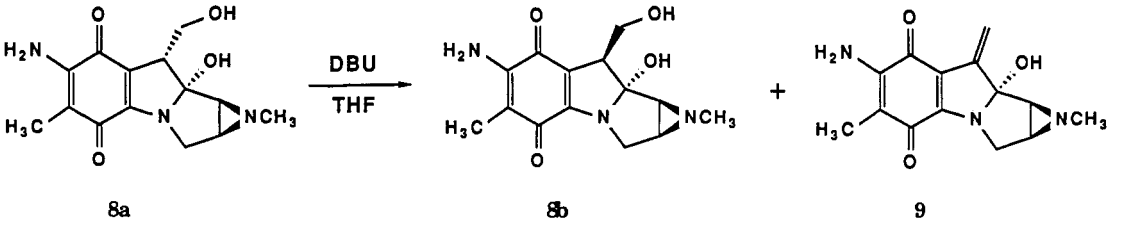
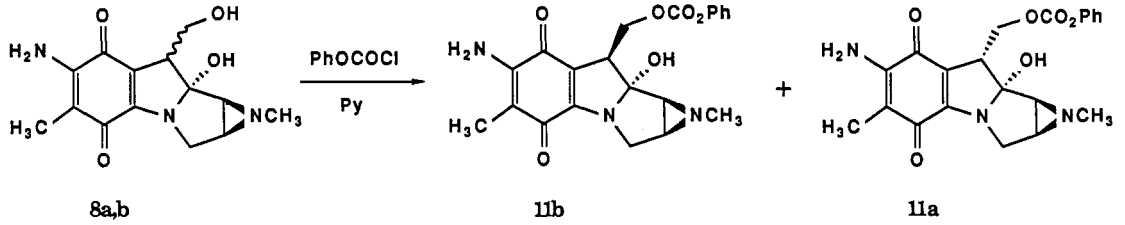
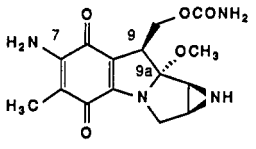
Scheme III



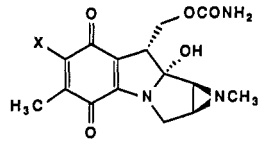
Scheme IV



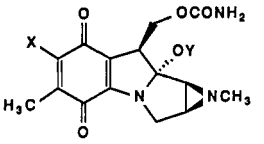


mitomycin C

1

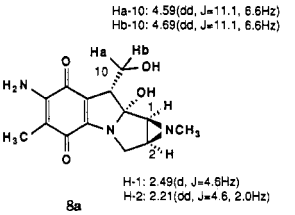


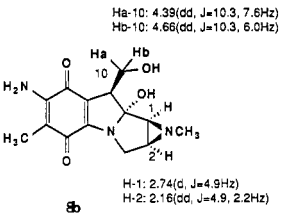
		X	
mitomycin B	OCH_3		**2a**
mitomycin D	NH_2		**3a**



		X	Y
9-epi-mitomycin B	OCH_3	H	**2b**
9-epi-mitomycin D	NH_2	H	**3b**
mitomycin F	OCH_3	CH_3	**4**

Figure 1.





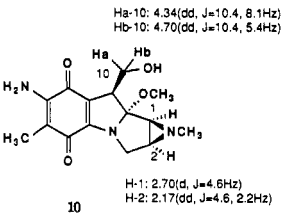


Figure 2. ^1H NMR data of **8a**, **8b**, and **10** (100 MHz, in Py-d_5).

notable, however, supporting the C-9 stereochemistry of **8b** (Figure 2).

Next, to facilitate their separation, phenoxycarbonylation was performed on the mixture of **8a** and **8b**. The difference in polarities between the product carbonates **11a** and **11b** rendered them easily separable (silica gel TLC, $CHCl_3$:Me_2CO = 1:1, R_f(**11b**) = 0.55, R_f(**11a**) = 0.42; Scheme IV). The carbonate **11a** was partly decomposed on treatment with a base such as sodium bicarbonate, indicating that it was extremely base labile. In the EI MS of **11b**, m/z 93 (PhO^+) was observed as the base peak, whereas the base peak of **11a** was m/z 94 ($PhOH^+$), and the relative intensity of m/z 93 was only 3.2%. A phenol might be generated by a proton transfer from the cis-9a-hydroxy group through a six-membered ring intermediate. Treatment of the carbonate **11a** with NH_3–MeOH to obtain mitomycin D (**3a**) immediately generated a red solution that contained many byproducts.[13] We assumed that the cyclic carbonate, which was not isolated and seemed to be extremely unstable, was generated by the attack of 9a-hydroxy at the carbonyl; subsequent decomposition of the cyclic carbonate was perhaps the source of the byproducts. In contrast, on treatment with NH_3–MeOH, **11b** afforded the desired system **3b** (yield 46% from **8b**).

To recover mitomycin D (**3a**), we examined the method applied by Kishi[13] for the preparation of carbamate in

(1) *Mitomycin C: Current Status and New Developments*; Carter, S. K., Crook, S. T., Eds.; Academic Press: New York, 1979.

(2) (a) Shirahata, K.; Morimoto, M.; Ashizawa, T.; Mineura, K.; Kono, M.; Saitoh, Y.; Kasai, M. The 21st Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, Nov 1981; Abstracts, p 421. (b) Urakawa, C.; Tsuchiya, H.; Nakano, K. *J. Antibiot.* **1981**, *34*, 243.

(3) Kono, M.; Saitoh, Y.; Shirahata, K. *J. Am. Chem. Soc.* **1987**, *109*, 7224.

(4) 1a-Demethylmitomycins G and K were derived from mitomycin C (1): Kono, M.; Kasai, M.; Shirahata, K., submitted for publication in *J. Antibiot.*

(5) Danishefsky reported the derivation of 9-*epi*-mitomycin B (**2b**) from mitomycin F (**4**) in 20–30% yield: Egbertson, M.; Danishefsky, S. J. *J. Org. Chem.* **1987**, *52*, 4424.

(6) (a) Urakawa, C.; Tsuchiya, H.; Nakano, K.; Nakamura, N. *J. Antibiot.* **1981**, *34*, 1152. (b) Kono, M.; Kasai, M.; Shirahata, K. *Synth. Commun.* **1989**, *19*, 2041.

(7) Kinoshita, S.; Uzu, K.; Nakano, K.; Takahashi, T. *J. Med. Chem.* **1971**, *14*, 109.

(8) Actually, the alcohol **7a** was easily decomposed under the condition of the epimerization (the condition is described later).

(9) Under the condition of the decarbamoylation, **3a** gave a complex mixture, the analysis of which highlighted the novel reactivity at the C-3 of mitomycins: Kasai, M.; Kono, M.; Shirahata, K., submitted for publication in *J. Antibiot.*

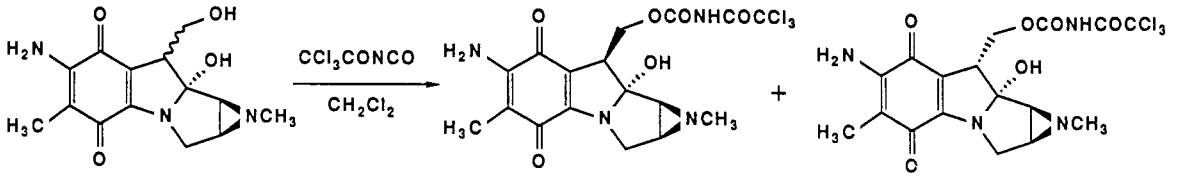
(10) Matsui, M.; Yamada, Y.; Uzu, K.; Hirata, T. *J. Antibiot.* **1968**, *21*, 189.

(11) Monoglyme, diglyme, dioxane, and tetrahydrofuran were examined as a solvent. Among them, tetrahydrofuran gave the best yield.

(12) Decarbamoylporfiromycin (**10**) was derived from porfiromycin according to the method described in the literature.[6]

(13) Kishi reported that mitomycin B (**2a**) could not be obtained from the phenyl carbonate: Kishi, Y. *J. Nat. Prod.* **1979**, *42*, 549.

Scheme V

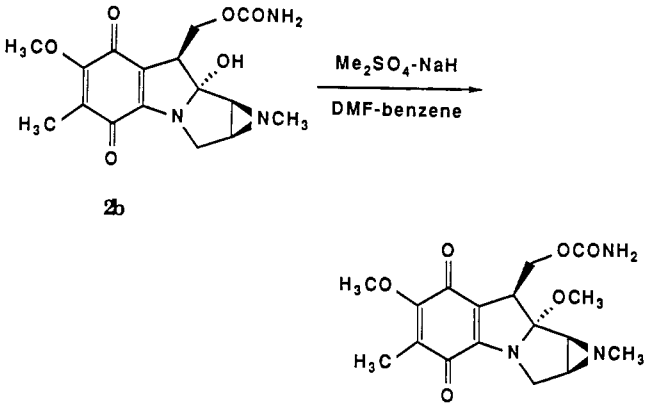


8a,b 12b 12a

mitomycin B (**2a**). Treatment of the alcohols **8a** and **8b** with trichloroacetyl isocyanate gave stable and readily separable trichloroacetyl carbamates **12a** and **12b** (silica gel TLC, $CHCl_3$:Me_2CO = 6:4, R_f(**12b**) = 0.33, R_f(**12a**) = 0.23; Scheme V). Hydrolysis of **12a** and **12b** in the presence of potassium carbonate proceeded in good yields to afford, respectively, recovered mitomycin D (**3a**, yield 41% from **8a**) and the desired 9-epimer **3b** (yield 49% from **8b**).

In the EI MS of **3b**, a molecular ion m/z 334 (M^+) was detected (calcd for $C_{15}H_{18}N_4O_5$ m/z 334.1277, found m/z 334.1274). The characteristic fragments of mitomycin D (**3a**)[14] such as m/z 316 ($M^+ - H_2O$), 291 (M^+ - NHCO), 273 (base peak, $M^+ - H_2NCO_2H$), and 70 ($CH_2{=}N^+(CH_3)CH{=}CH_2$) were also observed. Conversion of the amino group at C-7 in **3b** to the methoxy group was initiated with hydrolysis (NaOH/MeOH–H_2O). Subsequent methylation (CH_2N_2) yielded compound **2b** (36% from **3b**). For corroboration of the C-9 stereochemistry, **2b** was converted to mitomycin F (**4**, 1a-methylmitomycin A) by 9a-*O*-methylation (Me_2SO_4–NaH/DMF–benzene;[6b] Scheme VI).

Scheme VI



2b **4**

Conclusion

The potentially informative 9-*epi*-mitomycin B (**2b**), whose C-9 configuration is the same as that of mitomycin C (**1**), was derived from mitomycin B (**2a**) by utilizing the masked ketonic character of the 9a-hydroxy group. The conversion was accomplished in seven steps, consisting of decarbamoylation, C-7 amination, epimerization, carbamoylation, and introduction of the C-7 alkoxy group. Antitumor activity of 9-*epi*-mitomycin B (**2b**)[15] is anticipated on the basis of the C-9 stereochemistry. The elucidation of structure–activity relationships among these compounds as well as naturally occurring mitomycins will be of help in the design of novel, potent mitomycin analogues.

Experimental Section

Melting points were recorded on a Yanagimoto melting-point apparatus and are uncorrected. ^1H NMR spectra were recorded on a JEOL FX-100 and a JNM-PS-PFT-100 spectrometers. MS spectra were recorded on a JMS-01SG-2 spectrometer. IR spectra were recorded on a Shimadzu IR-27 G spectrometer. Electronic spectra were recorded on a Shimadzu MPS-50L spectrophotometer.

Preparation of 10-*O*-Decarbamoylmitomycin D (8a). Mitomycin B (**2a**, 1.0 g) was dissolved in anhydrous methanol/benzene (150 mL, 1:1) to which was added sodium methoxide (6.2 g), and the mixture was stirred for 72 h at ambient temperature. Then the mixture was neutralized with an excess amount of dry ice, and the resultant precipitate was separated by filtration. The filtrate was concentrated under reduced pressure to give a residue which was purified by column chromatography on silica gel by using chloroform/methanol (95:5 to 9:1). The more polar purple fractions were collected and concentrated to recover 234 mg of mitomycin B (**2a**, 23.4%). The less polar fractions were collected and concentrated to give dark purple **7a**, which was dissolved in ammonia (6%) solution in methanol. After stirring for 1 h at ambient temperature, the reaction mixture was concentrated to dryness. After recrystallization from acetone and benzene, 268.3 mg of greenish brown prisms of **8a** was gained (yield 42% from **2a**): mp 118–123 °C; IR (KBr) 3320, 1586, 1537, 1440, 1350 cm^{-1}; ^1H NMR (Py-d_5) δ 1.90 (3 H, s), 2.19 (3 H, s), 2.21 (1 H, dd, J = 4.6, 2.0 Hz), 2.49 (1 H, d, J = 4.6 Hz), 3.60 (1 H, dd, J = 12.9, 2.0 Hz), 3.98 (1 H, t, J = 6.6 Hz), 4.41 (1 H, d, J = 12.9 Hz), 4.51 (1 H, dd, J = 11.1, 6.6 Hz), 4.69 (1 H, dd, J = 11.1, 6.6 Hz); EI MS, m/z 291 (M^+), 273, 243 (base), 228, 70.

Preparation of 9-*epi*-10-*O*-Decarbamoylmitomycin D (8b). 10-*O*-Decarbamoylmitomycin D (**8a**, 72.6 mg) was dissolved in tetrahydrofuran (9 mL). After addition of 1,5-diazabicyclo-[5.4.0]undec-5-ene (86 mg), the solution was refluxed under a nitrogen atmosphere for 43 h. The reaction mixture was poured into brine, and ethyl acetate was used for extraction. The extract was dried over anhydrous sodium sulfate and concentrated under reduced pressure to dryness. The residue was purified by column chromatography on silica gel using chloroform/methanol (95:5). The first bluish green fractions were collected and concentrated under reduced pressure to dryness to give 9a-*O*-demethylmitomycin G (**9**) which was again purified by column chromatography on silica gel using ethyl acetate/methanol (97:3) to give dark green solids of **9** (2.9 mg; yield 4.3%). The second purple fractions were collected and concentrated under reduced pressure to dryness to give a mixture of **8a** and **8b**, which was again purified by column chromatography using ethyl acetate/methanol (9:1). The purple fractions were collected and concentrated under reduced pressure to dryness to give a 1:1 mixture of **8a** and **8b** (54.1 mg, yield of **8b**; 59.6% based on consumed **8a**). This mixture was separated by preparative TLC on silica gel using chloroform/methanol (9:1). The development was effected twice. The more polar band (R_f = 0.49) was scraped and eluted by chloroform/

(14) Van Lear, G. E. *Tetrahedron* **1970**, *26*, 2587.

(15) A preliminary evaluation of the antimicrobial effects of these compounds was made. 9-*epi*-Mitomycin B (**2b**) was superior to mitomycin B (**2a**) against several lines of pathogenic bacteria, and 9-*epi*-mitomycin D (**3b**) also exceeded mitomycin D (**3a**). These results suggested the possibility of antitumor activity for 9β-carbamoyloxymethyl-substituted mitomycins.

methanol (9:1). The solution was concentrated to dryness under reduced pressure to give brown solids of **8b**: mp 178–185 °C; IR (KBr) 3320, 2910, 1595, 1540, 1443, 1346 cm^{-1}; ^1H NMR (Py-d_5) δ 1.96 (3 H, s), 2.16 (1 H, dd, J = 4.9, 2.2 Hz), 2.24 (3 H, s), 2.74 (1 H, d, J = 4.9 Hz), 3.67 (1 H, dd, J = 12.9, 2.2 Hz), 3.91 (1 H, dd, J = 7.6, 6.0 Hz), 4.39 (1 H, dd, J = 10.3, 7.6 Hz), 4.56 (1 H, d, J = 12.9 Hz), 4.66 (1 H, dd, J = 10.3, 6.0 Hz); EI MS, m/z 291 (M^+), 273, 261, 258, 243, 228, 70 (base peak).

Preparation of 9-*epi*-10-*O*-Decarbamoyl-10-*O*-(phenoxycarbonyl)mitomycin D (11b). A mixture of 9-*epi*-10-*O*-decarbamoylmitomycin D (**8b**) and 10-*O*-decarbamoylmitomycin D (**8a**, 1:1, 18.3 mg) was dissolved in anhydrous pyridine (0.3 mL), to which was added of phenyl chloroformate (11.9 μL). The mixture was stirred for 4 h at 0 °C under a nitrogen atmosphere and poured into a cold aqueous saturated solution of sodium hydrogen carbonate. The mixture was extracted with ethyl acetate, and the extract was dried over anhydrous sodium sulfate, followed by removal of the solvent by evaporation under reduced pressure. The residue was purified by column chromatography on silica gel using chloroform/acetone (7:3). The less polar purple fractions were collected and concentrated under reduced pressure to give brown solids of **11b** (yield 67.9%). From the more polar fractions a small amount of 10-*O*-decarbamoyl-10-*O*-(phenoxycarbonyl)mitomycin D (**11a**, a brown paste) was obtained. **11b**: ^1H NMR (Py-d_5) δ 2.02 (3 H, s), 2.29 (4 H, s), 2.73 (1 H, d, J = 4.9 Hz), 3.71 (1 H, dd, J = 12.9, 2.0 Hz), 4.20 (1 H, dd, J = 11.0, 4.4 Hz), 4.57 (1 H, d, J = 12.9 Hz), 4.93 (1 H, dd, J = 11.0, 10.5 Hz), 5.46 (1 H, dd, J = 10.5, 4.4 Hz), 7.4 (5 H, m); EI MS, m/z 411 (M^+), 393, 273, 93 (base peak). **11a**: EI MS, m/z 411 (M^+), 393, 273, 94 (base peak).

Preparation of 9-*epi*-Mitomycin D (3b; from 11b). 9-*epi*-10-*O*-Decarbamoyl-10-*O*-(phenoxycarbonyl)mitomycin D (**11b**, 6.0 mg) was dissolved in chloroform (1.5 mL). While cooling in a dry ice–methanol bath, dry ammonia was blown into the solution for 30 min. The reaction was effected for 1.5 h under the cooling condition. Nitrogen gas was blown into the reaction mixture to remove ammonia, and the solvent was removed by evaporation under reduced pressure. The residue was purified by column chromatography on silica gel using chloroform/methanol (85:15) to give dark brown powder of **3b** (4.6 mg; yield 94.2%): mp >210 °C (dec); IR (KBr) 3430, 3350, 2920, 1710, 1590, 1545, 1340 cm^{-1}; ^1H NMR (Py-d_5) δ 2.00 (3 H, s), 2.20 (1 H, dd, J = 4.6, 2.0 Hz), 2.30 (3 H, s), 2.72 (1 H, d, J = 4.6 Hz), 3.69 (1 H, dd, J = 12.9, 2.0 Hz), 4.18 (1 H, dd, J = 11.4, 4.4 Hz), 4.58 (1 H, d, J = 12.9 Hz), 4.92 (1 H, dd, J = 11.4, 4.4 Hz), 5.46 (1 H, dd, J = 10.4, 4.4 Hz); EI MS, m/z 334 (M^+; calcd for $C_{15}H_{17}N_4O_5$ m/z 334.1277, found m/z 334.1274), 316, 291, 273 (base peak), 70.

Preparation of 9-*epi*-Mitomycin B (2b). 9-*epi*-Mitomycin D (**3b**, 17.5 mg) was dissolved in 0.1 N aqueous solution of sodium hydroxide (10 mL), which was stirred for 6 h at ambient temperature. The reaction solution was adjusted to pH 4.0 with a diluted hydrochloric acid solution and extracted with ethyl acetate. The extract was washed with brine and dried over anydrous sodium sulfate. The solvent was removed by evaporation under reduced pressure and the residue was dissolved in methanol (5 mL). An excess amount of diazomethane in ethyl ether was added dropwise to the solution, and the reaction was effected for 10 min at 0 °C. The solvent was removed from the reaction mixture by evaporation under reduced pressure, and the residue was purified by column chromatography on silica gel with chloroform/methanol (95:5) to give dark purple prisms of **2b** (4.8 mg; yield 26.3%): mp 173–175 °C; IR (KBr) 3460, 1707, 1623, 1570, 1448, 1320, 1292, 1210, 1070 cm^{-1}; ^1H NMR (Py-d_5) δ 1.80 (3 H, s), 2.20 (1 H, dd, J = 4.4, 2.0 Hz), 2.28 (3 H, s), 2.70 (1 H, d, J = 4.4 Hz), 3.58 (1 H, dd, J = 12.7, 2.0 Hz), 3.98 (3 H, s), 4.07 (1 H, dd, J = 11.5, 4.4 Hz), 4.22 (1 H, d, J =12.7 Hz), 4.85 (1 H, dd, J = 11.5, 10.5 Hz), 5.38 (1 H, dd, J = 10.5, 4.4 Hz); EI MS, m/z 349 (M^+; calcd for $C_{16}H_{19}N_3O_6$ m/z 349.1274, found m/z 349.1228).

Preparation of 9-*epi*-10-*O*-Decarbamoyl-10-*O*-[(trichloroacetyl)carbamoyl]mitomycin D (12b) and 10-*O*-Decarbamoyl-10-*O*-[(trichloroacetyl)carbamoyl]mitomycin D (12a). A mixture of 9-*epi*-10-*O*-decarbamoylmitomycin D (**8b**) and 10-*O*-decarbamoylmitomycin D (**8a**, 1:1, 137 mg) was dissolved in dry methylene chloride (20 mL), to which was added dropwise a solution of the same solvent containing trichloroacetyl isocyanate (106 mg). The mixture was stirred for 20 min at 0 °C under a nitrogen atmosphere, and methanol (3 mL) was added to quench the reaction. The mixture was extracted with ethyl acetate, and the extract was dried over anhydrous sodium sulfate, followed by removal of the solvent by evaporation under reduced pressure. The residue was purified by column chromatography on silica gel using chloroform/acetone (6:4). The less polar brownish green fractions were collected and concentrated under reduced pressure. From chloroform/*n*-hexane solution, a greenish brown powder of **12b** (68.8 mg; crude yield 61%) was obtained. From the more polar bluish green fractions a paste of **12a** (65.4 mg; crude yield 58%) was obtained. Compound **12a** was used in the next methanolysis without further purification. **12b**: mp >110 °C (dec); IR (KBr) 3340, 2940, 1795, 1737, 1597, 1534, 1447, 1352, 1185, 847 cm^{-1}; ^1H NMR (Py-d_5) δ 1.98 (3 H, s), 2.19 (3 H, s), 2.19 (1 H, overlapped), 2.58 (1 H, d, J = 4.9 Hz), 3.63 (1 H, dd, J = 12.7, 2.0 Hz), 4.01 (1 H, dd, J = 11.2, 4.4 Hz), 4.50 (1 H, d, J = 12.7 Hz), 4.86 (1 H, dd, J = 11.2, 10.7 Hz), 5.44 (1 H, dd, J = 10.7, 4.4 Hz), 8.47 (1 H, s). **12a**: ^1H NMR (Py-d_5) δ 1.97 (3 H, s), 2.07 (3 H, s), 2.17 (1 H, dd, J = 4.6, 1.5 Hz), 2.26 (1 H, d, J = 4.6 Hz), 3.60 (1 H, dd, J = 12.7, 1.5 Hz), 4.13 (1 H, dd, J = 9.5, 4.2 Hz), 4.42 (1 H, d, J = 12.7 Hz), 5.29 (1 H, dd, J = 10.5, 9.5 Hz), 5.47 (1 H, dd, J = 10.5, 4.2 Hz), 7.50 (2 H, br s), 9.58 (1 H, br s).

Preparation of 9-*epi*-Mitomycin D (3b; from 12b). 9-*epi*-10-*O*-Decarbamoyl-10-*O*-[(trichloroacetyl)carbamoyl]mitomycin D (**12b**, 44 mg) was dissolved in methanol (5 mL), to which was added potassium carbonate (55 mg). The mixture was stirred for 40 min at ambient temperature. The excess potassium carbonate was filtered from the reaction mixture, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography likewise the preparation of **3b** from **11b**. The yield of **3b** was 81%.

Recovery of Mitomycin D (3a; from 12a). Mitomycin D (**3a**) was prepared from 10-*O*-decarbamoyl-10-*O*-[(trichloroacetyl)-carbamoyl]mitomycin D (**12a**) by the same procedure used in the preparation of **3b** from **12b**. The yield was 70%.

Preparation of Mitomycin F (4; from 2b). 9-*epi*-Mitomycin B (**2b**, 1.1 mg) was dissolved in dry dimethylformamide/benzene (0.6 mL, 1:1). While this cooled at −10 °C under a nitrogen atmosphere, sodium hydride (15 mg, 50% oil dispersion) was added to the solution with stirring, followed by the addition of dimethyl sulfate (3 μL). The mixture was stirred for 15 min and quenched by the addition of water and ethyl acetate. The mixture was extracted with ethyl acetate, and the extract was dried over anhydrous sodium sulfate, followed by removal of the solvent under reduced pressure. The residue was purified by preparative silica gel TLC using chloroform/acetone (65:35). From the reddish purple band, purple solids (0.7 mg) were obtained. The silica gel TLC and EI MS of the obtained sample were consistent with the standard mitomycin F (**4**).

Registry No. **2a**, 4055-40-7; **2b**, 13164-90-4; **3a**, 10169-34-3; **3b**, 79026-43-0; **4**, 18209-14-8; **7a**, 26909-46-6; **8a**, 78879-23-9; **8b**, 78962-35-3; **9**, 74148-47-3; **11a**, 123482-47-3; **11b**, 78879-24-0; **12a**, 105616-80-6; **12b**, 105551-82-4; CCl_3CONCO, 3019-71-4.