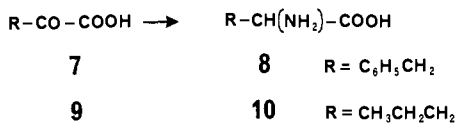
ANS, compared with 9.9×10^{-4} M for **4**. With this established, we have modified the structure to permit the attachment of interesting catalytic groups. We now wish to report the synthesis of the pyridoxamine derivative **6**. The cooperative interaction between the pyridoxamine unit and the hydrophobic binding cavity proved to be comparable in effectiveness to that in the cyclodextrin derivatives analogous to **6** which we have described previously.[9]

Catalyst **6** was synthesized from *N*-acetyl-*N'*-tosylbis(4-aminophenyl)methane (**11**)[10] by alkylation with 1,5-dibromopentane and then (after deacetylation and ditosylation) with 3-[(*tert*-butyldimethylsilyl)oxy]-1,5-dibromopentane. The resulting macrocycle was detosylated and desilylated with Na^0/n-BuOH,[11] and the resulting tetraamino alcohol was methylated with CH_2O and $NaBH_3CN$.[12] Conversion to the thioacetate with CH_3COSH, triphenylphosphine, and diethyl azodicarboxylate[13] was followed by quaternization to afford **5** as the tetraiodide. Alkaline hydrolysis in the presence of $NaBH_4$ and in situ alkylation with (bromomethyl)pyridoxamine dihydrobromide[14] afforded **6**. The product was isolated as the pentabicarbonate salt, a pale yellow solid (λ_{max} = 298 nm), in 3.3% yield (based on **11**) by Sephadex CM-25 chromatography with a 0–1 M ammonium bicarbonate gradient elution. Then the effectiveness of **6** in the amination of phenylpyruvic acid (**7**) to form phenylalanine (**8**)



and of α-ketovaleric acid (**9**) to form norvaline (**10**) was compared with the same aminations by simple pyridoxamine and by pyridoxamine cycloheptaamylose 6'-sulfide (resembling **6**, but with β-cyclodextrin instead of the synthetic macrocycle).

In our earliest studies of the cyclodextrin–pyridoxamine derivative,[9a] we found that simple pyridoxamine took 49 times as long to convert **7** to **8** as did the cyclodextrin derivative. However, this undoubtedly overestimates the rate difference, since in the slower reaction starting materials are also destroyed in side reactions. For this reason we have done direct kinetic studies on these reactions, comparing reaction rates in the first few percent of reaction in which the slopes were linear with time. Rates were studied at 0.5 mM concentrations[15] of keto acids **7** or **9** and 0.5 mM pyridoxamine derivative in 2.7 M phosphate buffer, pH 9.3, at 26 °C. Aliquots were taken, diluted with H_2O, dansylated, and analyzed by HPLC[16] with fluorescence detection (quantitatively calibrated with authentic dansyl amino acid solutions).

Macrocyclic derivative **6** converted **7** to **8** at a rate 31 ± 3 times as fast as did simple pyridoxamine; the conversion of **9** to **10** was 6 ± 1 times as fast with **6** as with pyridoxamine. Under these conditions the cyclodextrin analogue of **6** accelerated the reaction of **7** by a factor of 15 ± 2 and of **9** by a factor of 2, compared with the pyridoxamine rates. We had reported earlier[9a] that the attached cyclodextrin group did not accelerate the conversion of pyruvic acid to alanine by pyridoxamine.

These data indicate that binding of the phenyl group of **7** into the macrocyclic cavity of **6** contributes significantly to the rate, as it did for analogous cyclodextrin derivatives. We see a similar advantage for **6** in the conversion of indolepyruvic acid to tryptophan. Smaller effects are seen for the much less hydrophobic **9**. We had found[9] that the chirality of cyclodextrin induced chirality in the product amino acids, which is not possible with **6**. Furthermore, we have not yet achieved the kinds of high acylation rates[17] or selectivity in aromatic chlorinations[18] for hydroxymacrocycles (e.g., **3**, but X = OH) that has been possible with the hydroxyl groups of cyclodextrin. Thus it remains to be seen how well the cyclodextrin experience can be extrapolated to systems with synthetic binding groups. However, in terms of selective rate acceleration of transamination, the catalyst **6** is comparable to its cyclodextrin analogues.

Acknowledgment. We thank D. O'Krongly and S. Zimmerman for helpful contributions. This work was supported by the National Institutes of Health.

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Revised Absolute Configuration of Mitomycin C. X-ray Analysis of 1-*N*-(*p*-Bromobenzoyl)mitomycin C

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Received September 14, 1983

Mitomycin C is one of the most eminent antitumor antibiotics that are put to clinical use extensively and successfully today. The absolute configurations of mitomycin A and B, which are important members of mitomycin family, were determined by X-ray analysis using heavy-atom derivatives.[1,2] Mitomycin C has been chemically derived from mitomycin A.[3,4] Therefore the absolute configuration of mitomycin C must be identical with that of mitomycin A as shown in Figure 1. The studies on biosynthesis of mitomycins, however, are not consistent with the reported configurations of mitomycins. D-Glucosamine is incorporated into mitomycins efficiently by *Streptomyces verticillatus*, an mitomycin producer, and provides its C6 unit of C1, C2, C3, C9a, C9, and C10 and the nitrogen atom of the aziridine ring without any

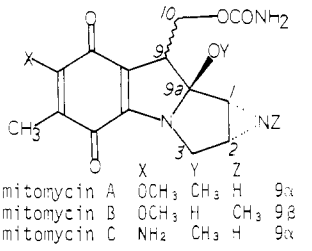

Figure 1. Structures of mitomycins.

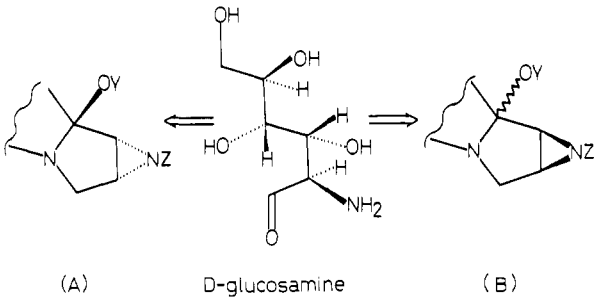

Figure 2. Absolute configurations of mitomycins: (A) determined previously, (B) predicted from the biosynthesis study.

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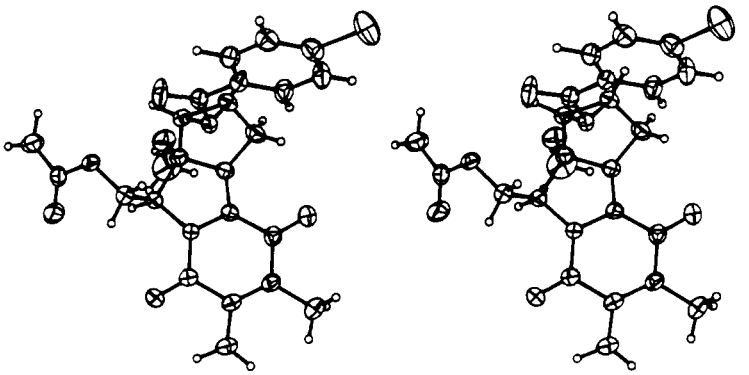

Figure 3. Stereoview of the molecule.

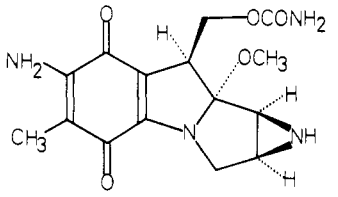

Figure 4. Revised absolute configuration of mitomycin C.

cleavage of C–C and C–N bonds of the amino sugar during biosynthesis.[5] On the other hand, feeding experiments with L-glucosamine and D-mannosamine, both have the configuration at C2 corresponding to the reported mitomycin structures, showed evidently that they can not be incorporated as a precursor of the C6 unit (Figure 2).[6] These results raised serious doubt on the reported stereochemistry, and we have tried reinvestigation of the problem. In this communication we report the determination of the absolute configuration of 1-*N*-(*p*-bromobenzoyl)mitomycin C by X-ray analysis.

The title compound was recrystallized from water–ethanol. Large hexagonal prismatic crystals of the compound belong to the hexagonal space group $P6_5$, with $a = 13.534$ (1) Å, $c = 21.146$ (2) Å, $V = 3355$ Å^3, and $Z = 6$. Intensities of 2356 reflections with $2\theta < 150°$ were measured on a Nonius CAD-4 automatic diffractometer, using graphite-monochromated Cu Kα radiation and employing ω–2θ scan technique. Out of the total, 2097 reflections were considered observed on the basis that $I > 3\sigma(I)$. The data were corrected for Lorentz and polarization factors.

The structure was solved by direct methods using MULTAN 11/82.[7] The phases of 255 reflections with $|E_o| > 1.56$ were assigned. The best set of phases was used to calculate an E map, which gave the location of Br atom and six aromatic carbon atoms of the *p*-bromobenzoyl group. The 26 other nonhydrogen atoms were located from the successive difference Fourier synthesis. The structural parameters were refined by full-matrix least squares with the CAD-4 structure determination package.[8] The position of H atoms were calculated geometrically. They were included in the calculation of structure factors, but not refined. The final refinement converged to an R factor of 0.0361 for 2097 observed reflections.

The absolute configuration was determined by the Bijvoet difference method. The structure was independently refined with the atoms in both enantiomorphic configurations, the f' and f'' values for C, N, O, and Br were taken from "International Tables for X-ray Crystallography".[9] Twenty-one reflections with F_{calcd} differing significantly at the end of the two refinements were remeasured with great care. The signs of ΔF_{calcd} and ΔF_{obsd} are the same for 20 reflections. The final R factors, 0.0361 and 0.0401, also justified the configuration on a basis of Hamilton's R factor test.[10] Figure 3 shows a stereoscopic drawing of the molecule.

Our result corresponds to the enantiomer of the stereochemistry reported previously, and the configurations at C1, C2, C9a, and C9 are *S*, *S*, *R*, and *S*, respectively. Thus the absolute configuration of mitomycin C, at least, must be revised as shown in Figure 4. Although we can not clearly trace out the reasons that led to the wrong absolute configurations in the analyses by Tulinsky et al.[1] and Yahashi et al.,[2] the high R values of both analyses seem to be responsible for them. We are now undertaking the redetermination of the absolute configuration of mitomycin A by X-ray analysis. The result and the details of the present work will be published in the near future.

Acknowledgment. We thank Kazuo Yamaguchi, Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., for providing the crystals.

Registry No. 1-*N*-6-Bromobenzoyl)mitomycin C, 87729-17-7; mitomycin C, 50-07-7.

Supplementary Material Available: Listings of structural parameters and structure factors (25 pages). Ordering information is given on any current masthead page.

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Carbon–Carbon Bond Formation by Light-Assisted B_{12} Catalysis. Nucleophilic Acylation of Michael Olefins[1]

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Received August 15, 1983

1,4-Dioxo compounds are valuable precursors for the synthesis of cyclopentanoids and furanoids.[2] 1,4-Dioxo compounds may

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