occurred, the 1.4:1.0 ratio of **6**:**7** did not change perceptibly. These results are consistent with a very rapid isomerization that maintained an equilibrium mixture of the compounds or with no isomerization at all as seen in the case of μ-ethylidyne complex **4**.

Aqueous HCO_3^- reacts rapidly with μ-pentylidyne complex **2** to produce the μ-pentenylidene complex **8**[4] in 87% yield whereas the μ-pentenyl complex **3** reacts only slowly with HCO_3^- over 24 h to give the β-hydroxy bridging carbene complex **9**[4] in 47% yield. Therefore it appeared possible that a pure sample of μ-alkenyl complex **7** might be obtained by selectively destroying μ-alkylidyne complex **6** by treatment with base. However, when the 1.4:1.0 mixture of **6** and **7** was treated with aqueous bicarbonate, all of the material was rapidly converted to the same vinylidene complex **10** which was isolated in 70% yield. The fact that both **6** and **7** were converted to **10** is consistent with a rapid equilibration of **6** and **7** at room temperature and selective deprotonation of **6** to **10**.[12] This deprotonation reaction could prove useful for converting synthetically unattractive mixtures of products from the reaction of **1** with 1,2-disubstituted alkenes into a single organometallic product.

Vinylidene complexes such as **8** are known to undergo protonation to give μ-alkylidyne complexes and not μ-alkenyl compounds.[6,13] When the cyclohexyl vinylidene complex **10** was reprotonated with $HBF_4 \cdot Et_2O$ in acetone-d_6 at −70 °C, only the BF_4^- salt of the cyclohexyl-substituted carbyne complex **6** was observed by ^1H NMR. Upon warming to −13 °C, pure **6** was converted to a 1.4:1.0 equilibrium mixture of **6**:**7**.[14] The rate of rearrangement of **6** to **7** was measured by ^1H NMR observation of the Cp resonances; the first-order rate constant for conversion of **6** to an 1.4:1 equilibrium mixture of **6**:**7** was found to be $k_e = 2.4 \pm 1.0 \times 10^{-4}$ s^{-1}. The rate constant for conversion of **6** to **7** is given by $k = k_e(1 + K_{eq}^{-1})^{-1} = 1.0 \pm 0.4 \times 10^{-4}$ s^{-1}, which corresponds to $\Delta G^{\ddagger} = 19.9 \pm 0.3$ kcal. Since we now know that the μ-alkylidyne and μ-alkenyl products **6** and **7** rapidly equilibrate, additional experiments will be required to determine the nature of the kinetic product from the reaction of **1** with 1,2-disubstituted alkenes.

The rate of rearrangement of μ-alkylidyne complexes to the corresponding μ-alkenyl complexes is increased dramatically by carbon substituents on the carbon α to the carbyne carbon. Thus, **4** with no α-carbon substituents does not rearrange at 88 °C ($\Delta G^{\ddagger} \geq 31.0$ kcal), **2** with one α-carbon substituent rearranges slowly at 88 °C ($\Delta G^{\ddagger} = 27.1 \pm 0.2$ kcal), and **6** with two α-carbon substituents rearranges rapidly at −13 °C ($\Delta G^{\ddagger} = 19.9 \pm 0.3$ kcal). This reactivity pattern suggests the buildup of positive charge at the carbon α to the carbyne carbon at the transition state for rearrangement; a transition state such as **11** is consistent with this reactivity pattern.

Acknowledgment. Support from the Department of Energy, Division of Basic Energy Sciences, and the National Science Foundation is gratefully acknowledged.

Supplementary Material Available: Spectral and analytical characterizations of compounds indicated by ref 4 (2 pages). Ordering information is given on any current masthead page.

(12) Similar aqueous HCO_3^- treatment of the 2.3:1.5:1.0 mixture of $[(C_5H_5)_2(CO)_2Fe_2(\mu\text{-}CO)(\mu\text{-}CCH(CH_3)CH_2CH_3)]^+PF_6^-$, $[(C_5H_5)_2(CO)_2Fe_2(\mu\text{-}CO)(\mu\text{-}\eta^1,\eta^2\text{-}(Z)\text{-}CH{=}C(CH_3)CH_2CH_3)]^+PF_6^-$, and $[(C_5H_5)_2(CO)_2Fe_2(\mu\text{-}CO)(\mu\text{-}\eta^1,\eta^2\text{-}(E)\text{-}CH{=}C(CH_3)CH_2CH_3)]^+PF_6^-$ obtained from reaction of *cis*-2-butene with **1** gave complete conversion to $(C_5H_5)_2(CO)_2Fe_2(\mu\text{-}CO)(\mu\text{-}C{=}C(CH_3)CH_2CH_3)$, which was isolated in 58% yield. Reprotonation with $HBF_4 \cdot O(CH_2CH_3)_2$ regenerated the BF_4^- salts in the 2.3:1.5:1.0 ratio in 47% yield.

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(14) When the sample was observed at −70 °C only the alkylidyne Cp's of **6** at δ 5.76 were observed. Upon warming to −13 °C both the alkylidyne Cp's of **6** at δ 5.76 and the μ-alkenyl Cp's at δ 5.68 were observed. The vinylic proton of **7** and the proton on the carbon α to the carbyne carbon of **6** were not observed by ^1H NMR presumably due to prior deuterium exchange of $HBF_4 \cdot O(CH_2CH_3)_2$ with $(CD_3)_2CO$.

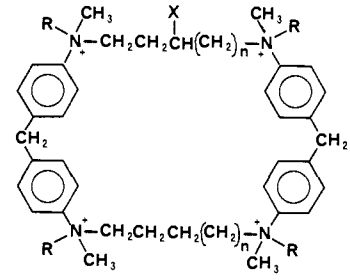
Artificial Transaminase Carrying a Synthetic Macrocyclic Binding Group

Jeffrey Winkler,[1] Evdoxia Coutouli-Argyropoulou,[2] Reinhard Leppkes,[3] and Ronald Breslow*

Department of Chemistry, Columbia University New York, New York 10027

Received July 11, 1983

Although various catalysts based on cyclodextrin binding groups[4] have been successful as enzyme mimics, it is obviously desirable to generalize them by using synthetic binding cavities. A number of macrocycles have been prepared that exhibit hydrophobic properties; of these, the systems such as **1**, described



1 n=1; R=H; X=H

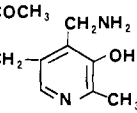
2 n=1; R=CH$_3$; X=H

3 n=2; R=CH$_3$; X=H

4 n=2; R=H; X=H

5 n=2; R=CH$_3$; X=SCOCH$_3$

6 n=2; R=CH$_3$; X=SCH$_2$-



by Koga[5] (based on earlier work by Stetter[6]) are particularly attractive because an X-ray structure determination[5] shows that a bound substrate, durene, is indeed located in the cavity. Since **1** dissolves and binds small hydrophobic molecules only in strong acid solution, we have prepared its quaternary derivative[7] **2** and find that **2** binds 2,7-dihydroxynaphthalene in neutral solution with upfield shifting of the ^1H NMR signals very similar (upfield shifting by 1.53, 0.48, and 1.34 ppm for H-1(8), H-3(6), and H-4(5), with 25 mM **2**, for 12.5 mM dihydroxynaphthalene in neutral D_2O) to those (upfield shifting by 1.36, 0.56, and 1.31 ppm for 25 mM dihydroxynaphthalene in D_2O/DCl) for Koga's complex. The dissociation constant for binding 8-anilino-1-naphthalenesulfonate (ANS), from a Hildebrand-Benesi plot[8] of fluorescence at 25 °C, was 6.6×10^{-5} M for **2** in neutral H_2O, compared with a reported 1.6×10^{-4} M for **1** in acid. Thus it is clear that **2** also binds substrates inside its cavity.

Similarly, we have prepared macrocycle **3**, analogous to Koga's **4**, and find that K_{diss} is 8.4×10^{-5} M for the complex of **3** with

(1) American Cancer Society Postdoctoral Fellow, 1981-1983. Current address: Department of Chemistry, University of Chicago, Chicago, IL 60637.

(2) On leave from the University of Thessalonika, 1980-1981.

(3) NATO Postdoctoral Fellow, 1982-1983.

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(7) Satisfactory ^1H NMR and CI-MS data were obtained for all new compounds. In the case of the quaternized macrocycles, clean molecular ions could not be obtained by using field-desorption mass spectroscopy, so **2** was analyzed. Anal. Calcd for $C_{42}H_{60}N_4I_4$ (Found): C, 44.69 (44.69); H, 5.37 (5.50); N, 4.97 (4.90); I, 44.97 (44.69). **6** was analyzed as a pentabicarbonate. Anal. Calcd for $C_{57}H_{80}N_6SO_{16} \cdot 7H_2O$ (Found): C, C, 54.18 (54.46); H, 7.50 (7.42); N, 6.65 (6.87).

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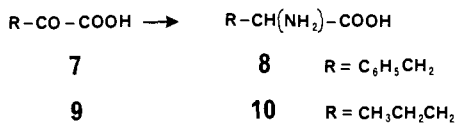
ANS, compared with 9.9×10^{-4} M for **4**. With this established, we have modified the structure to permit the attachment of interesting catalytic groups. We now wish to report the synthesis of the pyridoxamine derivative **6**. The cooperative interaction between the pyridoxamine unit and the hydrophobic 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

Kunikatsu Shirahata and Noriaki Hirayama*

Tokyo Research Laboratories
Kyowa Hakko Kogyo Company, Ltd.
3-6-6 Asahimachi, Machida, Tokyo 194, Japan

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

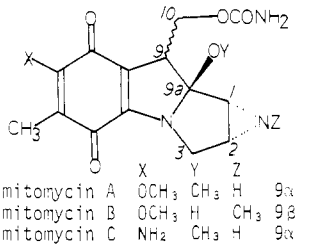

Figure 1. Structures of mitomycins.

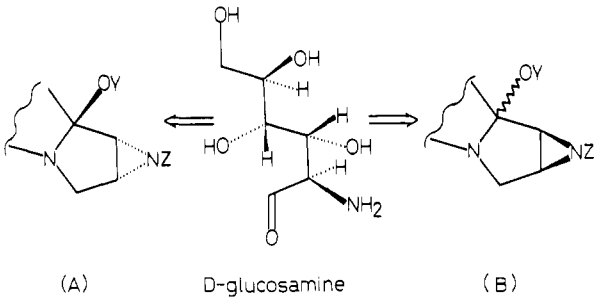

Figure 2. Absolute configurations of mitomycins: (A) determined previously, (B) predicted from the biosynthesis study.

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