9. The lack of symmetry in **10** is evidenced by the presence of 11 distinct carbon resonances and by an AB system ($J_{ortho}$ = 6.1 Hz) in the aromatic proton region for H6 and H7.[16] $Ag^{I}$-catalyzed methanolysis of **10** proceeds in an apparently regiospecific manner to deliver the *same* ether, **11** (Scheme II), as is obtained from **9** and as expected on the basis of electrophilic substitution involving attack at a $\sigma$-bond.[17]

The formation of **10** from **6** must involve initial 1,2-dehydrobromination and intervention of the "angular" cyclopropabenzyne, **8**. On the other hand, the appearance of adduct **9** requires an effective and highly regioselective[18] generation of the "linear" benzyne **7** from **5**. This is in no way untoward. The bond length and angle deformations present in the cyclopropabenzenes (C1a–C5a < C1a–C2 < C3–C4 ≲ C2–C3; ∠C1a23 ~ ∠C455a ~ 110°; ∠C234 ~ ∠C21a5a ~ 126°)[7,19] and those predicted[20] for **2** (short C1–C2 bond, ∠C123 widened) complement one another in the "linear" benzyne, **7**, but not in its "angular" isomer, **8**. We take this to imply that the distortions present in **1** are accentuated further in **7** but that serious structural modification is likely in order to accommodate the "angular" isomer, **8**.

**Acknowledgment.** We are grateful to Professor R. A. Bartsch for helpful comment and to the New Zealand Universities Grants Committee for equipment grants.

**Registry No. 5**, 63370-07-0; **6**, 60040-77-9; **7**, 86921-89-3; **8**, 86921-90-6; **9**, 86921-91-7; **10**, 86921-92-8; **11**, 573-57-9.

(16) Compound **10** may be named as 2,5-epoxy-2,5-dihydro-1*H*-cyclopropa[*a*]naphthalene: $^1$H NMR $\delta$ 3.19 (t, $J$ = 5 Hz, $CH_AH_B$), 5.70 (t, $J$ = 1.0 Hz, H2,5), 6.78 (d, $J$ = 6.1 Hz, H7), 6.99 (t, $J$ = 1.0 Hz, H3,4), 7.13 (d, $J$ = 6.1 Hz, H6); $^{13}$C NMR $\delta$ 18.4 (C1), 79.9/81.8 (C2/C5), 109.0 (C7), 115.0 (C1a), 120.2 (C6), 122.5 (C7a), 136.0 (C1b), 141.5/143.3 (C3/C4), 151.4 (C5a).

(17) Bee, L. K.; Garratt, P. J.; Mansuri, M. M. *J. Am. Chem. Soc.* **1980**, *102*, 7076–7079.

(18) Analysis of the $^{13}$C NMR spectrum of the product mixture indicates that adduct **10** is present to an extent of ca. 2%.

(19) Allen, F. H. *Acta Crystallogr., Sect. B* **1981**, *B37*, 900–906.

(20) Dewar, M. J. S.; Li, W.-K. *J. Am. Chem. Soc.* **1974**, *96*, 5569–5571. Wilhite, D. L.; Whitten, J. L. *Ibid.* **1971**, *93*, 2858–2864. Hoffman, R.; Imanura, A.; Hehre, W. H. *Ibid.* **1968**, *90*, 1499–1509. Millie, P.; Praud, L.; Serre, J. *Int. J. Quantum Chem.* **1971**, *4*, 187–193.

## Structure of Carzinophilin. 3.[1] Structure Elucidation by Nuclear Magnetic Resonance Spectroscopy. 1

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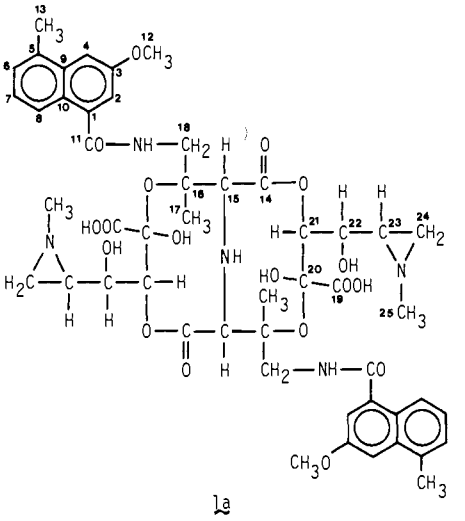
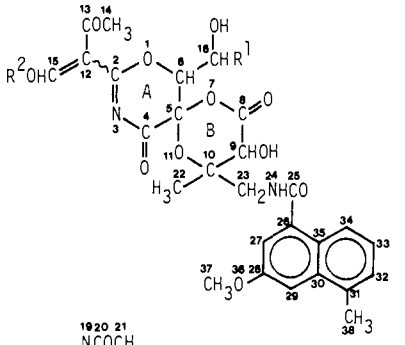
Carzinophilin (CZ, **1**) is an antitumor antibiotic isolated from *Streptomyces sahachiroi*.[2] Its molecular formula was given as $C_{60}H_{60}N_6O_{21}$,[3] which was later revised to be $C_{50}H_{58}N_5O_{18}$[4] or $C_{33}H_{35}N_3O_{12}$.[5] These formulas were based on the molecular weights obtained by Rast's method using camphor as solvent. It was therefore suspected that these scattered results were unreliable and that they might be responsible for thermal instability and low solubility of **1** in camphor. The molecular weight of **1** could not be obtained by conventional mass spectrometry. However, the molecular secondary-ion mass spectrum of dihydrocarzinophilin *p*-bromobenzoate using glycerol matrix provided the precise molecular weight[6] corresponding to $C_{31}H_{33}N_3O_{12}$ for **1**.[7] These findings suggested that the structure (**1a**) of CZ presented by Lown et al.[8] assuming the molecular formula to be $C_{50}H_{58}N_5O_{18}$ must be revised. We now report a revised structure (**1b**) for CZ.

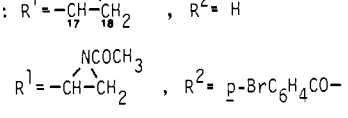


**1a**

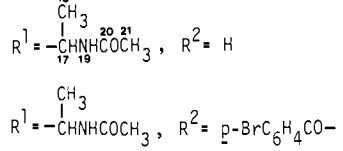
CZ (**1**) is an acidic compound. It afforded neutral carzinophilin *p*-bromobenzoate (**2**) on treatment with *p*-bromobenzoyl chloride. Hydrogenation of **1** over a platinum catalyst in dioxane afforded dihydrocarzinophilin (**3**), which provided neutral dihydrocarzinophilin *p*-bromobenzoate (**4**). The 100-MHz $^1$H and 25.2-MHz $^{13}$C NMR spectra of **1** showed 33 protons including 4 protons exchangeable with deuterium oxide and 31 carbons, respectively, which were consistent with the molecular formula



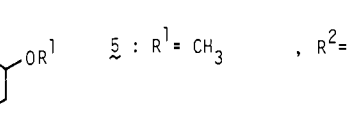
**1b**: $R^1$ = –CH(NCOCH$_3$)–CH$_2$, $R^2$ = H



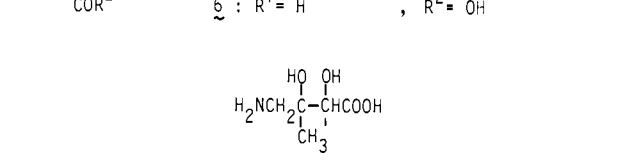
**2**: $R^1$ = –CH(NCOCH$_3$)–CH$_2$, $R^2$ = *p*-BrC$_6$H$_4$CO–



**3**: $R^1$ = –CH(CH$_3$)–CHNHCOCH$_3$, $R^2$ = H

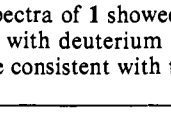


**4**: $R^1$ = –CH(CH$_3$)–CHNHCOCH$_3$, $R^2$ = *p*-BrC$_6$H$_4$CO–



**5**: $R^1$ = CH$_3$, $R^2$ = –NHCH$_2$C(OH)(CH$_3$)CHOHCONH$_2$

**6**: $R^1$ = H, $R^2$ = OH



**7**

(1) Part 2: Onda, M.; Konda, Y.; Ōmura, S.; Hata, T. *Chem. Pharm. Bull.* **1971**, *19*, 2013.

(2) Hata, T.; Koga, F.; Sano, Y.; Kanamori, K.; Matsumae, A.; Sugawara, R.; Shima, T.; Ito, S.; Tomizawa, S. *J. Antibiot., Ser. A* **1954**, *7*, 107.

(3) Unpublished observation by Dr. T. Hata at The Kitasato Institute.

(4) Tanaka, M.; Kishi, T.; Maruta, Y. *J. Antibiot., Ser. B* **1959**, *12*, 361.

(5) Unpublished observation by Prof. S. Shibata at University of Tokyo.

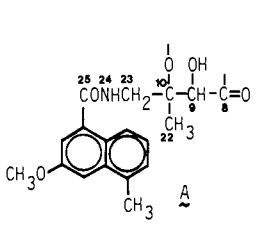
(6) Molecular weight was obtained from $m/z$ $(M + Na)^+$ 846 and 848 for $C_{38}H_{38}N_3O_{13}Br$.

(7) This formula was in accordance with elementary analysis data for CZ.

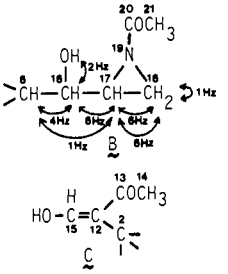
(8) Lown, J. W.; Hanstock, C. C. *J. Am. Chem. Soc.* **1982**, *104*, 3213.

0002-7863/83/1505-6311$01.50/0 

given above. The $^1H$ NMR spectrum was assigned by comparison with proton chemical shifts of related compounds as well as by spin-decoupling experiments. Carbon assignments were made by gated-decoupling and selective-proton-decoupling experiments. These data indicated that **1** consists of the following three structural units: A, B, and C.



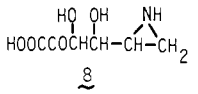
A



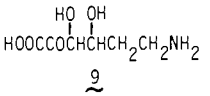
B



C



8



9

**Unit A.** Upon ammonolysis of **1**, (2*S*,3*S*)-2,3-dihydroxy-4-(3-methoxy-5-methylnaphthalene-1-carboxamido)-3-methylbutanamide (**5**) was formed from unit A.[1] The long-range coupling ($J_{CH}$ = 4 Hz) observed between 9-OH ($\delta_H$ 8.20) and C-8 ($\delta_C$ 164.3) suggested an $\alpha$-hydroxy carbonyl function.

**Unit B.** Spin-decoupling experiments on **1** showed the presence of a 1,1,3,4-tetrasubstituted-2-butanol structure. The long-range decouplings of 17-H ($\delta_H$ 3.39; $\delta_C$ 46.6 for C-17), 18-$H_2$ ($\delta_H$ 2.77 and 2.46; $\delta_C$ 36.7 for C-18) and 21-$H_3$ ($\delta_H$ 2.18; $\delta_C$ 20.8 for C-21) sharpened the signal of C-20 ($\delta_C$ 173.0), suggesting an acetylaziridine group at the 17- and 18-positions. Upon hydrogenation of **1** to **3**, the methylene group (C-18) was converted into a methyl group ($\delta_H$ 1.24, d, $J_{HH}$ = 5 Hz, and $\delta_C$ 14.1, q), and the resonance of C-17 shifted downfield by 11.5 ppm. These observations were consistent with ring opening of the aziridine ring to the amide.

**Unit C.** Two carbons (C-14 and -15) bearing protons were confirmed by one-bond proton-decoupling experiments. Long-range proton-decoupling experiments on **1** showed that 15-OH ($\delta_H$ 12.16) is coupled to both C-15 ($\delta_C$ 151.0) ($J_{CH}$ = 3 Hz) and C-12 ($\delta_C$ 118.7) (sharpened). Couplings between 15-H ($\delta_H$ ca. 7.35) and C-2 ($\delta_C$ 165.9) ($J_{CH}$ = 6 Hz) and between 15-H and C-12 (sharpened) were observed. In addition, coupling between 14-$H_3$ ($\delta_H$ 2.29) and C-12 (sharpened) was observed. It was confirmed by long-range decoupling of 14-$H_3$ ($J_{CH}$ = 4 Hz) that C-13 ($\delta_C$ 191.7) and C-14 ($\delta_C$ 24.3) constitute an acetyl group. Conversion of **1** and **3** into **2** and **4** shifted the resonances of 15-H downfield by ca. 1 ppm, respectively. Transformation of **3** to **4** shifted the resonance of C-15 upfield by 11.7 ppm.

Decoupling of 6-H ($\delta_H$ 5.50) sharpened the signals of C-4 ($\delta_C$ 162.1) and C-5 ($\delta_C$ 119.3). In addition, couplings between 6-H and C-2 ($J_{CH}$ = 4 Hz) and between 16-H ($\delta_H$ 4.64) and C-5 (sharpened) were observed in **1**.

The most reasonable combination of these structural units (A, B, and C) with the remaining nitrogen (one) and oxygen (three) atoms leads to the 5,6-dihydro-4*H*-1,3-oxazine as a partial structure for **1**, to which the 1,3-dioxane ring is combined in a spiro form.

As reported previously,[1] hydrolysis of **1** with 5% aqueous ammonia followed by 20% hydrochloric acid afforded two acids (**6** and **7**), which arose from partial structure A, glycine, and an unidentified compound. The latter compound has been identified as pyridine hydrochloride by direct comparison with an authentic sample. Hydrolysis of the 7-8 bond and retro-aldol cleavage of the 9-10 bond would give glycolic acid, which reacts with ammonia to yield glycine.[9] Since the formation of pyridine was also observed in the hydrolysis of **1** with 20% hydrochloric acid, the nitrogen atom in the pyridine should not arise from ammonia. Hydrolysis of the 1-2, 3-4, 5-11, and 7-8 bonds would afford 3,4-dihydroxy-5,6-imino-2-oxohexanoic acid (**8**). On the other hand, formic acid would be formed by retro-Claisen cleavage of **C**. Reduction of **8** with the formic acid to form the primary amine (**9**), ring closure, twice dehydration and final decarboxylation would account for the formation of pyridine.

(9) The formation of glycine from glycolic acid under the same conditions as those employed for hydrolysis of **1** was confirmed.

**Acknowledgment.** We are indebted to Kyowa Hakko Kogyo Co., Ltd., for the supply of carzinophilin.

**Registry No. 1b**, 1403-29-8.

**Supplementary Material Available:** Tables of proton and carbon NMR spectra for **1**, **2**, **3**, and **4** (4 pages). Ordering information is given on any current masthead page.

## Carbon-Carbon Bond Formation by Selective Coupling of Enol Silyl Ethers with Oxime Sulfonates

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*Received February 14, 1983*

We wish to outline a new reaction that leads to the formation of enaminones by the combination of enol silyl ethers and oxime sulfonates in the presence of organoaluminum reagents (Scheme I).[1,2] Enaminones (N—C=C—C=O) are an important class of compounds in view of the fruitful chemical properties and high synthetic utility, particularly as building blocks for the elaboration of fused carbocycles and polyheterocycles.[3,4] The general synthetic method involves reaction between $\beta$-diketones and amines that usually causes the lack of regiochemical control over the position of amino group in the enaminone moiety.[4]

A typical experimental procedure of the reaction is illustrated by the preparation of enaminone **3**. Diethylaluminum chloride (3 mmol, 3 mL of a 1 M hexane solution) was added to a mixture of *anti*-2-methylcyclohexanone oxime mesylate (**1**) (205 mg, 1 mmol)[5] and 2-(trimethylsiloxy)-1-octene (**2**) (220 mg, 1.1 mmol)[6] in dry methylene chloride at −78 °C. After 30 min, the solution was allowed to warm to 20 °C and stirred there for 1 h. The reaction was terminated by adding 10% NaOH. The crude

(1) For other classical reactions via nitrilium ions as intermediates, see reviews of the Ritter reaction: Johnson, F.; Madronero, R. In "Advances in Heterocyclic Chemistry"; Katritzky, A. R., Boulton, A. J., Eds.; Academic Press: New York, 1966; Vol. 6, p 95. Krimen, L. I.; Cota, D. J. *Org. React. (N.Y.)* **1969**, *17*, 213. Meyers, A. I.; Sircar, J. C. In "The Chemistry of Cyano Group"; Rappoport, Z., Ed.; Interscience: New York, 1970; p 341.

(2) For relevant reactions by organoaluminum reagents, see: Hattori, K.; Matsumura, Y.; Miyazaki, T.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1981**, *103*, 7368. Sakane, S.; Matsumura, Y.; Yamamura, Y.; Ishida, Y.; Maruoka, K.; Yamamoto, H. *Ibid.* **1983**, *105*, 672.

(3) The term enaminone was used to indicate any compound containing the conjugated system N—C=C—C=O. For the designation, see the reviews in ref 4.

(4) For reviews, see: Nishino, T.; Kajima, C.; Omote, Y. *J. Synth. Org. Chem., Jpn.* **1976**, *34*, 526. Greenhill, J. V. *Chem. Soc. Rev.* **1977**, *16*, 277. See also: Natale, N. R. *Tetrahedron Lett.* **1982**, *23*, 5009. For recent synthetic applications of enaminones, see: Horii, Z.; Morikawa, K.; Ninomiya, I. *Chem. Pharm. Bull.* **1969**, *17*, 2230. Oishi, T.; Nagai, M.; Onuma, T.; Moriyama, H.; Tsutae, K.; Ochiai, M.; Ban, Y. *Ibid.* **1969**, *17*, 2306. Yamada, Y.; Matsui, M. *Agric. Biol. Chem.* **1971**, *35*, 282. Iida, H.; Yuasa, Y.; Kibayashi, C. *J. Am. Chem. Soc.* **1978**, *100*, 3598. Patrick, J. B.; Saunders, E. K. *Tetrahedron Lett.* **1979**, 4009. Célérier, J.-P.; Eskénazi, C.; Lhommet, G.; Maitte, P. *J. Heterocycl. Chem.* **1979**, *16*, 953. Nagasaka, T.; Inoue, H.; Ichimura, M.; Hamaguchi, F. *Synthesis* **1982**, 848.

(5) Noncrystalline oxime mesylates may be conveniently stored at −20 °C or as a $CH_2Cl_2$ solution at 0 °C.

(6) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324.

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