under Contract DE-AC03-76SF00098. The work reported here was done at SSRL, which is supported by the Office of Basic Energy Sciences of DOE and the Division of Materials Research of NSF. We are especially indebted to the University of California, Berkeley, Graduate Division, for partial support of the work and to D. Outka, J. Gland and R. Koestner for assistance in the data collection.

Supplementary Material Available: Experimental procedure and analysis and Figure 4 for NEXAFS spectra for benzonitrile chemisorbed on Pt(111) (3 pages). Ordering information is given on any current masthead page.

Ab Initio Study of the Transition Structure of the [1,5]-Sigmatropic Hydrogen Transfer in *cis*-1,3-Pentadiene

B. Andes Hess, Jr.,* and L. J. Schaad*

Department of Chemistry, Vanderbilt University Nashville, Tennessee 37235

Received July 21, 1983

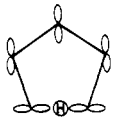
The simplest symmetry-allowed[1] [1,*n*]-sigmatropic rearrangement that can be readily observed thermally is the [1,5] hydrogen transfer in *cis*-1,3-pentadiene (**1**). In 1966 Roth and König using

1

deuterium-labeled derivatives of **1** reported that the hydrogen transfer from C-5 to C-1 in **1** occurs in the gas phase with an activation enthalpy of 35 kcal/mol and a k_H/k_D of 12.2.[2] From this they concluded that the rearrangement proceeds through the symmetric transition structure **2**. Recently Kwart and Acheson

2

have suggested that the data of Roth and König[2] demand that the transition structure for the [1,5]-sigmatropic rearrangement of **1** have a collinear arrangement of the two terminal carbons and the migrating hydrogen (**3**).[3] Their conclusion was based[4]



3

on the fact that the temperature dependence of k_H/k_D and an A_H/A_D ratio of 1.15 found by Roth and König are in line with the values predicted for a collinear hydrogen transfer by Schneider and Stern.[5]

Since Schneider and Stern used relatively simple model calculations in making their prediction, we thought it useful to undertake an ab initio study of the transition structure of the [1,5]-sigmatropic hydrogen transfer in **1**. The proposed collinear transition structure **3** as depicted by Kwart and Acheson has C_{2v} symmetry, while that of Roth and König (**2**) is of C_s symmetry. A third possible transition structure has C_2 symmetry, but this would involve the forbidden[1] antarafacial hydrogen transfer. In fact Roth and König have shown[6] that for a substituted 1,3-pentadiene the hydrogen transfer proceeds in a suprafacial fashion which could occur either via **2** or **3**. Since both **2** and **3** are of higher symmetry than the reactant (**1**), the task of locating the transition structure is greatly simplified. By imposing these higher symmetries the two potential transition structures can be readily located by energy minimization.

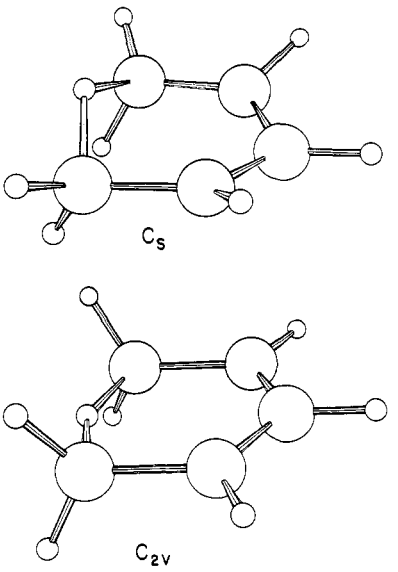


Figure 1. ORTEP drawings of the two transition structures considered.

Table I. Energies[a] (kcal/mol) of the Two Possible Transition Structures in the [1,5]-Sigmatropic Hydrogen Transfer in *cis*-1,3-Pentadiene

basis set	C_s	C_{2v}
3-21G	+54.6	+122.3
6-31G*	+58.7	+123.7

[a] Energies are given relative to the calculated *s-trans,cis*-1,3-pentadiene energy (3-21G: −192.879 58 au; 6-31G*: −193.956 25 au).

We have carried out these two minimizations with a 3-21G[7] wave function using the DEC 10 version of GAUSSIAN80.[8] The ORTEP[9] drawings in Figure 1 show the best C_{2v} and C_s structures. Single-point SCF energies and gradients were computed with the 6-31G* basis[10] at the best 3-21G geometries. The value of the gradient at these two points indicated, based on our experience, that these 6-31G* energies are most likely within 1 kcal/mol of the actual minima with this basis. Results are summarized in Table I where the energies of the proposed transition structures are given relative to that of the reactant **1**.[11] It is immediately seen that the proposed transition structure of C_{2v} symmetry is of considerably higher energy than that (C_s) suggested by Roth and König. The CHC angle of the migrating hydrogen in the C_s structure was found to be 129.9°. Further, this best C_{2v} structure

(1) Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Academic Press: New York, 1970; p 114.
(2) Roth, W. R.; König, J. *Liebigs Ann. Chem.* **1966**, *699*, 24.
(3) Kwart, H.; Brechbiel, M. W.; Acheson, R. M.; Ward, D. C., *J. Am. Chem. Soc.* **1982**, *104*, 4671.
(4) Kwart, H.; Brechbiel, M. W. *J. Am. Chem. Soc.* **1981**, *103*, 4650.
(5) Schneider, M. E.; Stern, M. J. *J. Am. Chem. Soc.* **1972**, *94*, 1517.
(6) Roth, W. R.; König, J. *Chem. Ber.* **1970**, *103*, 426.
(7) Binkley, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 939.
(8) Binkley, J. S.; Whiteside, R. A.; Krishnan, R.; Seeger, R.; DeFrees, D. J.; Schlegel, J. B.; Topiol, S.; Kahn, L. R.; Pople, J. A., GAUSSIAN80, Quantum Chemistry Program Exchange, Indiana University, Bloomington, IN. We thank Professor John Yates, University of Pittsburgh, for a DEC version of this program.
(9) Johnson, C. K. "ORTEP II: A FORTRAN Thermal-Ellipsoid Plot Program for Crystal Structure Illustrations"; Oak Ridge National Laboratory Report ORNL-5138, 1976.
(10) Pople, J. A. In "Modern Theoretical Chemistry"; Schaefer III, H. F., Ed.; Plenum Press: New York, 1977; Vol. 4, p 1–27.
(11) The energies of *cis*-1,3-pentadiene were obtained in a fashion similar to that of the two transition structures.

0002-7863/83/1505-7185$01.50/0

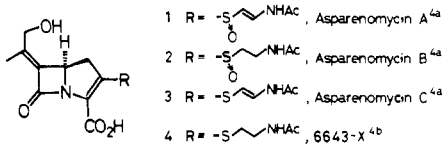
does not have a collinear arrangement of the two terminal carbon atoms and the migrating hydrogen. Such a collinear structure must be higher in energy. While inclusion of correlation might reduce the energy difference between **2** and **3**, we believe it unlikely that it would reverse the order of these two possible transition structures and conclude that the transition structure of the [1,5]-sigmatropic hydrogen transfer in **1** most likely possesses C_s symmetry and is therefore not a transition structure with a collinear hydrogen transfer.

Stereocontrolled Synthesis of an Ene-Carbapenem Antibiotic, (-)-Asparenomycin C

Kazuo Okano, Yoshinori Kyotani,[1] Hiroshi Ishihama,[1] Susumu Kobayashi, and Masaji Ohno*

Faculty of Pharmaceutical Sciences
University of Tokyo
Hongo, Bunkyo-ku, Tokyo 113, Japan
Received June 30, 1983

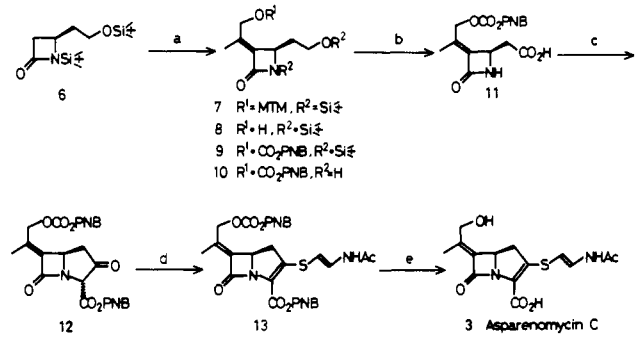
Naturally occurring carbapenem antibiotics can be classified into three groups (trans, cis, and ene types according to the structural mode of the side chain of the β-lactam ring.[2] Synthetically, trans-substituted carbapenem antibiotics have been most extensively studied by a number of research groups,[3a] and a cis-carbapenem antibiotic, (-)-carpetimycin A, was recently elaborated starting with (*S*)-3-[((benzyloxy)carbonyl)amino]-4-(methoxycarbonyl)butyric acid.[3b] However, there is no successful report for the enantioselective synthesis of asparenomycins **1**–**4**,



which belong to the third class of naturally occurring carbapenem antibiotics recently isolated.[4] They are structurally unique, because the common side chain at C-6 is a 1-(hydroxymethyl)-ethylidene group in *E* form and they have only one asymmetric carbon at C-5 with *R* configuration. We now wish to report here the first chiral and stereocontrolled synthesis of (-)-asparenomycin C starting with (*S*)-4-[(methoxycarbonyl)methyl]azetidin-2-one (**5**) as shown in Scheme I. The characteristic feature of the present synthesis includes a stereocontrolled elaboration of the required *E* tetrasubstituted olefin by a combination (one-pot reaction) of chelation-controlled aldol reaction and Peterson olefination as shown in Scheme II.

The fully silylated derivative **6** of 4-(hydroxyethyl)azetizin-2-one now easily available[5] from **5** was selected as the starting synthon. Introduction of alkylidene groups at C-3 of 2-azetidinone first studied by Shibuya et al.[6] showed that 3-alkylideneazetidin-2-ones are easily obtained by reaction of 3-(trimethylsilyl)azetidin-2-one with usual carbonyl compounds. We become interested in direct introduction of (*E*)-1-(hydroxymethyl)ethylidene group in a stereocontrolled manner by using hydroxyacetone derivatives. Thus, one-pot reaction of **6** with trimethylsilyl chloride (1 equiv)

Scheme I



a (i) 2 LDA, TMSCl, $CH_3COCH_2OCH_2SCH_3$/THF (6→7) (ii) $HgCl_2$, $CaCO_3$/aq CH_3CN (7→8) (iii) $ClCO_2PNB$, DMAP/CH_2Cl_2 (8→9) (iv) conc. HCl/MeOH (9→10); b CrO_3/Py; c (i) CDI/THF (ii) $(CO_2PNB\text{-}CO_2)_2Mg$ (iii) TsN_3, Et_3N/CH_3CN (iv) cat. $Rh_2(OAc)_4$/C_6H_6; d (i) $Cl\text{-}P(OPh)_2$, i-Pr_2NEt, DMAP/CH_3CN (ii) NaI, AgS-NHAc/CH_3CN; e H_2, Pd-C/pH 7.5 phosphate buffer, dioxane

in the presence of LDA (2.3 equiv) at −78 °C (15 min) and then with [(methylthio)methoxy]acetone[7] (1.6 equiv) at −78 °C (15 min) was studied and 3-(1-(((methylthio)methoxy)methyl)-ethylidene)azetidin-2-one (**7**) was obtained as the single product in 98% yield.[7] **7**: oil, $[\alpha]^{20}_D$ −25.26° (*c* 2.01, $CHCl_3$). The stereochemistry of the olefinic moiety was assigned the *E* form based on the comparison of ^1H NMR of **7** and reference compounds[8] and proved to be the desired *E* form by eventual conversion to natural asparemonycin C. The remarkable success of the stereoselectivity could be reasonably explained by the chelation-controlled aldol reaction from the α-face followed by Peterson olefination or syn elimination[9] of Me_3SiOLi, as depicted in Scheme II.

The similar complete stereoselectivity was also observed in each case of (((benzyloxy)carbonyl)oxy)- or ((methoxymethyl)oxy)-acetone, giving the corresponding *E* isomer as the sole product. These results clearly indicate that the chelation between lithium cation and oxygens[10] plays a key role at the transition state A to control the stereochemistry of the intermediate B. The MTM group was selectively cleaved by mercuric chloride–calcium carbonate in aqueous acetonitrile[11] at 40 °C, and the resultant unstable allyl alcohol **8**, $[\alpha]^{20}_D$ −38.6° (*c* 1.99, $CHCl_3$), was reprotected with *p*-nitrobenzyl (PNB) chloroformate and 4-(dimethylamino)pyridine to give **9** in 90% yield.[12] It was gratifying to be able to isolate **8** in 84% yield by catalytic hydrogenolysis (H_2–Pd/C) of **9**, showing that hydrogenolysis of the *p*-nitrobenzyl group is much faster than the hydrogenation of the double bond of the enone moiety of the β-lactam.[13] The confirmation of this crucial step allowed us to proceed the present synthetic path from monocyclic **9** to bicyclic **13**. Deprotection of the two silyl groups was quantitatively carried out with HCl in MeOH. Oxidation of **10** with Sarett reagent afforded an acid derivative **11**, $[\alpha]^{20}_D$

(1) Research chemists of Tokyo Research Laboratories, Kowa Co., Ltd.
(2) Recently, 6-unsubstituted and very unstable carbapenem, SQ27,860, was isolated and this may belong to a new class of carbapenems, but it is synthetically considered to be a simpler precursor. Parker, W. L.; Rathnum, M. L.; Wells, J. S.; Trejo, W. H.; Principe, P. A.; Sykes, R. B. *J. Antibiot.* **1982**, *35*, 653.
(3) (a) Okano, K.; Izawa, T.; Ohno, M. *Tetrahedron Lett.* **1983**, *24*, 217 and references cited therein. (b) Iimori, T.; Takahashi, Y.; Izawa, T.; Kobayashi, S.; Ohno, M. *J. Am. Chem. Soc.* **1983**, *105*, 1659, and references cited therein.
(4) Tsuji, N.; Nagashima, K.; Kobayashi, M.; Shoji, J.; Kato, T.; Terui, Y.; Nakai, H.; Shiro, M. *J. Antibiot.* **1982**, *35*, 24, and references cited therein.
(5) (a) Ohno, M.; Kobayashi, S.; Iimori, T.; Wang, Y.-F.; Izawa, T. *J. Am. Chem. Soc.* **1981**, *103*, 2405. (b) Kobayashi, S.; Iimori, T.; Izawa, T.; Ohno, M. *Ibid.* **1981**, *103*, 2406.
(6) Kano, S.; Ebata, T.; Funaki, K.; Shibuya, S. *Synthesis* **1978**, 746.
(7) ((Methylthio)methoxy)acetone was prepared directly from hydroxyacetone and (methylthio)methyl chloride according to Yamaguchi's method; Suzuki, K.; Inanaga, J.; Yamaguchi, M. *Chem. Lett.* **1979**, 1277. The intermediate **6a**, trimethylsilyl derivative of **6**, was able to be isolated and characterized.[16]
(8) 3-Isopropylidene derivative **C** was prepared from **6** and acetone in a similar manner, and we tentatively assigned the *E* stereochemistry for **7**. **7**: ^1H NMR ($CDCl_3$) δ 2.05. C: ^1H NMR ($CDCl_3$) δ 2.03 (cis methyl), 1.74 (trans methyl). See also: Johnston, D. B. R.; Schmitt, S. M.; Bouffard, E. A.; Christensen, B. G. *J. Am. Chem. Soc.* **1978**, *100*, 313.
(9) For reviews, see: (a) Weber, W. P. "Silicon Reagents for Organic Synthesis"; Springer-Verlag: Berlin and Heidelberg, 1983. Chapter 6. (b) Colvin, E. W. "Silicon in Organic Synthesis"; Butterworths: London 1981.
(10) For instance, see: Masamune, S.; Ellingboe, J. W.; Choy, W. *J. Am. Chem. Soc.* **1982**, *104*, 5526.
(11) Corey, E. J.; Bock, M. G. *Tetrahedron Lett.* **1976**, 3269.
(12) The direct preparation of **9** from **6** with [(((*p*-nitrobenzyl)oxy)-carbonyl)oxy]acetone in the similar manner was found to be unsuccessful.
(13) This point was considered to be a crusial step in the present synthesis, since we previously observed that a simple double bond conjugated to the carbonyl of the β-lactam was easily hydrogenated during the synthesis of PS-6 series. Okano, K.; Ohno, M., unpublished results.

0002-7863/83/1505-7186$01.50/0