Steric vs. Stereoelectronic Effects in Carbocation Reactions of the 2-Bicyclo[6.1.0]nonyl System

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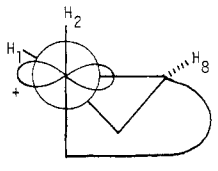
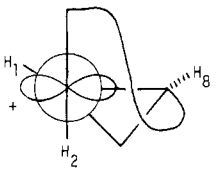
An investigation of *anti*-9-methyl substituent effects upon the kinetics and products of hydrolysis of the cis-ring-fused *endo*- and *exo*-2-bicyclo[6.1.0]nonyl 3,5-dinitrobenzoates in 80% aqueous acetone has been carried out. In the exo system, the *anti*-9-methyl substituent produced only a small rate-accelerating effect of 1.8 at 80 °C. However, for the endo system acceleration by a factor of 4.7 was observed. In neither system did the *anti*-9-methyl substituent affect the exo:endo product ratio. With the *anti*-6-methyl-2-bicyclo[3.1.0]hexyl 3,5-dinitrobenzoates, which were studied for comparison, the *anti*-6-methyl substituent exhibited an identical rate-accelerating effect of 8.3 in both the endo and the exo isomers. Also, with both isomers an identical exo:endo product ratio was observed. On the basis of these results, it is proposed that the stereoselectivities observed in product formation in the 2-bicyclo[6.1.0]nonyl system are not due primarily to electronic factors but result mainly from steric effects upon structurally different, noninterconverting intermediates with bisected delocalization.

It is generally agreed[1] that the energetically most favorable conformation of the cyclopropylcarbinyl cation is that in which the p orbital on the carbinyl carbon overlaps simultaneously with both bonds of the cyclopropane ring. In such a bisected form, solvent attack should take place simultaneously from both sides of the carbinyl carbon. However, in certain cyclopropylcarbinyl systems such as with the cis-ring-fused *endo*- and *exo*-2-bicyclo[6.1.0]nonyl 3,5-dinitrobenzoates,[2] mutually exclusive sets of products are obtained (Scheme I).

For the 2-bicyclo[6.1.0]nonyl system, the product-forming behavior has been rationalized[3a] in terms of the intermediacy of conformationally different bicyclobutonium-type intermediates **1** and **2** in which electron-releasing effects of the ring residue at carbon 8 cause preferential overlap of one lobe of the p orbital at carbon 2 with the C_1–C_8 cyclopropane bond. However, Poulter and Spillner[4] later commented, in connection with other results, that it is unlikely that the electronic effect of the alkyl-ring residue at carbon 8 is large enough to explain the high stereospecificity in the reactions of the 2-bicyclo[6.1.0]nonyl system.



1 (from endo)

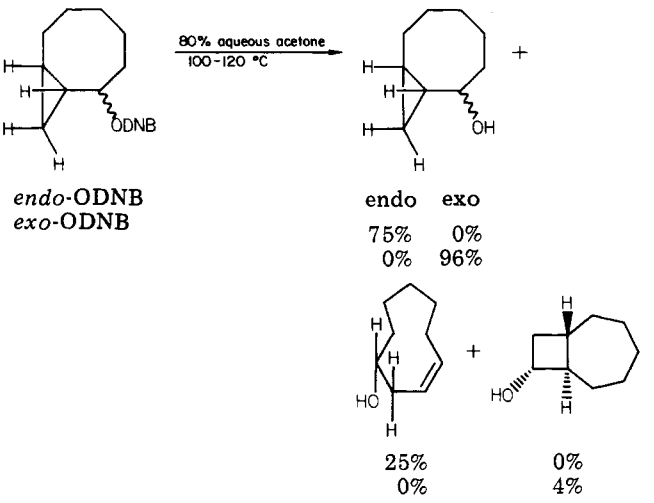


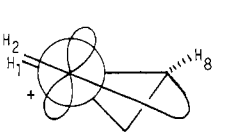
2 (from exo)

Although one cannot find fault with the conclusion that the endo and exo [6.1.0] derivatives react via conformationally isomeric intermediates, it is not obvious why these should necessarily be of the bicyclobutonium types **1** and **2** rather than the energetically more favorable bisected types **3** and **4**. Molecular models reveal that these are both possible without introducing much strain in the system. Also, kinetic data for the [6.1.0] derivatives[2] show that they are at least as reactive as the corresponding 2-bicyclo[3.1.0]hexyl derivatives,[5] which are known to react via bisected activated complexes and intermediates. The postulation of bisected intermediates in the 2-bicyclo[6.1.0]nonyl system does, however, cause problems in explaining the solvolysis product stereochemistries as some crossover of endo and exo products would be expected. The only way this would not happen is if severe steric problems strongly hinder solvent attack from one side of the bisected intermediate.

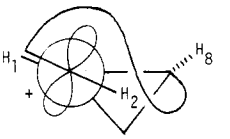
The investigation described below was carried out to obtain a better understanding of the factors involved in

Scheme I





3 (from endo)



4 (from exo)

(1) For reviews, see: (a) Richey, G. "Carbonium Ions"; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley-Interscience: New York, 1972; Vol. III, Chapter 25. (b) Wiberg, K. B.; Hess, B. A., Jr.; Ashe, A. J., ref 1a, Vol. III, Chapter 26. (c) Haywood-Farmer, J. *Chem. Rev.* **1974**, *74*, 315. (d) Brown, H. C. "The Nonclassical Ion Problem"; Plenum Press: New York, 1977; Chapter 5.

(2) Wiberg, K. B.; Nakahira, T. *J. Am. Chem. Soc.* **1971**, *93*, 5193. Similar results were also found with the corresponding *p*-nitrobenzoates.[3]

(3) (a) Poulter, C. D.; Friedrich, E. C.; Winstein, S. *J. Am. Chem. Soc.* **1970**, *92*, 4274. (b) Gassman, P. G.; Williams, E. A.; Williams, F. J. *Ibid.* **1971**, *93*, 5199.

(4) Poulter, C. D.; Spillner, C. J. *J. Am. Chem. Soc.* **1974**, *96*, 7591.

(5) Friedrich, E. C.; Saleh, M. A. *J. Am. Chem. Soc.* **1973**, *95*, 2617.

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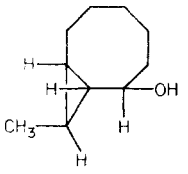
the carbocation reactions of the 2-bicyclo[6.1.0]nonyl system. In this study special emphasis was placed on determining the nature of the delocalization in the intermediate cyclopropylcarbinyl cation species and of their conformations and stereochemistries for reaction with solvent.

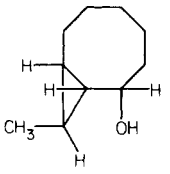
Results and Discussion

The initial approach used in this investigation was to examine the effects of *anti*-9-methyl substitution upon the rates and products of hydrolysis of the *endo*- and *exo*-2-bicyclo[6.1.0]nonyl 3,5-dinitrobenzoates. It was anticipated that the *anti*-9-methyl substituent would exert only electronic and no steric effects at the carbon-2 reaction site and that this would thus allow a clear distinction of the steric and electronic influences upon the reactions of the system to be made. However, brief studies of *anti*-6-methyl substituent effects on the *endo*- and *exo*-2-bicyclo[3.1.0]hexyl 3,5-dinitrobenzoates were also carried out to test this.

Synthesis of Starting Materials. The preparations of the isomeric *anti*-9-methyl-*endo*- and -*exo*-2-bicyclo-[6.1.0]nonyl derivatives required for this investigation were carried out as follows. Methylcyclopropanation of cyclooctene-3-ol with 1,1-diiodoethane and zinc dust–cuprous chloride in ether[6] gave a 72:28 mixture of *syn*- and *anti*-9-methyl-*exo*-2-bicyclo[6.1.0]nonanols. A pure sample of the *anti*-9-methyl *exo* alcohol **5** was separated from the



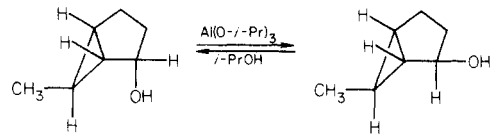
5



6

reaction mixture by GLC. The corresponding endo alcohol **6** was separated from a mixture prepared by $LiAlH_4$ reduction[7] of the mixture of ketones obtained by oxidation of the exo alcohol mixture. In the ketone reduction less than 10% of the exo alcohols were formed. Preparations of the corresponding 3,5-dinitrobenzoates from the *anti*-9-methyl alcohols **5** and **6** were accomplished in the usual manner without any difficulties.

Syntheses of the *anti*-6-methyl *endo*- and *exo*-2-bicyclo[3.1.0]hexyl derivatives needed as model systems for this study were accomplished as follows. Methylcyclopropanation of cyclopenten-3-ol with 1,1-diiodoethane and a 30-mesh granular zinc–copper couple in ether gave a 62% yield of a 78:22 mixture of *anti*- and *syn*-6-methyl-*endo*-2-bicyclo[3.1.0]hexanols.[6] A pure sample of the anti-endo alcohol **7** obtained by GLC was equilibrated by using



7 **8**

aluminum isopropoxide in isopropanol to obtain a 40:60 mixture of the anti-endo and anti-exo alcohols **7** and **8** from which **8** was separated by GLC. Preparations of the corresponding 3,5-dinitrobenzoates were accomplished in the usual manner.

(6) Friedrich, E. C.; Biresaw, G. *J. Org. Chem.* **1982**, *47*, 1615.
(7) Kawabata, N.; Nakagawa, T.; Nakao, T.; Yamashita, S. *J. Org. Chem.* **1977**, *42*, 3031.

Table I. Comparison of $LiAlH_4$ Reduction and $Al(O\text{-}i\text{-}Pr)_3$ Equilibration Results for Several 2-Bicyclo[3.1.0]hexyl and 2-Bicyclo[6.1.0]nonyl Systems

process	2-bicyclo[*n*.1.0]alkyl derivative	2-bicyclo-[*n*.1.0]alkanol product, % endo	exo
$LiAlH_4$ in ether redn at room temperature	unsubstituted [3.1.0][a]	91	9
	anti-6-methyl [3.1.0]	91	9
	unsubstituted [6.1.0][b]	98	2
	anti-9-methyl [6.1.0]	99	1
$Al(O\text{-}i\text{-}Pr)_3$ in *i*-PrOH equil at 100 °C	unsubstituted [3.1.0][c]	37	63
	anti-6-methyl [3.1.0]	40	60
	unsubstituted [6.1.0]	0.2	99.8
	anti-9-methyl [6.1.0]	0.1	99.9

[a] Data of: Hanack, M.; Allmendinger, H. *Chem. Ber.* **1969**, *97*, 1669. [b] Data of: Poulter, C. D.; Friedrich, E. C.; Winstein, S. *J. Am. Chem. Soc.* **1970**, *92*, 4274. [c] Data of: Thornton, R. I. Ph.D. Thesis, MIT., Cambridge, MA, 1961.

Table II. Rates of Hydrolysis of Some *endo*- and *exo*-2-Bicyclo[3.1.0]hexyl and 2-Bicyclo[6.1.0]nonyl 3,5-Dinitrobenzoates in 80% Aqueous Acetone at 80 °C

2-bicyclo[*n*.1.0]-alkyl derivative	$10^5 k_1$, s^{-1}	k_{endo}/k_{exo}	k_{Me}/k_H	k_{rel}
2-Bicyclo[3.1.0]hexyl 3,5-Dinitrobenzoates				
unsubstituted[a]				
endo-ODNB	0.184	1.2		1.2
exo-ODNB	0.152			1
anti-6-methyl				
endo-ODNB	1.52	1.2	8.3	10
exo-ODNB	1.26		8.3	8.3
2-Bicyclo[6.1.0]nonyl 3,5-Dinitrobenzoates				
unsubstituted[b]				
endo-ODNB	2.81	22		22
exo-ODNB	0.128[c]			1
anti-9-methyl				
endo-ODNB	13.1	56	4.7	102
exo-ODNB	0.234		1.8	1.8

[a] Data of: Friedrich, E. C.; Saleh, M. A. *J. Am. Chem. Soc.* **1973**, *95*, 2617. [b] Data of: Wiberg, K. B.; Nakahira, T. *Ibid.* **1971**, *93*, 5193. [c] Calculated from data at higher temperatures.

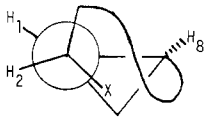
Before proceeding with the kinetic and product studies, we investigated whether the *anti*-6- or *anti*-9-methyl substituents exert any steric effects at the carbon-2 reaction site. This was accomplished by comparing the $LiAlH_4$ in ether ketone reduction stereochemistries and the aluminum isopropoxide in isopropyl alcohol equilibration stereochemistries for the unsubstituted and methyl-substituted systems. These data are given in Table I and reveal that within experimental error the methyl-substituted and unsubstituted systems afford the same results, indicating the absence of steric effects of the *anti*-6- or *anti*-9-methyl substituents at carbon 2.

Kinetic Studies. Kinetic data for the hydrolyses of the unsubstituted and methyl-substituted 2-bicyclo[3.1.0]hexyl and 2-bicyclo[6.1.0]nonyl 3,5-dinitrobenzoates in 80% aqueous acetone at 80 °C are given in Table II. The results reveal for the 2-bicyclo[3.1.0]hexyl derivatives, which react via bisected activated complexes, that the *anti*-6-methyl substituent causes an identical rate acceleration of 8.3 for both the endo and exo derivatives. However, for the 2-bicyclo[6.1.0]nonyl system, the acceleration of 4.7 for the endo isomer is more than twice as large as that of 1.8 for the exo isomer. Control experiments showed that no ion-pair return to rearranged or epimeric

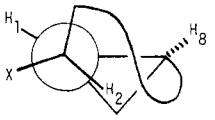
3,5-dinitrobenzoates occurred during the course of any of the hydrolyses.

These kinetic results clearly negate the possibility that both the endo and exo [6.1.0]dinitrobenzoates ionize to give bicyclobutonium-type intermediates such as **1** and **2** involving delocalization only with the C_1–C_8 cyclopropane bond. Had this been true, the *anti*-9-methyl substitution would have been expected to have a minor effect on the reaction rates of both the endo and exo esters. Thus, both epimers must be reacting via activated complexes involving bisected-type delocalization. However, because of conformational problems unequal amounts of C_1–C_8 and C_1–C_9 cyclopropane-bond overlap must be involved for one or both of the epimers. Otherwise one would have expected to observe equal k_{Me}/k_H values for both the *endo*- and *exo*-2-bicyclo[6.1.0]nonyl derivatives as was found in the 2-bicyclo[3.1.0]hexyl system. Since the k_{Me}/k_H value for the endo derivatives is larger than that for the exo derivatives, the endo-activated complex must involve more C_1–C_9 cyclopropane-bond overlap than does the exo isomer.

Information regarding conformational preferences in the 2-bicyclo[6.1.0]nonyl system may be obtained from ^1H NMR data. The fact that the protons on carbon 2 for the exo derivatives absorb about 1 ppm upfield from those for the endo derivatives can be attributed[3b] to shielding by the cyclopropane ring of the endo-directed protons on carbon 2 of the exo derivatives. A conformation for the 2-bicyclo[6.1.0]nonyl system that is consistent with the NMR data is illustrated in the Newman projections **9** and **10** for the endo and exo derivatives, respectively. This



9 (endo)

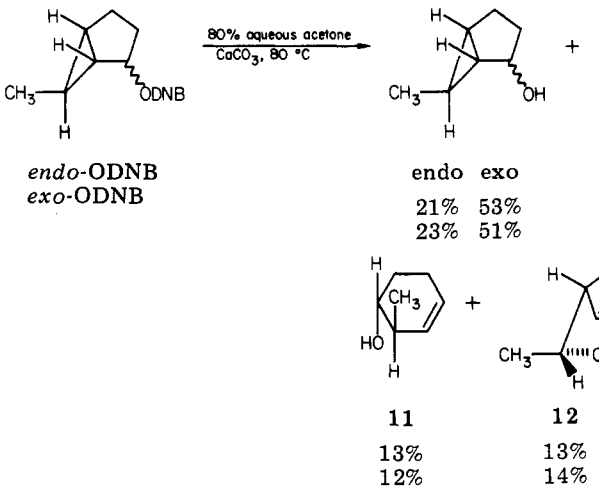


10 (exo)

conformation agrees well with the $LiAlH_4$ ketone reduction and $Al(O\text{-}i\text{-}Pr)_3$ alcohol equilibrium data (Table I) as well as with the endo–exo rate ratio data, which indicate that the endo side of the 2-bicyclo[6.1.0]nonyl molecule should be considerably more hindered than is the exo side. Also, it is in accord with the suggestion made earlier from consideration of k_{Me}/k_H values that the activated complex for reaction of thhe endo [6.1.0] 3,5-dinitrobenzoate takes part in more C_1–C_9 cyclopropane-band overlap than does the corresponding exo derivative.

Hydrolysis Product Studies. The products of hydrolysis of the *anti*-6-methyl-substituted *endo*- and *exo*-2-bicyclo[3.1.0]hexyl 3,5-dinitrobenzoates in 80% aqueous acetone are given below. Control experiments showed that all of the products are stable under the reaction conditions. Within experimental error, identical products were obtained from both the endo and exo *anti*-6-methyl 3,5-dinitrobenzoates, indicating the intermediacy of a bisected cyclopropylcarbinyl cation species. Also, the cyclohexen-4-ol (**11**) and 1-(cyclopenten-3-yl)ethanol (**12**) products are each one specific stereoisomer as would be expected from solvent attack on a delocalized cyclopropylcarbinyl cation intermediate. Evidence regarding their precise stereochemistries is presented in the Experimental Section.

The products of hydrolysis of the *anti*-9-methyl-substituted 2-bicyclo[6.1.0]nonyl 3,5-dinitrobenzoates were also determined at 80 °C in 80% aqueous acetone buffered with calcium carbonate. The endo ester gave a 78% yield of endo alcohol together with a mixture of three minor products but no exo alcohol. The exo ester gave a 98% yield of exo alcohol and 2% of one minor product but no endo alcohol. Further information regarding the nature



of the minor products is provided in the Experimental Section.

Comparison of the hydrolysis products for the *anti*-9-methyl esters with those for the corresponding unsubstituted esters (Scheme I) reveals for the exo derivative that the *anti*-9-methyl substituent has virtually no effect upon the regio- or stereoselectivity for solvent attack. This is in agreement with the kinetic results for the exo 3,5-dinitrobenzoate in that the *anti*-9-methyl substituent exerted only a small accelerating effect. In any case, no solvent attack would have been expected at carbon 9 in the exo system as the resulting 1-(cycloocten-3-yl)ethanol product would necessarily have a trans double bond if it was derived from a delocalized intermediate.

As to why the exo system gives exclusively the exo-[6.1.0] and no endo-[6.1.0] product could be due in part to a stereoelectronic effect in an intermediate resembling structure **2** with more C_1–C_8 than C_1–C_9 cyclopropane-bond participation as is suggested by the kinetic results. Thus, attack by solvent should be more favorable at the less interacting exo lobe of the p orbital on carbon 2. However, steric effects might also be expected to favor exo product. Thus, $LiAlH_4$ reduction of 2-bicyclo[6.1.0]nonanone (Table I) proceeds with almost exclusive exo attack. For these reasons, it is believed that in the *exo*-2-bicyclo[6.1.0]nonyl system both stereoelectronic and steric effects are important in explaining the behavior observed in product formation.

For the endo-[6.1.0] system, the k_{CH_3}/k_H results (Table II) would appear to require an activated complex and subsequent intermediate in which bisected delocalization close to that in structure **3** is taking place. Thus, the exclusive formation of endo-[6.1.0] hydrolysis product cannot be due to a stereoelectronic effect as is depicted in structure **1**. Instead it must be due to a steric effect.

The problem with a steric explanation is that both $LiAlH_4$ reduction and $Al(O\text{-}i\text{-}Pr)_3$ equilibration studies (Table I) have shown the exo side of the molecule to be less sterically hindered than the endo side. However, this is misleading as it assumes the ring conformation for the endo-[6.1.0] intermediate to be similar to that for the [6.1.0] ketone. Instead the structure of the endo intermediate probably resembles **3** while the structure for the ketone most likely resembles **4**, where H_2 has been replaced by oxygen. A model of **3** reveals that its endo side is clearly less sterically hindered than the exo side, owing to cross-ring hydrogen interactions.

Experimental Section

General Methods. Melting and boiling points are uncorrected. NMR spectra were run on a Varian Associates EM390 instrument

with chemical shifts measured in parts per million (δ) downfield from tetramethylsilane as an internal standard. GLC analyses and separations were carried by using Varian Series 1400 or Aerograph A90P3 instruments fitted with Pyrex injector inserts. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. Mass spectra were run at the U.C. Davis Advanced Instrumentation Facility.

Preparation of 9-Methyl-2-bicyclo[6.1.0]nonanols. The two isomeric 9-methyl-2-bicyclo[6.1.0]nonanols were prepared by following the procedure of Kawabata and co-workers[7] with some modifications.[6] The reaction of 19 g (0.15 mol) of cycloocten-3-ol, 93 g (0.33 mol) of 1,1-diiodoethane, 65 g (0.60 mol) of zinc dust, and 5.9 g (0.060 mol) of cuprous chloride in 75 mL of ether was carried out at reflux for 20 h. Workup and distillation gave 21 g (88% yield) of a 72:28 mixture of *syn*- and *anti*-9-methyl-*exo*-2-bicyclo[6.1.0]nonanols: bp 105–106 °C (10 mm). The *anti*-9-methyl-*exo*-2-bicyclo[6.1.0]nonanol was separated by GLC on a 10% diethylene glycol succinate on 60/80 mesh nonacid-washed Chromosorb W column: NMR (CCl_4) δ 0.2–2.2 (m, 13 H), 1.1 (d, J = 6 Hz, 3 H, CH_3), 2.3 (s, 1 H, OH), 3.2 (m, $W_{1/2}$ = 20 Hz, 1 H, CHOH).

Oxidation of 8.3 g (0.054 mol) of the 72:28 syn–anti alcohol mixture in 50 mL of acetone with 16 mL of a 2.67 M chromium trioxide in aqueous sulfuric acid solution gave after workup and distillation 7.9 g (90% yield) of a 71:29 mixture of *syn*- and *anti*-9-methyl-2-bicyclo[6.1.0]nonanones: bp 97–98 °C (10 mm); IR (neat) ν 1690 cm^{-1} (C=O stretch). Reduction of 7.0 g (0.046 mol) of the ketone mixture with 1.9 g (0.05 mol) of $LiAlH_4$ in 75 mL of ether at room temperature gave after workup and distillation 6.6 g (93% yield) of a mixture of 9-methyl-2-bicyclo-[6.1.0]nonanols: bp 103–105 °C (10 mm). GLC analysis on a 47-m Carbowax 20M glass capillary column revealed the presence of <1% *anti-exo*-, 28% *anti-endo*-, 8% *syn-exo*-, and 64% *syn-endo*-9-methyl-2-bicyclo[6.1.0]nonanol. The *anti*-9-methyl-*endo*-2-bicyclo[6.1.0]nonanol, which solidified during collection and melted at 78–80 °C after recrystallization from mixed hexanes, and separated by GLC on a 10% diethylene glycol succinate on 60/80 mesh nonacid-washed Chromosorb W column: NMR (CCl_4) δ 0.2–2.1 (m, 13 H), 1.1 (d, J = 6 Hz, 3 H, CH_3), 1.6 (s, 1 H, OH), 4.4 (m, $W_{1/2}$ = 14 Hz, 1 H, CHOH).

***anti*-9-Methyl-*exo*-2-bicyclo[6.1.0]nonyl 3,5-Dinitrobenzoate.** A solution of 0.20 g (1.3 mmol) of *anti*-9-methyl-*exo*-2-bicyclo[6.1.0]nonanol in 20 mL of pyridine was treated with 0.37 g (1.6 mmol) of 3,5-dinitrobenzoyl chloride and allowed to react at 0 °C for 14 h. The reaction mixture was worked up in the usual manner, and the crude product was recrystallized from 25 mL of mixed hexanes to give 0.28 g (62% yield) of white crystals: mp 131–132 °C; NMR ($CDCl_3$) δ 0.2–2.6 (m, 13 H), 1.0 (d, J = 6 Hz, 3 H, CH_3), 5.0 (m, $W_{1/2}$ = 24 Hz, 1 H CHODNB), 9.2 (m, 3 H, Ar).

Anal. Calcd for $C_{17}H_{20}N_2O_6$: C, 58.62; H, 5.75. Found: C, 58.58; H, 5.87.

***anti*-9-Methyl-*endo*-2-bicyclo[6.1.0]nonyl 3,5-Dinitrobenzoate.** Reaction of 0.30 g (1.9 mmol) of *anti*-9-methyl-*endo*-2-bicyclo[6.1.0]nonanol in 30 mL of dry pyridine with 0.56 g (2.4 mmol) of 3,5-dinitrobenzoyl chloride was allowed to proceed at 0 °C for 14 h. The solid obtained after workup was recrystallized from mixed hexanes to give 0.39 g (57% yield) of flakey crystals: mp 90–92 °C; NMR ($CDCl_3$) δ 0.3–2.5 (m, 13 H), 1.1 (d, J = 6 Hz, 3 H, CH_3), 5.9 (m, $W_{1/2}$ = 13 Hz, 1 H, CHODNB), 9.2 (m, 3 H, Ar).

Anal. Calcd for $C_{17}H_{20}N_2O_6$: C, 58.62; H, 5.75. Found: C, 58.44; H, 5.78.

Preparation of 6-Methyl-2-bicyclo[3.1.0]hexanols. A 78:22 mixture of *anti*- and *syn*-6-methyl-*endo*-2-bicyclo[3.1.0]hexanols was prepared by cyclopropanation of cyclopenten-3-ol with ethylidine iodide as described earlier.[6] Equilibration of a portion of this mixture using aluminum isopropoxide and acetone in isopropyl alcohol under reflux gave a mixture of 45% *anti-exo*-, 31% *anti-exo*-, 18% *syn-exo*-, and 6% *syn-endo*-6-methyl-2-bicyclo[3.1.0]hexanol. A sample of the *anti*-6-methyl-*exo*-2-bicyclo[3.1.0]hexanol was separated by GLC on a 20% 3-nitro-3-methylpimelonitrile on 60/80 mesh nonacid-washed Chromosorb W column: NMR (CCl_4) δ 0.4 (m, 1 H, cyclopropyl), 0.8–2.0 (m, 6 H), 1.0 (d, J = 6 Hz, 3 H, CH_3), 1.9 (s, 1 H, OH), 4.1 (d, J = 4 Hz, 1 H, CHOH).

***anti*-6-Methyl-*endo*-2-bicyclo[3.1.0]hexyl 3,5-Dinitrobenzoate.** The reaction of 1.0 g (8.9 mmol) of *anti*-6-methyl-*endo*-2-bicyclo[3.1.0]hexanol (separated by GLC from an anti–syn mixture using a 20% Carbowax 20M column) and 2.5 g (11 mmol) of 3,5-dinitrobenzoyl chloride in 20 mL of dry pyridine was allowed to proceed at 0 °C for 8 h. The crude product obtained was recrystallized from 40 mL of warm methylcyclohexane to give 1.7 g (61% yield) of white crystals: mp 106–108 °C; NMR ($CDCl_3$) δ 0.8–2.3 (m, 7 H), 1.0 (br s, 3 H, CH_3), 5.7 (m, 1 H, CHODNB), 9.2 (m, 3 H, Ar).

Anal. Calcd. for $C_{14}H_{14}N_2O_6$: C, 54.90; H, 4.58. Found: C, 54.78; H, 4.56.

***anti*-6-Methyl-*exo*-2-bicyclo[3.1.0]hexyl 3,5-Dinitrobenzoate.** A sample of *anti*-6-methyl-*exo*-2-bicyclo[3.1.0]hexanol (0.40 g, 3.6 mmol), separated from the aluminum isopropoxide equilibration mixture by GLC as described earlier, was reacted with 1.0 g (4.3 mmol) of 3,5-dinitrobenzoyl chloride in 10 mL of dry pyridine at 0 °C for 4 h. The crude product obtained after workup was recrystallized from 20 mL of methylcyclohexane to obtain 0.50 g (59% yield) of light yellow crystals: mp 79–82 °C; NMR ($CDCl_3$) δ 0.5 (m, 1 H, cyclopropyl), 0.9–2.0 (m, 6 H), 1.0 (d, J = 6 Hz, 3 H, CH_3), 5.5 (d, J = 4 Hz, 1 H, CHODNB), 9.3 (m, 3 H, Ar).

Anal. Calcd for $C_{14}H_{14}N_2O_6$: C, 54.90; H, 4.58. Found: C, 54.75; H, 4.67.

Kinetic Procedures. The 80 volumn % aqueous acetone solvent, kinetic method, and controls for possible ion-pair return with rearrangement were similar to those reported earlier.[5] No ion-pair return with rearrangement was observed for any of the 3,5-dinitrobenzoates.

Hydrolysis Products from the *anti*-6-Methyl-2-bicyclo-[3.1.0]hexyl 3,5-Dinitrobenzoates. As an example of the usual procedure, approximately 0.10 g of the 3,5-dinitrobenzoate and 0.10 g of calcium carbonate in 5 mL of 80% aqueous acetone was sealed in a Pyrex ampule and heated at 80 °C for 5 half-lives for acid production. The ampule was then opened and the contents poured into 50 mL of ether. The ether solution was washed with three 10-mL portions of saturated aqueous NaCl and dried over $MgSO_4$. Most of the ether solvent was removed by careful distillation through a fractionating column filled with glass beads, and the product composition was determined by using a combination of GLC and NMR techniques. On a 47-m Carbowax 20M glass capillary column the 1-(cyclopenten-3-yl)ethanol and *anti*-6-methyl-*exo*-2-bicyclo[3.1.0]hexanol products were well resolved. However, *anti*-6-methyl-*endo*-2-bicyclo[3.1.0]hexanol and *trans*-2-methylcyclohex-3-en-1-ol were eluted together. Thus, ^1H NMR integration data for the total vinylic proton absorptions and the endo and exo alcohol two-proton absorptions had to be combined with the GLC data to enable complete analysis of the reaction mixture to be made. A control experiment with the anti-endo alcohol, the most reactive of the products, showed that it was stable under the reaction conditions.

Perchloric acid in acetic acid catalyzed rearrangement of a sample of the anti-endo alcohol followed by lithium aluminum hydride in ether reduction[5] gave a 60:40 mixture of the 1-(cyclopenten-3-yl)ethanol and *trans*-2-methylcyclohex-3-en-1-ol products that could be conveniently separated on a 3-nitro-3-methylpimelonitrile column. The identification of the *trans*-2-methylcyclohex-3-en-1-ol was made by comparing its ^1H NMR and IR spectra with the spectra of a known sample provided by Professor B. Rickborn.[8] The 1-(cyclopenten-3-yl)ethanol was identified by independent synthesis as described below.

1-(Cyclopenten-3-yl)ethanol. A highly reactive magnesium powder[9] was prepared from 30 g (0.32 mol) of $MgCl_2$ and 25 g (0.64 mol) of potassium metal in 200 mL of dry THF. This was treated at −78 °C while stirring by dropwise addition of 30 g (0.29 mol) of 3-chlorocyclopentene[10] over a period of 2 h. Then 13 g (0.30 mol) of acetaldehyde was added at −78 °C over a period of 15 min. After allowing the mixture to stir overnight at room temperature, it was worked up and distilled to give 20 g of a light yellow liquid, bp 60–69 °C (15 mm), which consisted of approx-

(8) Staroscik, J.; Rickborn, B. *J. Am. Chem. Soc.* **1971**, *93*, 3046.
(9) Chapman, O. L.; Mattes, K. C.; Sheridan, R. S.; Klun, J. A. *J. Am. Chem. Soc.* **1978**, *100*, 4878.
(10) Alder, K.; Flock, F. H. *Chem. Ber.* **1956**, *89*, 1732.

imately a 60:40 mixture of the desired 1-(cyclopenten-3-yl)ethanol and the coupling product 3-(cyclopenten-3-yl)cyclopentene. About 3 g of the product mixture was chromatographed on a 2 × 15 cm activity grade 3 alumina column using pentane and ether. The alcohol-containing fraction was dried and distilled; bp 81–82 °C (32 mm). GLC analysis on a 46-m Carbowax 20M glass capillary column showed the material was a 65:35 mixture of diastereomers: NMR (CCl_4) δ 1.1 (d, J = 6 Hz, 3 H, CH_3), 1.3–2.9 (m, 5 H), 3.2 (s, 1 H, OH), 3.5 (quintet, J = 6 Hz, 1 H, CHOH), 5.4–5.8 (m, 2 H, vinylic).

Anal. Calcd. for $C_7H_{12}O$: C, 75.00; H, 10.71 Found: C, 74.78; H, 10.69.

Samples of the 1-(cyclopenten-3-yl)ethanol diastereomers were collected from a 20% Carbowax 20M column. NMR analysis showed that they have identical absorptions except in the vinylic region. For the major product, NMR δ (CCl_4) 5.5 and 5.7 (a pair of symmetrical multiplets); for the minor product, NMR δ (CCl_4) 5.7 ppm (a singlet). The major product was identical with the material obtained from hydrolysis of the *anti*-6-methyl-2-bicyclo[3.1.0]hexyl 3,5-dinitrobenzoates. Thus, it was assigned as being the (*RR*)(*SS*) isomer and the minor product was assigned as being the (*RS*)(*SR*) isomer.

Hydrolysis Products from the *anti*-9-Methyl-2-bicyclo[6.1.0]nonyl 3,5-Dinitrobenzoates. The hydrolysis products in 80% aqueous acetone at 80 °C were obtained by following a similar procedure to that described above for the 2-bicyclo[3.1.0]hexyl system, and the product compositions were determined by using a combination of 47-m Carbowax 20M glass capillary column GLC and ^1H NMR techniques. A control experiment with the anti-endo alcohol, the most reactive of the various product alcohols, showed that it was stable under the reaction conditions.

Of the three minor hydrolysis products obtained from the anti-endo 3,5-dinitrobenzoate, the one that was formed in about 3% yield has an identical GLC retention time as one of the diastereomeric 1-(cycloocten-3-yl)ethanols prepared independently as described below. The other two, present in about equal amounts, have similar GLC retention times as those of the other C_{10} alcohols encountered in this study. However, they could not be isolated in sufficient quantities for identification.[11]

The sole minor product (2% yield) from hydrolysis of the anti-exo 3,5-dinitrobenzoate had the same GLC retention time as the major product (95% yield) obtained from perchloric acid in acetic acid catalyzed rearrangement of the anti-exo alcohol followed by lithium aluminum hydride in ether reduction of the acetates formed. On the basis of its spectra and from mechanistic expectations, this has been tentatively identified as *trans*-8-hydroxy-*cis*-9-methyl-*trans*-bicyclo[5.2.0]nonane: NMR (CCl_4) δ 1.1 (d, J = 7 Hz, 3 H, CH_3), 1.1–2.1 (m, 13 H), 1.7 (s, 1 H, OH), 3.1 (t, J = 7 Hz, 1 H, CHOH). A precise molecular weight was determined by mass spectrometry. Calcd for $C_{10}H_{18}O$: 154.1358. Found: 154.1375.

1-(Cycloocten-3-yl)ethanol. Following an analogous procedure to that described above for preparing 1-(cyclopenten-3-yl)ethanol but starting with 3-chlorocycloocteene,[12] a 60:40 mixture of two diastereomeric 1-(cycloocten-3-yl)ethanols together with some 3-(cycloocten-3-yl)cycloocteene coupling product was obtained. The major isomer had the same GLC retention time as that of one of the minor hydrolysis products of *anti*-9-methyl-*endo*-2-bicyclo[6.1.0]nonyl 3,5-dinitrobenzoate. A sample of the 1-(cycloocten-3-yl)ethanol mixture was collected by GLC and a precise molecular weight determined by mass spectrometry. Calcd for $C_{10}H_{18}O$: 154.1358. Found: 154.1354. For the major product, NMR (CCl_4) δ 1.1 (d, J = 6 Hz, 3 H, CH_3), 1.0–2.6 (m, 11 H), 1.6 (s, 1 H, OH), 3.5 (quintet, J = 6 Hz, 1 H, CHOH), 5.0–5.7 (m, 2 H, vinylic); for the minor product, NMR (CCl_4) 1.1 (d, J = 6 Hz, 3 H, CH_3), 1.0–2.6 (m, 11 H), 1.5 (s, 1 H, OH), 3.6 (quintet, J = 6 Hz, 1 H, CHOH), 5.2–5.9 ppm (m, 2 H, vinylic).

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Registry No. (±)-**5**, 85249-33-8; (±)-**5** 3,5-DNB, 85203-30-1; (±)-**6**, 85249-34-9; (±)-**6** 3,5-DNB, 85249-35-0; (±)-**7**, 85203-31-2; (±)-**7** 3,5-DNB, 85203-32-3; (±)-**8**, 85203-33-4; (±)-**8** 3,5-DNB, 85203-34-5; (±)-**12**, 85203-35-6; (±)-*anti*-6-methyl-2-bicyclo[3.1.0]hexanone, 85249-36-1; bicyclo[6.1.0]nonan-2-one, 29800-55-3; (±)-cycloocten-3-ol, 62249-35-8; 1,1-diiodoethane, 594-02-5; (±)-*syn*-9-methyl-2-bicyclo[6.1.0]nonanone, 85249-37-2; (±)-*anti*-9-methyl-2-bicyclo[6.1.0]nonanone, 85249-38-3; (±)-*syn*-9-methyl-*endo*-2-bicyclo[6.1.0]nonanol, 85249-39-4; (±)-*syn*-6-methyl-*endo*-2-bicyclo[3.1.0]hexanol, 85203-36-7; (±)-cyclopenten-3-ol, 62894-08-0; (±)-*syn*-6-methyl-*exo*-2-bicyclo[3.1.0]-hexanol, 85203-37-8; (±)-3-chlorocyclopentene, 62894-09-1; acetaldehyde, 75-07-0; 3-(cyclopenten-3-yl)cyclopentene, 2690-18-8; (±)-(*R**,*S**)-1-(cyclopenten-3-yl)ethanol, 85203-38-9; (±)-*trans*-8-hydroxy-*cis*-9-methyl-*trans*-bicyclo[5.2.0]nonane, 85203-39-0; (±)-(*R**,*R**)-1-(cycloocten-3-yl)ethanol, 85203-40-3; (±)-(*R**,*S**)-1-(cycloocten-3-yl)ethanol, 85203-41-4; (±)-3-chlorocycloocteene, 85249-40-7; (±)-*syn*-9-methyl-*exo*-2-bicyclo[6.1.0]nonanol, 85249-41-8.

(11) For information concerning further rearrangements of 2-bicyclo[6.1.0]nonyl cations, see: Olah, G. A.; Prakash, G. R. S.; Rawdah, T. N. *J. Org. Chem.* **1980**, *45*, 965.

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Synthesis of the Carbapenam System from Glutamic Acid and Acetoacetic Acid Derivatives[1]

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A synthesis of carbapenam-3-carboxylates is described. Ethyl pyroglutamate was converted into the corresponding thioamide **6** which was subjected to an alkylative sulfide contraction with ethyl 2-bromoacetoacetate. The resulting enamino keto ester **7** was hydrogenated to give, after appropriate manipulations with protecting groups, the two diastereoisomeric 2-[2-(*p*-nitrobenzyloxycarbonyl)-5-pyrrolidinyl]butanoic acids **22a** and **22b**. Dehydration with 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride afforded the *p*-nitrobenzyl (±)-6β-ethylcarbapenam-3-carboxylate **25a** and its 6α epimer **25b**.

The discovery of the highly potent and broad-spectrum antibiotic thienamycin **1**[2] (Chart I) was followed by the isolation of other antibiotics deriving from the carbapenem-3-carboxylic acid **2** and bearing alkyl or hydroxyalkyl

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