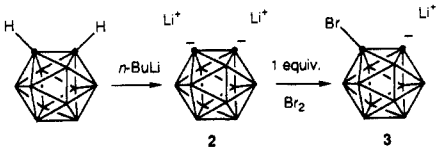
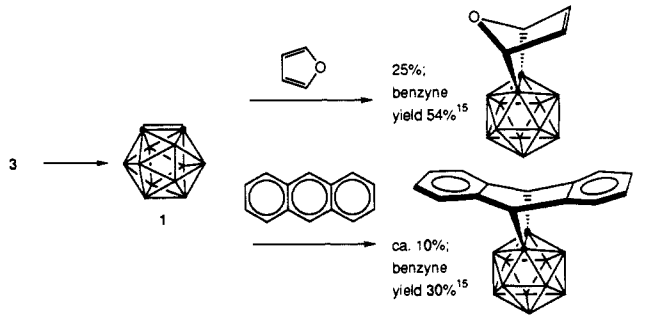
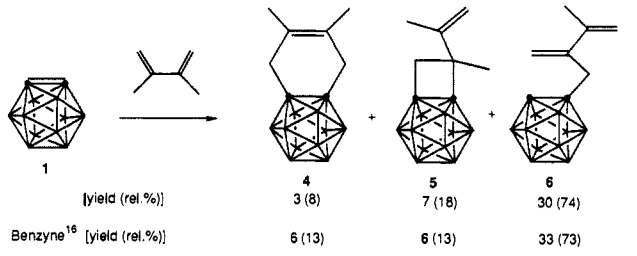
3 owes its relative stability to the presence of the negative charge on a carborane carbon (pK_a = 19-23)[12] and to the length of the carbon-carbon bond, estimated at 1.634 Å in *o*-carborane itself.[13]



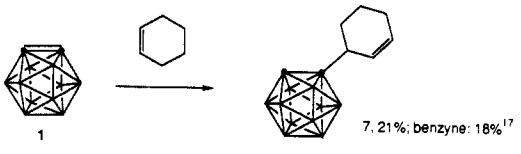
Warming 3 in the presence of dienes to 35 °C leads to products in which 1 has been trapped in Diels-Alder fashion.[14]



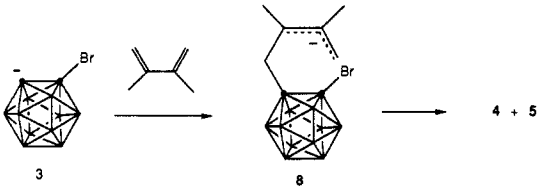
An acylic diene, 2,3-dimethyl-1,3-butadiene, gives three products, **4** (4 + 2 reaction), **5** (2 + 2 reaction), and **6** (ene reaction), all of which have equivalents in the related chemistry of benzyne.[16]



The relative yields of the three kinds of products are comparable for 1 and benzyne. Ene product dominates the reactions of both 1 and benzyne, although for 1 the 2 + 2 cycloaddition is favored somewhat over 2 + 4 addition. Simple alkenes do not give 2 + 2 addition, however. As for benzyne,[17] the product of the ene reaction, 7, is the sole isolable product from reaction with cyclohexene.



We attribute all the reactions described here to 1. Are there not other possible mechanistic explanations? Might not 2 or 3 be involved, for example? Dianion 2 can be eliminated by a simple control experiment. No products are isolated if the addition of bromine is eliminated from the reaction sequence. The bromo anion 3 poses a more difficult problem. One can imagine stepwise processes in which the 2 + 2 and 2 + 4 products are generated by an initial formation of an allyl anion (8), which then displaces bromine from the cage.[18]



This mechanism suffers a number of implausibilities. The first step must be substantially endothermic as the pK_a of *o*-carborane is 19-23[12] whereas pK_a's of simple allyl compounds are ca. 40.[19] Moreover, nucleophiles do not react with bromo carboranes to displace bromide and form an alkyl carborane. The formations of the ene products 6 and 7 are even harder to rationalize using 3 as the active ingredient. We think these reactions are best described in terms of the new reactive intermediate 1.[20]

Supplementary Material Available: Experimental details of the trapping of 1,2-dehydro-*o*-carborane with furan and with anthracene, isolation of the Diels-Alder adduct in each case, and reaction of 1,2-dehydro-*o*-carborane with 2,3-dimethyl-1,3-butadiene and with cyclohexene (4 pages). Ordering information is given on any current masthead page.

(11) Reference 8, pp 43-44.
(12) Shatenstein, A. I.; Zakharkin, L. I.; Petrov, E. S.; Yakovleva, E. A.; Yakoshin, F. S.; Vokmirovich, Z.; Isavera, G. G.; Kalinin, V. N. *J. Organomet. Chem.* **1970**, *23*, 313.
(13) Ott, J. J.; Gimarc, B. M. *J. Comput. Chem.* **1986**, *7*, 673.
(14) All new compounds reported here have been characterized spectroscopically. Elemental analyses have been obtained or precise masses determined by mass spectrometry.
(15) Wittig, G.; Hoffmann, R. W. *Chem. Ber.* **1962**, *95*, 2718.
(16) Wittig, G.; Dürr, H. *Justus Liebigs Ann. Chem.* **1964**, *672*, 55. For reactions of benzyne with other dienes, see: DeCamp, M. R.; Levin, R. H.; Jones, M., Jr. *Tetrahedron Lett.* **1974**, 3575. Jones, M., Jr.; Levin, R. H. *J. Am. Chem. Soc.* **1969**, *91*, 6411.
(17) Reference 8 reports a personal communication from L. Friedman to the effect that cyclohexene does yield a 2 + 2 adduct (p 239, ref 20a), but neither earlier nor later workers find such a product. See ref 8 and, especially, the following reference, by Ahlgren and Akerman, who explicitly discuss this problem: Ahlgren, G.; Akerman, B. *Tetrahedron Lett.* **1970**, 3047.
(18) Of course direct, front-side displacement is out of the question, but a two-step process in which the allyl anion adds to the cage at the carbon bearing the bromine might give an intermediate that could later expel bromide. Such a process is not known.
(19) Vollhardt, K. P. C. *Organic Chemistry*; Freeman: New York, 1987.
(20) Two referees have suggested a sensible variant of the anion mechanism in which intermediates such as 8 first transfer bromine from the cage carbon to the allyl anion and then close. We have now found that norbornadiene reacts with "1" to give good yields of the product of the homo-Diels-Alder reaction.[21] If the bromo anion were active in this reaction, 3 would have to add to the diene to give, not an allyl anion, but a homoallyl anion. Moreover, the cage structure requires that the transferred bromine appear in an endo position. The final displacement of bromide is no longer possible! The case for 1 is strengthened.
(21) Ghosh, T., unpublished work.

Rearrangement of an Allyl Vinyl Rhenium Complex to a Rhenium Allyl Vinyl Ketone Complex via Two Consecutive Concerted Organometallic Rearrangements

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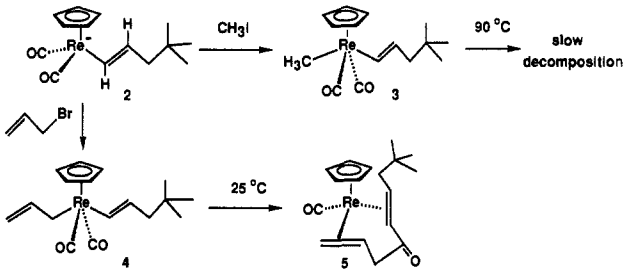
We recently discovered a new synthesis of rhenium carbene complexes $C_5H_5(CO)_2Re{=}CHR$ from the reaction of $(C_5H_5)_2Zr(\eta^2\text{-}COR)Cl$ and $K^+C_5H_5(CO)_2ReH^-$.[1] These rhenium carbene complexes display amphiphilic reactivity: both nucleophiles and electrophiles add to the carbene carbon.[2] Here we report that the vinylrhenium anions obtained by deprotonation of these carbene complexes are alkylated at rhenium by allyl halides to produce (σ-allyl)vinylrhenium intermediates that undergo facile rearrangement to allyl vinyl ketone complexes by two consecutive concerted organometallic rearrangements.

As reported earlier, deprotonation of $C_5H_5(CO)_2Re{=}CHCH_2CH_2CMe_3$ (1) with $KOC(CH_3)_3$ produced the vinyl-

(1) Casey, C. P.; Nagashima, H. *J. Am. Chem. Soc.* **1989**, *111*, 2352.
(2) Casey, C. P.; Vosejpka, P. C.; Askham, F. R. *J. Am. Chem. Soc.*, in press.

0002-7863/90/1512-4083$02.50/0

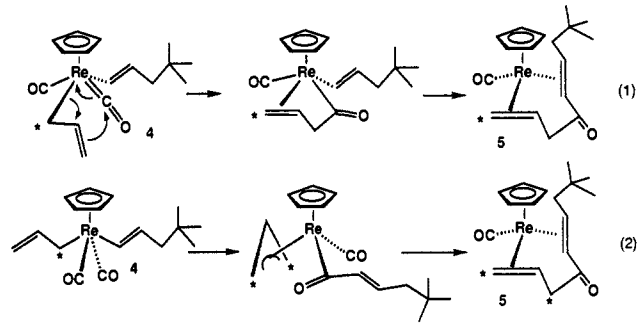
rhenium complex $K^+C_5H_5(CO)_2Re[(E)\text{-}CH{=}CHCH_2CMe_3]^-$ (**2**) as a pale yellow solid.[2] Reaction of **2** with CH_3I resulted in alkylation at rhenium to produce *trans*-$C_5H_5(CO)_2Re(CH_3)[(E)\text{-}CH{=}CHCH_2CMe_3]$ (**3**),[3] which decomposed slowly at 90 °C ($t_{1/2}$ = 1 day).



The reaction of **2** with allyl bromide also led to alkylation at rhenium and formation of an allylvinylrhenium complex, *trans*-$C_5H_5(CO)_2Re(CH_2CH{=}CH_2)[(E)\text{-}CH{=}CHCH_2CMe_3]$ (**4**).[3] Surprisingly, **4** rearranged rapidly ($t_{1/2}$ = 10 min) at room temperature to produce the rhenium complex of an allyl vinyl ketone, $C_5H_5(CO)Re(\eta^2,\eta^2\text{-}CH_2{=}CHCH_2COCH{=}CHCH_2CMe_3)$ (**5**).[3] This transformation involves coupling of CO with both the vinyl and allyl groups and coordination of both carbon–carbon double bonds to rhenium.

The structure of **5** was established spectroscopically[3] and confirmed by X-ray crystallography (Figure 1). An interesting feature of **5** is that the allyl double bond is approximately parallel to the Cp ring while the vinyl double bond is approximately perpendicular to the Cp ring.[4]

The rapid rearrangement of allylrhenium complex **4** stands in stark contrast to the stability of the related methylrhenium complex **3** and strongly suggests that the allyl group assists in the migration to CO. Two possible roles for allyl assistance were initially considered. The allyl group might migrate to CO with allylic inversion and produce an acyl derivative in which the allyl double bond is coordinated to rhenium; this would require inversion of a labeled allyl system (sequence 1). Alternatively, the migration



of a vinyl group to CO might be aided by concerted η^1 to η^3 rearrangement of the allyl ligand; depending on the details of the allyl rearrangement, this might lead to either retention or inversion of an allylic label (sequence 2). Both of these alternatives avoid a high-energy coordinatively unsaturated rhenium intermediate and provide an explanation of the high kinetic reactivity of allylrhenium complex **4**.

Reaction of vinylrhenium anion **2** with $CH_2{=}CHCD_2Cl$ occurred with predominant retention of allylic regiochemistry to

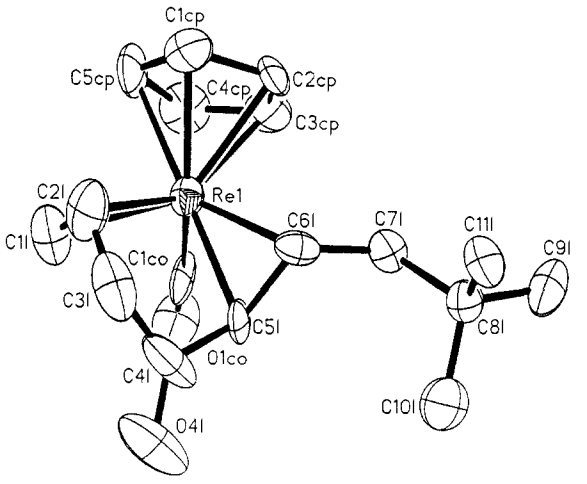
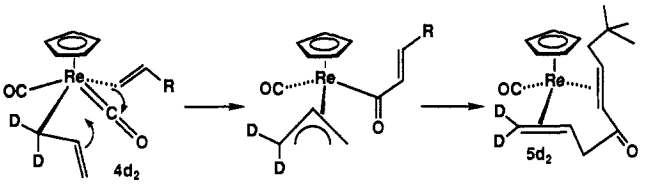


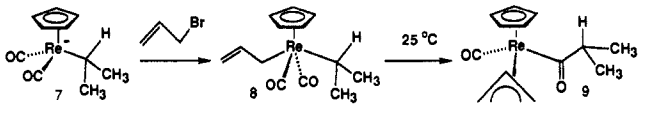
Figure 1. Structure of $C_5H_5(CO)Re(\eta^2,\eta^2\text{-}CH_2{=}CHCH_2COCH{=}CHCH_2CMe_3)$ (**5**).

Scheme I



produce **4d$_2$**.[6] Rearrangement of **4d$_2$** to allyl vinyl ketone complex **5d$_2$** occurred with essentially complete inversion of allylic regiochemistry. This result is consistent with either of the mechanisms mentioned above.

An allylalkylrhenium complex was synthesized to probe the role of the vinyl ligand. Reaction of $LiCuMe_2$ with $C_5H_5(CO)_2Re{=}CHCH_3$ (**6**)[1] produced the isopropylrhenium anion $Li^+C_5H_5(CO)_2ReCH(CH_3)_2^-$ (**7**),[3] which reacted with allyl bromide to give *trans*-$C_5H_5(CO)_2Re(CH_2CH{=}CH_2)[CH(CH_3)_2]$ (**8**).[3] Allyl isopropyl complex **8** rearranged cleanly at room temperature ($t_{1/2}$ = 2 days) to produce the (π-allyl)acylrhenium complex $C_5H_5(CO)Re(\eta^3\text{-}CH_2CHCH_2)[COCH(CH_3)_2]$ (**9**).[3] The transformation of **8** to **9** involves isopropyl migration to CO concerted with η^1- to η^3-allyl rearrangement. In the absence of a vinyl double bond for coordination, no coupling of the acyl and η^3-allyl ligands of **9** occurred.



The results obtained here allow a very detailed description of the mechanism of formation of allyl vinyl ketone complex **5** (Scheme I). Vinyl migration to CO is assisted by η^1- to η^3-allyl rearrangement, which avoids generation of a high-energy coordinatively unsaturated rhenium species. In the allyl rearrangement, the double bond of the allyl swings toward the newly forming acyl ligand to produce an exo η^3-allyl unit. This explains the inversion of regiochemistry of the deuterium label and the conformation of the allyl portion of the complexed ketone. In a second concerted organometallic reaction, the reductive coupling of the η^3-allyl unit and the acyl ligand is assisted by complexation of the vinyl double bond. Once again the concerted nature of this reaction avoids the generation of a high-energy coordinatively unsaturated rhenium intermediate. The complexation of the vinyl double bond can occur most readily from the s-trans configuration of the α,β-unsaturated acyl ligand, which leads directly to the

(3) See supplementary material for full spectral characterization.

(4) The angle between the plane of the Cp centroid, Re, and the centroid of the allylic double bond and the plane of Re and the two carbon atoms of the allylic double bond [C(1L) and C(2L)] is 82.5°. The angle between the plane of the Cp centroid, Re, and the centroid of the vinylic double bond and the plane of Re and the two carbon atoms of the vinylic double bond [C(5L) and C(6L)] is 8.6°. Other examples of "crossed" double bonds coordinated to a transition metal are known.[5]

(5) (a) Rakowsky, M. H.; Woolcock, J. C.; Wright, L. L.; Green, D. B.; Rettig, M. F.; Wing, R. M. *Organometallics* **1987**, *6*, 1211. (b) Crossed double bonds have been theoretically addressed: Albright, T. A.; Hoffmann, R.; Thibeault, J. C.; Thorn, D. L. *J. Am. Chem. Soc.* **1979**, *101*, 3801.

(6) Reaction of **2** with excess $CH_2{=}CHCD_2Cl$ (96% d_2) in CD_3CN led to formation of **4d$_2$** with 91% retention of allylic regiochemistry as determined by ^1H NMR. After evaporation of excess allyl chloride, **4d$_2$** rearranged at room temperature to **5d$_2$** in which 89% of the deuterium was located on the terminal carbon of the allyl unit as determined by ^1H NMR.

parallel-perpendicular conformation of allyl vinyl ketone complex **5**.

Acknowledgment. Support from the National Science Foundation is gratefully acknowledged. P.C.V. thanks BP America for a fellowship.

Supplementary Material Available: Complete spectral characterization of complexes **2-5** and **7-9** and X-ray crystallographic data for **5** (9 pages); table of observed and calculated structure factors for **5** (8 pages). Ordering information is given on any current masthead page.

Novel Strategy for the Construction of the Oligosaccharide Fragment of Calicheamicin $\gamma_{1\alpha}^{I}$. Synthesis of the ABC Skeleton

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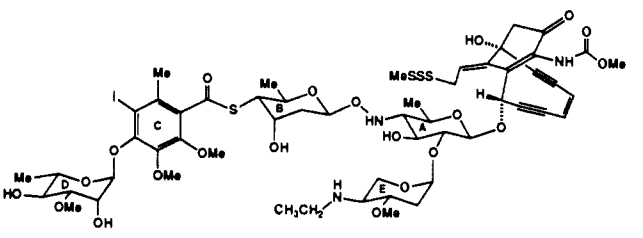
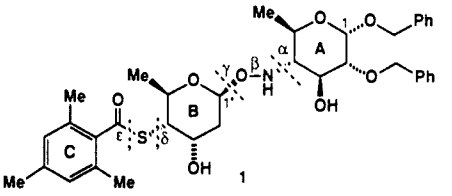
The highly unusual structures of the calicheamicins, of which calicheamicin $\gamma_{1\alpha}^{I}$ is the most prominent member,[1] coupled with their phenomenal biological activity have spurred a flurry of investigations. Whereas most of the synthetic efforts in this area have focused on biological mimics[2] and the bicyclic enediyne skeleton,[3] reports relating to the oligosaccharide fragment have been few.[4] In this communication we describe the first synthetic study that provides solutions to the stereoselective construction of the crucial bonds α-ϵ (see structure **1**) present in the calicheamicin $\gamma_{1\alpha}^{I}$ oligosaccharide, and which delivers the ABC skeleton **1** in optically active form.

On close inspection of the oligosaccharide fragment of calicheamicin $\gamma_{1\alpha}^{I}$, one identifies the following challenging synthetic features (shown in target **1**): (a) the unusual alkoxylamine bond β, linking carbohydrate units A and B via bonds α and γ; (b) the β-stereochemistry of the glycoside bond γ, which, taken in combination with the 2-deoxy nature of saccharide B, offers a unique challenge to synthetic construction; (c) the sulfur bridge, linking carbohydrate unit B with a heavily substituted aromatic system via bonds δ and ϵ; and (d) the α-stereochemistry of the N- and



Calicheamicin $\gamma_{1\alpha}^{I}$



S-bearing stereogenic centers of saccharide units A and B, respectively. Our studies provide clean and rather novel solutions to all the above challenges.

The synthetic design was based on the retrosynthetic disconnections indicated in structure **1**, which led to thiocarbonyldiimidazole ($Im_2C{=}S$) as the sulfur source, *N*-hydroxyphthalimide (HO-NPhth) as the origin of the alkoxyamino group, and precursors to rings A, B, and C as potential starting points. Scheme I outlines the synthetic strategy as designed from the above analysis, and which, in addition to solving the above-mentioned problems, avoids a potentially difficult deoxygenation step to generate the methylene group of the B ring. Thus intermediate I (Scheme I) was designed with an ester group at position 2 to assure the desired stereochemical outcome of the glycosidation reaction (I → II, β-stereochemistry) as well as a means to stereoselectively deliver the sulfur atom at position 4 via a sigmatropic rearrangement (II → III → IV). Intermediate IV was then expected to serve as a precursor to V.

Scheme II outlines the sequence leading to target **1**. Thus, following selective deprotection (DIBAL, 72%) of the diester **2**,[5] epoxidation of **3**[6] with *m*-chloroperoxybenzoic acid (MCPBA) followed by regio- and stereoselective epoxide opening by *m*-chlorobenzoic acid afforded diol **4** in 55% yield. Selective silylation (-Si^{t}BuMe$_2$, 67%) of the 3-hydroxyl group of **4** followed by exposure to Swern conditions resulted in the formation of enone **6** via an oxidation-elimination sequence (88%). 1,2-Reduction of enone **6** using $Zn(BH_4)_2$-NH_4Cl in ether[7] proceeded smoothly from the β-face and was followed by the expected, in situ, ester migration,[8] to afford the desired α-lactol **7** in good yield (ca. 8:1 α:β ratio by ^{1}H NMR). Rapid workup followed by immediate addition of HO-NPhth, Ph_3P, and diisopropyl azodicarboxylate[9] resulted in the formation of the β-glycoside **9**, presumably via intermediate **8** (53% overall yield). While the mechanism of this glycosidation is not fully understood, an S_N2 process may be occurring since the α:β ratio of the resulting glycoside **9** is dependent upon the ratio of starting lactol anomers.[10] Liberation (NH_2NH_2) of the amino group led to hydroxylamine derivative **10**, which was condensed with ketone A[5] under acidic conditions, to afford compound **11**[11] (92% overall yield from **9**). Silylation (-Si^{t}BuMe$_2$, 99%) of **11** gave **12**, which on exposure to DIBAL led to the hydroxy compound **13** (91%). Reaction of **13** with

(1) Lee, M. D.; Dunne, T. S.; Siegel, M. M.; Chang, C. C.; Morton, G. O.; Borders, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 3464. Lee, M. D.; Dunne, T. S.; Chang, C. C.; Ellestad, G. A.; Siegel, M. M.; Morton, G. O.; McGahren, W. J.; Borders, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 3466.

(2) Nicolaou, K. C.; Ogawa, Y.; Zuccarello, G.; Kataoka, H. *J. Am. Chem. Soc.* **1988**, *110*, 7247. Nicolaou, K. C.; Zuccarello, G.; Ogawa, Y.; Schweiger, E. J.; Kumazawa, T. *J. Am. Chem. Soc.* **1988**, *110*, 4866.

(3) Haseltine, J. N.; Danishefsky, S. J.; Schulte, G. *J. Am. Chem. Soc.* **1989**, *110*, 7638. Danishefsky, S. J.; Mantlo, N. B.; Yamashita, D. S.; Schulte, G. *J. Am. Chem. Soc.* **1988**, *110*, 6890. Danishefsky, S. J.; Yamashita, D. S.; Mantlo, N. B. *Tetrahedron Lett.* **1988**, *29*, 4681. Screiber, S. L.; Kiessling, L. L. *Tetrahedron Lett.* **1989**, *30*, 433. Screiber, S. L.; Kiessling, L. L. *J. Am. Chem. Soc.* **1988**, *110*, 631. Magnus, P.; Lewis, R. T. *Tetrahedron Lett.* **1989**, *30*, 1905. Magnus, P.; Lewis, R.; Bennett, F. *J. Chem. Soc., Chem. Commun.* **1989**, 916. Magnus, P.; Lewis, R. T.; Huffman, J. C. *J. Am. Chem. Soc.* **1988**, *110*, 6921. Magnus, P.; Carter, P. A. *J. Am. Chem. Soc.* **1988**, *110*, 1626. Kende, A. S.; Smith, C. A. *Tetrahedron Lett.* **1988**, *29*, 4217. Tomioka, K.; Fujita, H.; Koga, K. *Tetrahedron Lett.* **1989**, *30*, 851.

(4) (a) For the synthesis of the aromatic system of calicheamicin $\gamma_{1\alpha}^{I}$, see: Nicolaou, K. C.; Ebata, T.; Stylianides, N. A.; Groneberg, R. D.; Carrol, P. J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1097. (b) For the synthesis of a methyl-α-glycoside of the thio sugar, see: Van Laak, K.; Scharf, H. D. *Tetrahedron Lett.* **1989**, *30*, 4505. (c) For a synthesis of the esperamycin isopropylamino sugar, see: Golik, J.; Wong, H.; Vyas, D. M.; Doyle, T. W. *Tetrahedron Lett.* **1989**, *30*, 2497. For a synthesis of the calicheamicin $\gamma_{1\alpha}^{I}$ ethylamino sugar, see: Kahne, D.; Yang, D.; Lee, M. D. *Tetrahedron Lett.* **1990**, *31*, 21.

(5) For the synthesis of this compound, see the supplementary material.

(6) All new compounds exhibited satisfactory spectral and analytical and/or exact mass data. Yields refer to spectroscopically and chromatographically homogeneous materials.

(7) In the absence of NH_4Cl, silicon migration from O-3 to O-2 was a competing process following initial 1,2-reduction of the enone.

(8) For an example of 1,2-ester migration in a *cis*-1-*O*-acyl-2-hydroxy sugar, see: Pederson, C.; Fletcher, H. B., Jr. *J. Am. Chem. Soc.* **1960**, *82*, 3215.

(9) Grochowski, E.; Jurczak, J. *Carbohydr. Res.* **1976**, *50*, C15.

(10) For a similar observation involving glycosyl ester formation, see: Smith, A. B., III; Hale, K. J.; Rivero, R. A. *Tetrahedron Lett.* **1986**, *27*, 5813.

(11) While a single geometrical isomer about the oxime bond was obtained, the stereochemistry has not been determined.

0002-7863/90/1512-4085$02.50/0