

Treatment of the lithio enolate of 4 (from 4 and 1.5 equiv of LHMDS as described above) with 1 at -78°C resulted in a single hydroxy lactone, 5a in 62% yield. When KHMDS is used to generate the enolate the isolated yield of 5a increased to 91%. The major hydroxy lactone product, 5a, is presumed to have the cis stereochemistry based on the fact that chiral 2-sulfonyloxaziridines¹⁶ and MoOPH¹⁷ attack the face of the enolate from the sterically least hindered direction.^{18,20}

The chiral synthesis of (+)-kjellmanianone (44% yield, 38% ee), using optically active 2-sulfonyloxaziridines, has previously demonstrated the application of these reagents in the oxidation of enolates of 1,3-dicarbonyl compounds.¹⁹ However, attempts to oxidize the 1,3-dicarbonyl enolates of dibenzoylmethane and ethyl benzoylacetate have been unsuccessful to date.

In summary, direct enolate oxidation (Scheme I) using 2-sulfonyloxaziridine 1 results in better yields of α -hydroxy carbonyl compounds than does O_2 or MoOPH. The fact that 1 is easily prepared, stable, and aprotic makes this oxidant the reagent of choice for direct enolate oxidation, particularly when high stereoselectivity is desired.

Acknowledgment. We thank Dr. Orum Stringer, SmithKline Beckman, for helpful discussion, the National Science Foundation (CHE-8114769), and the Petroleum Research Fund, administered by the American Chemical Society, for generous support of this research.

Registry No. 1, 63160-13-4; 2, 13909-34-7; 3, 90867-72-4; 4, 90867-73-5; 5a, 90867-74-6; 5b, 90867-01-4; PhCH₂COPh, 451-40-1; PhCO(CH₂)₃CH₃, 1009-14-9; PhCH(Me)CO₂Me, 31508-44-8; PhCH₂CO₂Et, 101-97-3; PhCH₂CO₂Me, 101-41-7; PhCOCH(OH)CH₂CH₂CH₃, 20907-23-7; PhCOCOCH₂CH₂CH₃, 20895-66-3; PhC(Me)(OH)CO₂Me, 20731-95-7; PhCH(OH)CO₂Et, 774-40-3; PhCH(OH)CO₂Me, 771-90-4; PhCH(OH)COPh, 119-53-9; PhCOCOPh, 134-81-6; 1,7,7-trimethylbicyclo[2.2.1]heptan-2-one, 76-22-2; 1-hydroxy-18,19-dinorpregn-5-en-20-one, 90867-75-7; dichloroketene, 4591-28-0; 1-[(3,4-methylenedioxy)phenyl]cyclohexene, 90867-76-8; 1,7,7-trimethyl-3-hydroxybicyclo[2.2.1]heptan-2-one, 21488-68-6; 1,17-dihydroxy-18,19-dinorpregn-5-en-20-one, 90867-77-9.

Supplementary Material Available: ¹H NMR, IR, and physical data for adduct 3, lactone 4, and hydroxy lactones 5a,b (1 page). Ordering information is given on any current masthead page.

(13) Prepared by addition of 1-lithio-3,4-(methylenedioxy)benzene to cyclohexanone followed by acid-catalyzed dehydration according to procedures previously described. See: Jeffs, P. W.; Cortese, N. A.; Wolfram, J. J. *Org. Chem.* 1982, 47, 3881.

(14) Finn, J.; Jeffs, P., manuscript in preparation.

(15) Hydroxy lactones 5a,b were isolated by preparative TLC (silica gel), eluting with petroleum ether/ether (1:1).¹⁰

(16) Chiral 2-sulfonyloxaziridines epoxidize alkenes and oxidized sulfides to sulfoxides, approaching in the least hindered direction. See ref 5a,b.

(17) Grieco, P. A.; Ferrino, S.; Vidari, G. *J. Am. Chem. Soc.* 1980, 102, 7586.

(18) Inspection of Dreiding molecular models indicate that 5a would be sterically favored.

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(20) Note Added in Proof: The structure of the major hydroxy lactone was confirmed as 5a by X-ray crystallography.

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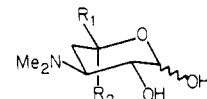
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Received February 22, 1984

Synthesis of 5-*epi*-Desosamine via a Stereoselective Intramolecular *N*-Sulfinyl Diels-Alder Cycloaddition

Summary: 5-*epi*-Desosamine (2) has been synthesized in six steps from diene alcohol 3 through a key intramolecular *N*-sulfinyl dienophile Diels-Alder process which establishes the relative stereochemistry of the three chiral centers of the amino sugar.

Sir: We recently reported a diastereoselective method for synthesis of unsaturated vicinal amino alcohols from 3,6-dihydrothiazine 1-oxides, which are readily prepared by Diels-Alder reactions of *N*-sulfinyl dienophiles.^{1,2} It seemed to us that this methodology should be applicable to construction of amino sugars of various types provided one could employ intramolecular [4 + 2] cycloadditions to control both regiochemistry and stereochemistry. Although we reported the first to examples of intramolecular *N*-sulfinyl Diels-Alder reactions in our initial paper,¹ nothing is currently known about the stereochemistry of the process. Thus, as a means of probing salient stereochemical features of this sort of cycloaddition, a synthetic sequence was explored which was directed at the common amino sugar desosamine 1³ and/or its unnatural C-5 epimer 2.



1, R₁ = Me; R₂ = H
2, R₁ = H; R₂ = Me

The starting (*E,E*)-diene alcohol 3 required for this route was prepared by the method of Corey and Kang.⁴ The dianion generated from triphenylmethylphosphonium bromide (2 equiv of *sec*-butyllithium, ether, -78°C , 2 h) was treated with propylene oxide, followed by crotonaldehyde, affording 3 in 57% yield as one geometric isomer. This alcohol was converted to carbamate 4 with sodium cyanate/trifluoroacetic acid (PhH, room temperature, sealed tube, 80%).⁵ When 4 was treated with thionyl chloride/pyridine (PhMe, 0°C to room temperature) a single Diels-Alder adduct 6 was formed (80%). The structure and stereochemistry of this dihydrothiazine oxide was determined by single-crystal X-ray analysis.

Our rationale for the stereoselectivity in this cycloaddition is shown in Scheme I. This explanation is completely consistent with that offered for two intramolecular imino Diels-Alder reactions⁶ and an "all carbon" cycloaddition⁷ which stereoselectively produced 6/6 fused ring systems containing a chiral center in the connecting chain. The *N*-sulfinyl carbamate derived from 4 can potentially react as the *E* or *Z* isomer. Although *N*-sulfinylaniline⁸

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(2) For reviews of this cycloaddition, see: Kresze, G.; Wucherpfnig, W. *Angew. Chem., Int. Ed. Engl.* 1967, 6, 49. Weinreb, S. M.; Staib, R. R. *Tetrahedron* 1982, 38, 3087.

(3) Previous syntheses of 1: Richardson, A. *J. Chem. Soc.* 1964, 5364. Baer, H. H.; Chiu, C.-W. *Can. J. Chem.* 1974, 52, 122.

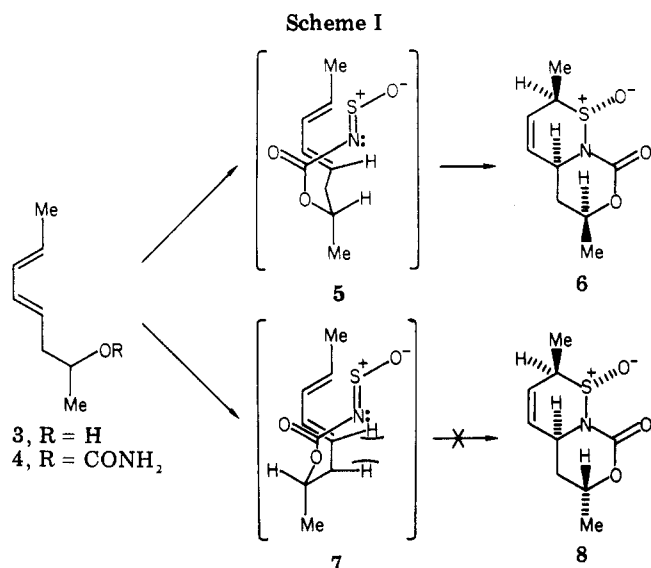
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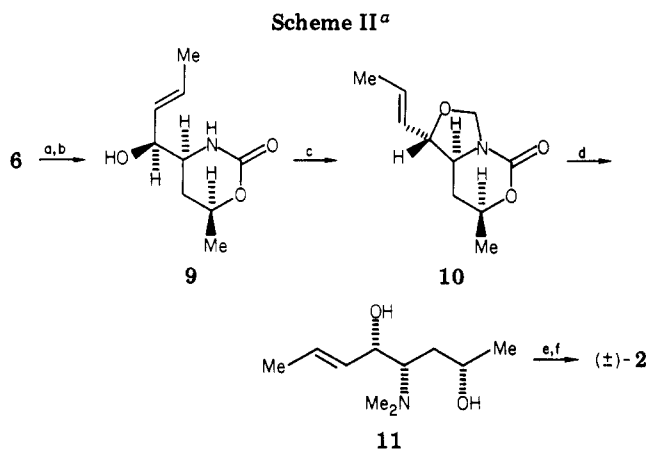
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and *N*-sulfinyl-*p*-toluenesulfonamide⁹ exist as the *Z* isomers, it does appear that *E/Z* isomerization may be quite facile.¹⁰ Nothing has yet been reported concerning the configuration of *N*-sulfinyl carbamates, but it is not unreasonable that such a compound might react preferably in the *E* form. Thus, if the intermediate *N*-sulfinyl carbamate underwent the cycloaddition through a transition state having the carbonyl group endo and the sulfinyl oxygen exo (cf. 5), the observed sulfur stereochemistry would be produced. Furthermore, if the bridging atoms assumed a quasi-boat conformation as shown in 5, with the methyl group quasi-equatorial, product 6 would result. The alternative quasi-chair transition-state conformation 7 which leads to epimeric adduct 8 may be destabilized relative to 5 due to the vicinal hydrogen eclipsing indicated in the drawing.¹¹ As alluded to above, the preference for a transition state like 5 vs. 7 has previously been noted.^{6,7}

Diels-Alder adduct 6 was cleaved (Scheme II) with phenylmagnesium bromide to give an allylic sulfoxide which upon [2,3]-sigmatropic rearrangement and desulfurization of the resulting sulfenate ester yielded allylic alcohol 9 as a *single* stereoisomer (90%) which has the *E*-threo configuration as anticipated from our previous work.¹ A novel two-step sequence was used to convert 9 to the desired *N,N*-dimethylamino compound.¹² Reaction of 9 with paraformaldehyde using a catalytic amount of *p*-TsOH gave 10, which upon reduction with lithium



^a (a) PhMgBr, THF, -50 °C; (b) piperidine/EtOH, reflux, 12 h; (c) (HCHO)_n, catalytic *p*-TsOH, PhH, reflux; (d) LiAlH₄, THF, reflux, 12 h; (e) TFA, CH₂Cl₂; (f) O₃/silica gel, -78 °C; Zn, HOAc.

aluminum hydride afforded amino diol 11 (68% from 9).

Oxidative cleavage of the double bond of 11 proved considerably more difficult than first envisioned. A number of standard methods were attempted unsuccessfully on 11 and various protected derivatives. Finally, it was discovered that dry silica gel ozonization¹³ of the trifluoroacetate salt of amino diol 11 led to (±)-5-epidesosamine (2) in 70% yield. This material had spectral data similar but different from naturally derived desosamine (1).¹⁴

Acknowledgment. We are grateful to the National Science Foundation for financial support (CHE-81-00132) and to the John Simon Guggenheim Memorial Foundation for a fellowship to S.M.W. We also thank R. Garigipati for valuable advice.

Registry No. 2, 91126-84-0; 3, 91126-85-1; 4, 91126-86-2; 6, 91126-87-3; 9, 91126-88-4; 10, 91126-89-5; 11, 91126-90-8; 11-F₃CCO₂H, 91199-10-9; (methyl)triphenylphosphonium bromide, 1779-49-3; propylene oxide, 75-56-9; crotonaldehyde, 4170-30-3; thionyl chloride, 7719-09-7; paraformaldehyde, 30525-89-4.

Supplementary Material Available: Experimental and spectroscopic details for all new compounds; tables of X-ray data for compound 6 (13 pages). Ordering information is given on any current masthead page.

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(11) Molecular mechanics calculations on a closely related "all carbon" systems indicate that a conformation like 5 is ~3 kcal/mol more stable than 7, and that this eclipsing is the primary destabilizing effect. We thank T. Stouch and Professor P. Jurs for these calculations.

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Received March 20, 1984