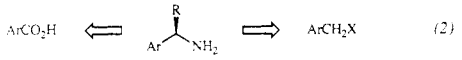
mentation, but the general route that evolved is shown in Scheme III. The oxazolidinone nucleus of **6** is exceptionally robust, but yielded to hydrolysis when subjected to Gassman's recipe[10] for unsolvated KOH in ether (6 equiv of KO-*t*-Bu, 2 equiv of H_2O, ether, 4–24 h). The single exception was **6f**, which afforded only cinnamic acid derivatives under a variety of acidic and basic hydrolysis conditions.[11] Oxidative cleavage of the amino alcohols **7a–e** to the imines **8a–e** occurred in excellent yield ($Pb(OAc)_4$, 2:1 CH_2Cl_2–MeOH, 0 °C, 2 min), at which point hydrolysis to the liberated primary amines **9a–e** was routine (HCl, EtOH, 6–24 h). Table II details the yields for the conversion of **6a–e** to **9a–e**.

The absolute configuration and enantiomeric excess (ee) of the amines **9a–e** were determined by Pirkle analysis of the corresponding naphthamides.[8] The results are summarized in Table II. In all cases, the absolute configuration was *R*, although the percent of the products was diminished from the percent of the oxazolidinones **6a–d**. Thus, there appears to be some racemization in the conversion **6** to **9** for some of the substrates studied. The lead tetraacetate oxidation step is most likely the culprit, since cyclization of **7b** and **7e** with phosgene afforded **6b** and **6e** of undiminished diastereomeric excess.

The starting *N*-benzyloxazolidinones **5** may be prepared in either of two ways. Most obviously, the parent oxazolidinone may be alkylated with the appropriate benzyl halide (KH, THF, BnX, cat. Bu_4NI). Alternatively, **5** is available by cyclization of the corresponding *N*-benzylvalinol derivatives, which are in turn prepared by $LiAlH_4$ reduction of benzoyl valines.[12]

Conclusion

We have reported the first examples of acyclic stereoselection in the alkylation of chiral dipole stabilized organolithiums. A comparison of 1,5- vs 1,3-induction revealed significantly greater selectivity for the latter. The successful conversion of oxazolidinones **5** to chiral primary amines **9** constitutes a new method for the synthesis of primary amines by asymmetric alkylation. The resultant overall transformations, illustrated in eq 2, convert benzyl halides or carboxylic acids into chiral primary amines by a self-immolative chirality transfer from valine.



(2)

Supplementary Material Available: Experimental details for the synthesis and characterization of all compounds (7 pages). Ordering information is given on any current masthead page.

(10) Gassman, P. G.; Hodgson, P. K. G.; Balchunis, R. J. *J. Am. Chem. Soc.* **1976**, *98*, 1275–6.

(11) We had intended **6f** to be a precursor of β-tyrosine. For a recent synthesis of a β-tyrosine derivative, and leading references to the occurence of this rare amino acid in peptide antibiotics, see: Grieco, P. A.; Hon, Y. S.; Perez-Medrano, A. *J. Am. Chem. Soc.* **1988**, *110*, 1630–1631.

(12) For example, the reduction of *N*-benzoylvaline to *N*-benzylvalinol is achieved in 76% yield: Smith, G. A.; Hart, G.; Chemburkar, S.; Goicoechea-Pappas, M.; Rein, K.; Anklekar, T. V.; Smith, A. L.; Gawley, R. E. *Organic Syntheses*; Wiley: New York, 1989; Collect. Vol. VII, in press.

Inside–Outside Stereoisomerism. 4.† An Unusual Rearrangement of the *trans*-Bicyclo[5.3.1]undecan-11-yl Radical

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Summary: Deoxygenation of 11-hydroxy-*trans*-bicyclo[5.3.1]undecane leads to the formation of both the trans- and the cis-bridged hydrocarbons. The mechanistic studies described herein are consistent with the formation of *cis*-bicyclo[5.3.1]undecane via a sequence of transannular hydrogen atom abstractions leading to the formation of the bicyclo[5.3.1]undecan-1-yl tertiary radical, which, on reduction with tri-*n*-butyltin hydride, leads to the formation of the cis-fused hydrocarbon.

Sir: The intramolecular dioxenone photocycloaddition reaction provides unique synthetic approaches for the preparation of carbocyclic structures with unusual structural and chemical properties.[2] We have recently reported the application of this methodology to the synthesis of trans or "inside–outside"[3] bicyclo[5.3.1]undecan-11-one, **1** (Scheme I), which is ca. 10 kcal/mol less stable than the corresponding cis isomer, **2**.[2a] In an effort to prepare the parent hydrocarbon, *trans*-bicyclo[5.3.1]undecane, **6**, the deoxygenation of **1** was examined. We report herein that treatment of the *trans*-bicyclo[5.3.1]undecan-11-yl xanthate, **4**, with a stoichiometric amount of tri-*n*-butyltin hydride[4] leads to the predominant formation of *cis*-bicyclo[5.3.1]undecane, **5**. Our preliminary studies directed toward the elucidation of the mechanism of this unusual stereochemical isomerization are outlined below.

While **1** was inert to standard thioketalization conditions and even to reduction with sodium borohydride (2 equiv, ethanol, 25 °C), treatment with lithium aluminum hydride (2 equiv, tetrahydrofuran, 25 °C, 83%) led to the formation of 11-hydroxy-*trans*-bicyclo[5.3.1]undecane, whose structure was assigned as the α-epimer, **3**, the result of hydride

†Dedicated to Professor Josef Fried on the occasion of his 75th birthday. For the previous paper in this series, see: Winkler, J.; Hey, J.; Williard, P. *Tetrahedron Lett.* **1988**, 4691.

(1) Recipient of the American Cyanamid Young Faculty Award (1989–1992) and a National Institutes of Health Research Career Development Award (1988–1993). Fellow of the Alfred P. Sloan Foundation (1987–1989).

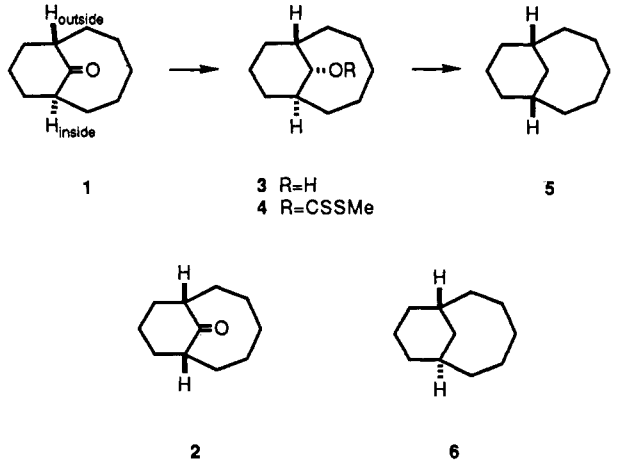
(2) For examples of the use of the intramolecular dioxenone photocycloaddition reaction, see: (a) Winkler, J.; Hey, J.; Williard, P. *J. Am. Chem. Soc.* **1986**, *108*, 6425. (b) Winkler, J.; Hey, J.; Darling, S. *Tetrahedron Lett.* **1986**, 5959. (c) Winkler, J.; Hey, J.; Hannon, F.; Williard, P. *Heterocycles* **1987**, *25*, 55. (d) Henegar, K.; Winkler, J. *Tetrahedron Lett.* **1987**, 1051. (e) Winkler, J.; Henegar, K.; Williard, P. *J. Am. Chem. Soc.* **1987**, *109*, 2850. (f) Winkler, J.; Hey, J.; Williard, P. *Tetrahedron Lett.* **1988**, 4691. For the intermolecular photocycloaddition of dioxenones, see: Baldwin, S.; Wilkinson, J. *J. Am. Chem. Soc.* **1980**, *102*, 3634.

(3) For a recent review, see: Alder, R. *Acc. Chem. Res.* **1983**, *16*, 321. For other syntheses of inside-outside bicycloalkanes, see: (a) References 2e and 2f. (b) Funk, R.; Olmstead, T.; Parvez, M. *J. Am. Chem. Soc.* **1988**, *110*, 3298. (c) McMurry, J.; Hodge, C. *J. Am. Chem. Soc.* **1984**, *106*, 6450. (d) Gassman, P. G.; Hoye, R. *J. Am. Chem. Soc.* **1981**, *103*, 215, 2496, 2498. (e) Haines, A.; Harntiang, P. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2577. (f) Gassman, P.; Thummel, R. *J. Am. Chem. Soc.* **1972**, *94*, 7183. (g) Park, C.; Simmons, J. *J. Am. Chem. Soc.* **1972**, *94*, 7184.

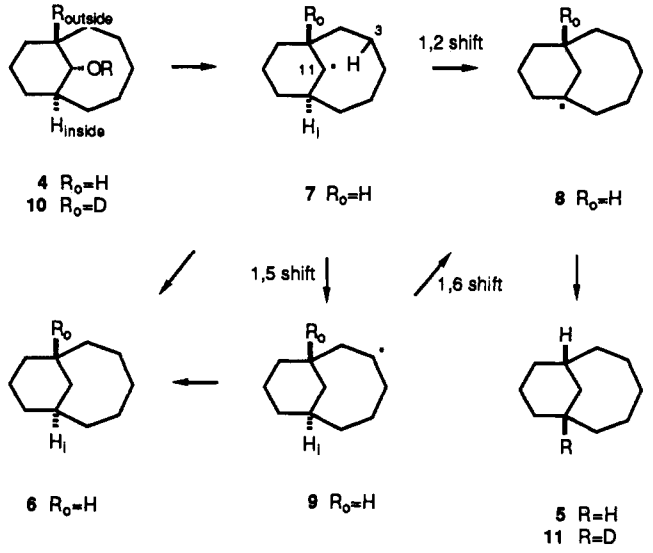
(4) Barton, D.; McCombie, S. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.

0022-3263/89/1954-3004$01.50/0

Scheme I



Scheme II



attack from the less hindered β-face of 1.[5] Generation of the xanthate 4 of 3 (2 equiv of NaH, 6 equiv of CS_2, 6 equiv of MeI, tetrahydrofuran, 75%), followed by treatment with tri-*n*-butyltin hydride (0.01 M in benzene, 1.1 equiv of stannane), led to the formation of a 5:1 mixture of isomeric hydrocarbons in 53% yield, which could be separated by preparative gas chromatography (OV-101, 100 °C). The seven-line ^{13}C spectrum (16.06, 25.51, 28.25, 31.34, 31.58, 31.72, 32.83) of the major product was identical with that previously reported for the symmetrical *cis*-bicyclo[5.3.1]undecane, **5**,[6] while the eleven-line spectrum (24.90, 25.11, 28.70, 29.14, 29.61, 30.71, 32.21, 32.80, 33.52, 33.80, 33.92) of the minor product was consistent with *trans*-bicyclo[5.3.1]undecane, **6**, which, unlike *cis*-**5**, contains neither a plane nor an axis of symmetry.

The effect of stannane concentration on the cis/trans product ratio (1.1 equiv, 5.4/1; 5 equiv, 1/1; 10 equiv, 1/2) is consistent with the intermediacy of the *trans*-bicyclo[5.3.1]undecan-11-yl radical, which can partition between reduction to *trans*-**6**, or rearrangement, followed by reduction, leading to *cis*-**5**. With high stannane concentration (10 equiv), reduction of the *trans*-bicyclo[5.3.1]undecan-11-yl radical is faster than rearrangement, and **6** is the major product. Alternatively, with only stoichiometric stannane, rearrangement is faster than reduction and the major product is *cis*-**5**. A mechanistic scheme incorporating these different pathways is outlined in Scheme II.

The positions of the radical centers which are generated in the course of the rearrangement of **7** to **8** could be determined by establishing the location of the deuterium in the cis- and trans-monodeuterated bicyclo[5.3.1]undecanes formed on reduction of **4** with *n*-Bu_3SnD. The isolation of **11** as only cis-bridged deuterated product[7] is consistent with the intermediacy of the tertiary radical **8** in the formation of *cis*-**5**. The coupling of a single resonance (29.14 ppm) to deuterium in the ^{13}C spectrum of the trans hydrocarbon formed in the reduction of **4** with *n*-Bu_3SnD was consistent with the presence of a unique trans-bridged deuterated product (vide infra).

Two different pathways for the isomerization of **7** to **8**, the key step leading to the formation of *cis*-**5**, are outlined in Scheme II. While a 1,2-shift of the "inside" hydrogen atom would be the most direct method for the conversion of **7** to **8**, it is a step for which there is no precedent in organic chemistry. Alternatively, the isomerization of **7** to **8** could proceed via a combination of 1,5- and 1,6-transannular hydrogen atom abstractions, steps for which there exists ample precedent,[8] particularly in medium-ring systems.[9] Transannular hydrogen atom abstraction by the C-11 radical, i.e., of the hydrogen at C-3, would generate **9**, which could then abstract one of the bridgehead hydrogens, presumably the "inside" position, to generate the teritary radical **8**. To determine which of the two bridgehead hydrogen atoms (H_{inside} or $R_{outside}$) is abstracted from **7** to give **8**, the reduction and isomerization of xanthate **10**,[10] labeled with deuterium at the "outside" position (R_o) was examined. The formation of **11**, as the only monodeuterated *cis*-bicyclo[5.3.1]undecane formed on deoxygenation of **10**, is consistent with the exclusive migration of the "inside" bridgehead hydrogen in the course of the rearrangement.

(5) The stereochemical assignment was confirmed by examination of the ^1H NMR spectrum of **3**. Observed for H_{C-11}: δ 3.59 (J = 2.8, 9.3 Hz). Coupling constants for the α- and β-alcohols were calculated to be 1.6, 8.3 Hz and 0.6, 3.6 Hz, respectively, based on conformations obtained for **3** and its C-11 epimer by the Gajewski/Gilbert modification of the Allinger MM2 program (No. 395, Quantum Chemistry Program Exchange, Indiana University).

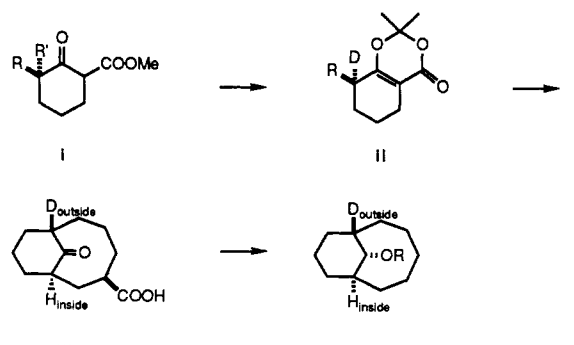
(6) Martin, S.; White, J.; Wagner, R. *J. Org. Chem.* **1982**, *47*, 3191.

(7) The unique resonance (31.72 ppm) coupled to deuterium in the ^{13}C spectrum of **11** was assigned to C-1 (tertiary carbon) by APT (attached proton test).

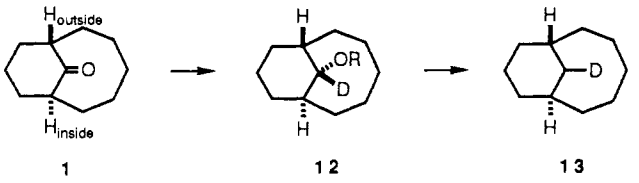
(8) Wentrup, C. *Reactive Molecules: The Neutral Reactive Intermediates in Organic Chemistry*; Wiley: New York, 1984; pp 90–97.

(9) Breslow, R.; Khanna, P. *J. Am. Chem. Soc.* **1976**, *98*, 1297. Fisch, M.; Ourisson, G. *J. Chem. Soc., Chem. Commun.* **1965**, 407. Traynham, J.; Courillon, T. *J. Am. Chem. Soc.* **1965**, *87*, 5806.

(10) The "outside"-deuterated xanthate **10** was prepared from i (R = 4-pentenyl, R′ = H) as outlined below. Deuteration of i, via the corresponding dianion, followed by dioxenone formation, led to the formation of ii (R = 4-pentenyl). Photoaddition and fragmentation according to ref 2a led to the formation of iii. The stereochemical relationships indicated in iii are based on the X-ray structure of the corresponding keto acid in ref 2a. Barton decarboxylation, followed by ketone reduction, and xanthate formation, produced **10**, with deuterium at the "outside" position.



Scheme III



1 12 13

The location of the deuterium in the monodeuterated *trans*-bicyclo[5.3.1]undecane obtained via *n*-Bu_3SnD reduction of **4** could permit the distinction between a sequence of transannular hydrogen atom abstractions and the 1,2-shift as the pathway for the conversion of **7** to **8**. While the presence of deuterium at C-11 in the trans-monodeuterated product would be consistent with both mechanistic possibilities, the absence of deuterium at C-11, i.e., deuteration at any other position, would be consistent only with the series of transannular hydrogen abstractions for the conversion of **7** to **8**, thereby excluding the possibility of a 1,2-shift. To establish whether the deuterium in the trans-monodeuterated product was indeed at C-11, an authentic sample of **13**, the C-11 deuterated trans-bridged hydrocarbon, was prepared as outlined in Scheme III.

Reduction of **1** with lithium aluminum deuteride, followed by treatment of the derived xanthate with 10 equiv of *n*-Bu_3SnH, led, after preparative gas chromatography, to the isolation of the 11-deuterio-*trans*-bicyclo[5.3.1]undecane, **13**. The ^{13}C NMR spectrum of this monodeuterated *trans*-bicyclo[5.3.1]undecane **13** showed a different resonance (33.52 ppm) coupled to deuterium than had been observed in the monodeuterated trans product obtained by reduction of **4** with *n*-Bu_3SnD (29.14 ppm). These preliminary experiments clearly indicate that the rearrangement of **7** to **8** is not a consequence of a 1,2-shift of hydrogen, but instead the result of a sequence of transannular hydrogen atom abstractions which lead to the formation of **8**, and ultimately to the cis product **5**. Further studies directed toward the determination of the precise location of the radical center in the initial rearrangement product, and the establishment of the scope of this unusual rearrangement, are currently under way in our laboratory.

Acknowledgment. We would like to thank Professor Thomas Hoye for stimulating discussions, Professor Stephen Martin for providing an authentic sample of *cis*-bicyclo[5.3.1]undecane, **6**, and Professor David Lynn and Mr. Timothy Logan for invaluable assistance in obtaining the NMR spectral data. Support from the Petroleum Research Fund, administered by the American Chemical Society, the National Institutes of Health (Grants CA40250 and CA45686), the Alfred P. Sloan Foundation, American Cyanamid, Merck, Sharp and Dohme, and Glaxo is gratefully acknowledged. The NMR instruments used were funded in part by the NSF Chemical Instrumentation Program and by the NCI via the University of Chicago Cancer Research Center (Grant CA 14599).

Structure of the Fatty Acid Component of an Antibiotic Cyclodepsipeptide Complex from the Genus *Fusarium*

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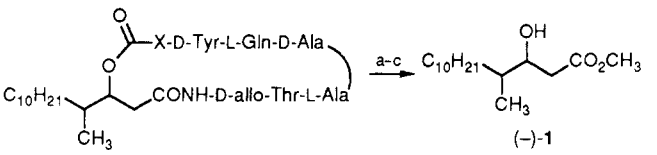
Summary: The fatty acid component of the *Fusarium* cyclodepsipeptide complex CDPC 3510 is (−)-*anti*-3-hydroxy-4-methyltetradecanoic acid. A diastereoselective synthesis of the racemic methyl ester of CDPC 3510 fatty acid is described.

Sir: A recent report by Carr et al.[1] concerning the structure of a novel cyclodepsipeptide complex isolated from several species of the genus *Fusarium* intrigued us in part because a β-hydroxy carboxylic acid obtained by hydrolytic degradation of the complex was postulated to be 3-hydroxy-4-methyltetradecanoic acid. Murai and co-workers[2] have recently shown that the fatty acid unit common to the *Bacillus circulans* cyclodepsipeptide metabolites polypeptin A, permetin A, and BMY-28160 is (−)-*syn*-3-hydroxy-4-methylhexanoic acid; therefore characterization of a structurally similar 3-hydroxy-4-methylalkanoic acid[3] from depsipeptide metabolites of the deuteromycete *Fusarium* could provide a unique opportunity to compare the lipid biosynthesis steps of cyclodepsipeptide anabolism in a prokaryotic organism (*B. circulans*) with that of a eukaryote (*Fusarium sporotrichiodes*). However, the structural characterization of the *Fusarium* depsipeptidic fatty acid was based solely on a mass spectrometric analysis of its methyl ester derivative without the benefit of authentic samples of the syn and anti diastereomers[4] of methyl 3-hydroxy-4-methyltetradecanoate, thus nothing could be deduced concerning the C(3)–C(4) relative stereochemistry of the degradation product.

Scheme I[a]



CDPC 3510: X = L-Leu (60 mol %), L-Ileu (30 mol %), L-Val (10 mol %)

[a] (a) 5 M HCl, 100 °C, 2 h. (b) Diazomethane in ether. (c) Column chromatography (silica gel; 19:1 hexane–ether).

We isolated the three-component cyclodepsipeptide complex, CDPC 3510, from methanol extracts of *F. sporotrichiodes* NRRL 3510 grown on white corn grit medium;

(1) Carr, S. A.; Block, E.; Costello, C. E.; Vesonder, R. F.; Burmeister, H. R. *J. Org. Chem.* **1985**, *50*, 2854.

(2) Murai, A.; Amino, Y.; Ando, T. *J. Antibiot.* **1985**, *38*, 1610.

(3) For additional examples of fungal cyclodepsipeptide metabolites that contain the 3-hydroxy-4-methylalkanoic acid unit, see: (a) Elsworth, J. F.; Grove, J. F. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1795. (b) Grove, J. F. *J. Chem. Soc, Perkin Trans. 1* **1980**, 2878. It should be noted that the fatty acid residues described in these two papers were characterized by mass spectrometric methods and currently remain unassigned with respect to their C(3)–C(4) stereochemistry.

(4) The descriptors "syn" and "anti" are employed here in the sense described in the following: Masamune, S.; Ali, S. A.; Snitman, D. L.; Garvey, D. S. *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 557.

0022-3263/89/1954-3006$01.50/0