Synthesis of Conduramines from *N-tert*-Butoxycarbonylpyrrole†

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Two related synthetic strategies were devised to convert the Diels−Alder adduct **3c** of Boc-pyrrole and *p*-toluenesulfonylacetylene into various racemic and optically pure conduramines. One process consists of the regio- and stereoselective hydroxylation of **3c** to the tri- and dihydroxylated azabicyclo-[2.2.1]heptane derivatives **10b** (Scheme 2) and the exo−endo mixture **13**−**14** (Scheme 3). Anionic fragmentation of **10b** (methylmagnesium bromide) and of the **13**−**14** sulfone mixture (lithium bis-(trimethylsilyl)amide) generated the corresponding tri- and dihydroxylated aminocyclohexenes **17** and **16** (Scheme 3). Compound **17** is an aminocyclitol with a stereochemistry and partial aminotriol sequence identical to that found in neoinosamine. Compound **16** served as a source of the protected and free aminodiols **35b** and **35a** (Scheme 6), which were stereospecifically epoxidized to **36** (Scheme 6) and **40** (Scheme 7). Phenylselenide cleavage of these epoxides provided **37** (Scheme 6) and **41a** (Scheme 7), which after selenoxide cycloelimination and protecting group manipulation were converted into (±)-conduramine C-1 (**39a**, Scheme 6) and the previously unreported, *all-cis*-conduramine D-1 (**43a**, Scheme 7). In a second process, anionic fragmentaion of the bicyclic system is effected prior to introduction of the hydroxyl groups, as exemplified by the high-yielding conversion of the exo−endo mixture of azabicycloheptenes **11** and **12** into the aminocyclohexadiene **15** (Scheme 3). Osmate catalyzed cis-dihydroxylation of the derived bis-Boc derivative **20** (Scheme 4) led stereospecifically to the α-*cis*-diol **21** which was transformed into (±)-conduramine A-1 (**27a**) and its tetraacetyl derivative **27b** via the epoxy compound **24**. On the other hand, peracid oxidation of the diene **15** gave the *β*-epoxide **28** (Scheme 5) which was cleaved to the *trans*-diol **29** with aqueous sulfuric acid. This diol was converted into (±)-conduramine F-1 (**34a**) and its tetraacetyl derivative (**34b**) by a reaction sequence similar to that used for the other conduramine syntheses. Fractional crystallization of the diastereomeric mixture of Michael adducts obtained from (±)-**3c** and (−)-methyl lactate gave (−)-**44a** and (−)-**45a** both in ≥47% yield (Scheme 8). Both the carboxylic acid (+)-**44b** and the primary alcohol (+)-**46** derived from (−)-**44a** were converted into (−)-**3c** with excess methylmagnesium bromide (ca. 40% overall yield). In the same way (−)-**45a** was transformed into optically pure (+)-**3c**. (−)-**3c** and (+)-**3c** were then converted into (−)-conduramine C-1 [(−)-**39a**] and (+)-conduramine D-1 [(+)-**43a**] by procedures identical to those used for the racemic compounds.

Introduction

Conduramines are purely synthetic aminocyclohexen-etriols[1] formally derived from conduritols. (Two conduritols are naturally occurring. See, Balci et al.,[1b] p 3724 and references cited therein.) Some conduramines have significant glycosidase inhibitory activity,[2] but they are of much greater importance as synthetic precursors of amino- and diaminocyclitols,[3] many of which constitute the aglycon portions of the therapeutically useful aminoglycoside antibiotics. In addition, conduramines have been utilized as intermediates in the preparation of azasugars,[4] aminosugars,[5] sphingosines,[6] and narcissus alkaloids.[7] Given the importance of conduramines as synthetic building blocks, it is not surprising that so much effort has been devoted to the development of useful preparative routes to these compounds[3a,e,o,8] and their derivatives.[3d,f−h,j−l,n,4−7,9] Hudlicky et al. (op. cit.) have devised a very effective synthetic strategy which produces either (+)- or (−)-conduramines from a single, optically pure 1-halo-*cis*-2,3-dihydrobenzene-2,3-diol. The

† Dedicated to Dr. Yvon G. Perron, mentor and friend, on the occasion of his 73rd birthday.

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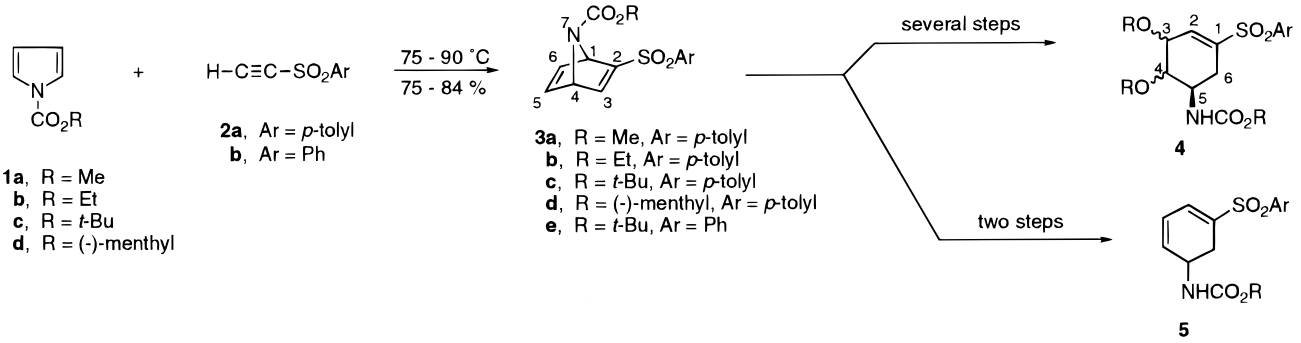
Scheme 1



diols are obtained from the corresponding inexpensive halobenzenes by fermentation with a strain of *Pseudomonas putida*. We were interested in examining a similar strategy whereby the 7-azabicyclo[2.2.1]heptadiene derivative **3** (Scheme 1) might serve as a universal conduramine precursor. The bicyclic system was expected to exert predictable control over the stereochemistry of hydroxylation, after which anionic fragmentation[10] initiated by the sulfonyl group would provide an hydroxylated aminocyclohexene derivative **4** suitable for elaboration to various conduramines. Alternatively, fragmentation of the bicyclic system, after conjugate reduction of the α,β-unsaturated sulfone, would lead to the aminocyclohexadiene derivative **5**, a potential conduramine progenitor in which all the ring carbon atoms are chemically differentiated. If, in addition, **3** could by some means be generated in both enantiopure forms, then it could provide access, in principle, to any desired enantiopure conduramine.

This article gives a full description of the successful utilization of **3c**[11] for the synthesis of both racemic and optically pure conduramines.[12]

Results and Discussion

A. Synthesis of the 7-Azabicyclo[2.2.1]heptadiene Derivatives (3). Altenbach, et al.[13a] first described the synthesis of **3a** by the Diels−Alder reaction of *N*-methoxycarbonylpyrrole (**1a**) with ethynyl-*p*-tolyl sulfone (**2a**). We found that one set of optimum conditions to effect the cycloaddition reaction was to heat a 2:1 molar ratio of the alkoxycarbonylpyrrole and the acetylenic sulfone without solvent at 75−90 °C for 16−48 h.[13b] Removal of the excess pyrrole derivative (recoverable) by column chromatography on silica gel gave the azabicyclo-[2.2.1]heptadienes **3a**−**e** in good yields. For example, by using these conditions, the Boc derivative **3c** was easily and routinely prepared in over 80% yield on a 100 g scale. It is important to note that the diastereomeric mixture **3d** derived from (−)-*N*-menthyloxycarbonylpyrrole (**1d**) could not be induced to crystallize, and it could not be separated by chromatographic techniques. Thus, other means of obtaining both enantiomeric forms of the azabicyclo[2.2.1]heptadienes had to be devised.

One of the disadvantages of using **3** as conduramine progenitors is that the room-temperature NMR spectra of these compounds are complicated because of restricted rotation about the NCO bond. The spectra do become simpler when they are recorded at higher temperatures (310−410 °K). This operation was inconvenient, but it was vital in the confirmation of the stereochemistry of the bicyclic compounds derived from **3** by functionalization of one or both double bonds. This operation was also necessary for the Boc-protected cyclohexenylamines obtained by anionic fragmentation of the bicyclic compounds and for the Boc-protected compounds derived from them.

B. Functionalization of 3c. Oxygenation (Scheme 2). Compound **3c** is admirably suited for site specific oxygenation because of the greatly different electron density of the double bonds. Thus, osmium tetroxide catalyzed hydroxylation[14] occurred regiospecifically at the more nucleophilic double bond to give the exo-cis-diol **7** exclusively (73%). This compound was produced in somewhat better yield (81%)[15] when the dihydroxylation was conducted in two steps via the phenyl boronate **6**. The

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(11) After some initial studies using **1b**, we chose to use **1c** as the starting material because the Boc moiety gave rise to simpler NMR spectra and because of its facile removal with trifluoroacetic acid.

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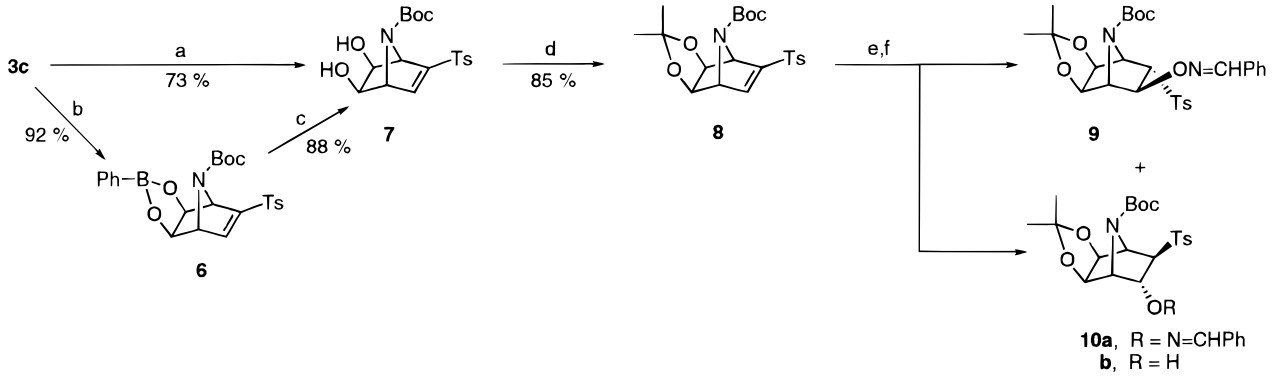
Scheme 2[a]



[a] Reagents and conditions: (a) OsO_4, NMO/$NaHCO_3$, *t*-BuOH, H_2O, THF/rt; (b) OsO_4, NMO, $PhB(OH)_2$/*t*-BuOH, CH_2Cl_2/rt; (c) 30% H_2O_2/THF, CH_2Cl_2, H_2O/rt; (d) $Me_2C(OMe)_2$, Me_2CO/TsOH/rt; (e) *syn*-PhCH=NOH, PhCH=NONa (cat.)/DMSO/rt; (f) $NaBH_4$, TFA/THF, reflux.

regio- and stereochemistry of this hydroxylation was readily apparent from the ^{1}H NMR spectra of the phenyl boronate **6**, the diol **7**, or the acetonide **8**, all of which still retained an absorption for the olefinic hydrogen H-3 at ca. δ 7.2, and also showed characteristically small[16] values for $J_{1,6}$ and $J_{4,5}$ (Table 1). Hydroxylation of the less nucleophilic 2,3-double bond of the bicyclic system could also be readily effected. Specifically, conjugate addition of *syn*-benzaldoxime to **8** at room temperature, catalyzed by sodium benzaldoximate, gave a 1:7.5 mixture of the *exo*- and *endo*-oximates **9** and **10a**, the stereochemistries of which were deduced from NOE effects and the appropriate *J* values (Table 1). It is not known whether this isomer ratio is a consequence of kinetic or thermodynamic control. Reduction of the *endo*-oximate **10a** with sodium trifluoroacetoxyborohydride, which is known to reductively cleave oxime ethers,[17] gave the 3-*endo*-hydroxy-2-*exo*-tosyl compound **10b** in high yield. This is another example of the use of *syn*-benzaldoxime as a formal OH^- equivalent.[18]

2. Anionic Ring Cleavage of the Functionalized 7-Azabicyclo[2.2.1]heptane Derivatives. Synthesis of a (±)-Conduramine C Derivative with a 3,5,6-Trihydroxy-4-amino Sequence (Scheme 3). One strategy which we envisioned using to trigger fragmentation of the bicyclic systems required a hydrogen atom α to the sulfone moiety. Compound **10b** is already appropriately functionalized for this purpose, but **3c** and **8** are not. These compounds were brought to the required oxidation level by reduction with excess methanolic sodium borohydride. In each case, easily separable mixtures of *exo*- and *endo*-sulfones were obtained for which the exo:endo ratios differed considerably from system to system, e.g., **11**:**12** = 0.13; **13**:**14** = 10. The exo isomer is the thermodynamically more stable one, at least for **13**. For example, generation of the anion from the *endo*-sulfone **14** with lithium bis(trimethylsilyl)amide in THF at −78 °C, followed by quenching at this temperature after 1 h, gave **13** exclusively. The sulfone stereochemistry is, thus, inconsequential because of this equilibration and because the equilibrium will shift constantly in the direction of the anion undergoing fragmentation.[10] Indeed, addition of THF solutions of **11** and **12** or of **13** and **14** to 1.5−2 equiv of lithium bis(trimethylsilyl)amide[10b] at −78 °C, followed by warming to rt cleanly gave the fragmentation products **15** and **16**, respectively, in yields approaching 80%.

Whereas lithium bis(trimethylsilyl)amide efficiently triggered anionic cleavage of **11**−**14**, it was completely without effect on the *endo*-hydroxy compound **10b**, even at 50 °C. Excess *n*-butyllithium in THF, both alone[19] and admixed with sodium *tert*-butoxide, gave similar results. Surprisingly, however, the addition of excess (6 equiv) methylmagnesium bromide to a THF solution of **10b** at rt produced the fragmentation product **17** in over 80% yield.[20] Although it was not done, desulfonylation and deprotection of **17** would generate an aminotriol with the stereochemistry of a conduramine C, but with a 4-amino-3,5,6-triol substituent sequence, identical to that found in neoinosamine.[1a] This approach to aminocyclitols, in which an hydroxyl group is installed at C-3 prior to fragmentation of the azabicyclo[2.2.1]heptane system, merits further study.

C. Synthesis of (±)-Conduramines from (±)-1-*tert*-Butoxycarbonylamino-5-*p*-toluenesulfonyl-2,4-cyclohexadiene (15). 1. (±)-Conduramine A-1 (Scheme 4). The cyclohexadiene derivative **15** is a substrate in which chemoselective functionalization of the double bonds is anticipated to be facile. Although the synthesis of conduramines could, in principle, be initiated at either double bond, we chose to functionalize the nonconjugated one first because the proximal *tert*-butoxycarbonylamino group was expected to exert greater stereochemical control over reactions at this site than over those at the more remote double bond.

The synthesis of (±)-conduramine A-1 from **15** required the introduction of cis-vicinal hydroxyl groups trans to the protected amino moiety. Osmate catalyzed hydroxylation of this diene gave a 1:1 mixture of *cis*-diols **18** (see also Scheme 6) and **19a** which was converted into a mixture of acetonides, one of which was identical to the *all-cis*-acetonide **16** (Scheme 3). In contrast, the easily

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(19) Anion formation did occur, since quenching with D_2O gave **10b** with >95% deuterium at C-2.

(20) This cleavage method was discovered near the end of this study. We hope to study this process in detail in the future. A referee has suggested that this reactivity difference might be a function of the preferred octahedral coordination of magnesium versus that of lithium (tetrahedral).

Table 1. ^{1}H NMR Spectral Data for Some 7-Azabicyclo[2.2.1]heptyl Compounds

compd no.	solvent[a] (*T*, K)	δ (ppm)	J_{Values} (Hz)	NOE's
(−)-**3c**	A (330)	1.31 (s, 9H), 2.43 (s, 3H), 5.18 (m, 1H), 5.34 (bq, 1H), 6.85 (dd, 1H), 6.96 (dd, 1H), 7.32 (d, 2H), 7.49 (dd, 1H), 7.74 (d, 2H)	$J_{1,3} = 0.7$, $J_{1,4} = 1.8$, $J_{1,5} = 0.7$, $J_{1,6} = 2.5$, $J_{3,4} = 2.4$, $J_{4,5} = 2.5$, $J_{4,6} < 0.5$, $J_{5,6} = 5.3$	
6	A (probe)[b]	1.14 (s, 9H), 2.44 (s, 3H), 4.60 (dd, 1H), 4.75 (dd, 1H), 4.81 (m, 1H), 4.94 (m, 1H), 7.05 (dd, 1H), 7.31−7.48 (m, 5H), 7.76 (d, 2H), 7.82 (d, 2H)	$J_{1,3} = 0.5$, $J_{1,6} = 0.7$, $J_{3,4} = 2.2$, $J_{4,5} = 0.5$, $J_{5,6} = 5.5$	
(−)-**7**	B (360)	1.18 (s, 9H), 2.42 (s, 3H), 3.57 (d, 1H), 3.67 (dd, 1H), 4.38 (dd, 1H), 4.48 (t, 1H), 7.13 (d, 1H), 7.47 (d, 2H), 7.75 (d, 2H)	$J_{1,4} = 1.7$, $J_{3,4} = 2.3$, $J_{5,6} = 6.0$	
(−)-**8**	A (330)	1.25 (s, 9H), 1.29 (s, 3H), 1.43 (s, 3H), 2.44 (s, 3H), 4.32 (d, 1H), 4.49 (d, 1H), 4.64 (dd, 1H), 4.79 (dd, 1H), 7.02 (dd, 1H), 7.35 (d, 2H), 7.78 (d, 2H)	$J_{1,3} = 0.6$, $J_{1,4} = 0.6$, $J_{1,6} \leq 0.5$, $J_{3,4} = 2.3$, $J_{5,6} = 5.5$	
9	B (380)	1.29 (s, 3H), 1.36 (s, 12H), 2.33 (s, 3H), 3.72 (dd, 1H), 4.37 (d, 1H), 4.43 (d, 1H), 4.47 (dd, 1H), 4.72 (d, 1H), 5.02 (d, 1H), 7.32−7.44 (m, 7H), 7.82 (d, 2H), 7.93 (s, 1H)	$J_{1,2} = 5.0$, $J_{1,4} = 1.8$, $J_{2,3} = 3.4$, $J_{5,6} = 5.5$	1 ↔ 2, 3 ↔ 4, 3 ↔ 5, 5 ↔ 6
10a	B (390)	1.21 (s, 3H), 1.30 (s, 3H), 1.41 (s, 9H), 2.35 (s, 3H), 3.34 (d, 1H), 4.41 (bm, 1H), 4.47 (bm, 1H), 4.48 (d, 1H), 4.59 (d, 1H), 4.91 (t, 1H), 7.39−7.44 (m, 5H), 7.53−7.56 (m, 2H), 7.79 (d, 2H), 8.12 (s, 1H)	$J_{1,4} = 1.6$, $J_{2,3} = 4.1$, $J_{3,4} = 4.4$, $J_{5,6} = 5.4$	2 ↔ 3, 2 ↔ 6
10b	B (370)	1.22 (s, 3H), 1.31 (s, 3H), 1.40 (s, 9H), 2.43 (s, 3H), 2.89 (d, 1H), 4.12 (bm, 1H), 4.22 (bm, 1H), 4.32 (d, 1H), 4.43 (bm, 1H), 4.72 (d, 1H), 7.42 (d, 2H), 7.77 (d, 2H)	$J_{2,3} = 4.1$, $J_{5,6} = 5.4$	2 ↔ 3, 2 ↔ 6, 3 ↔ 4, 4 ↔ 5, 5 ↔ 6
11	B (330)	1.32 (s, 9H), 1.52 (dd, 1H), 2.08 (dt, 1H), 2.41 (s, 3H), 3.21 (dd, 1H), 4.62 (m, 1H), 4.76 (d, 1H), 6.38 (m, 1H), 6.47 (dd, 1H), 7.43 (d, 2H), 7.75 (d, 2H)	$J_{1,6} = 2.1$, $J_{2,3-endo} = 8.5$, $J_{2,3exo} = 4.3$, $J_{3exo-3endo} = 12.4$, $J_{3exo,4-} = 4.2$, $J_{4,5} \approx 2$, $J_{5,6} = 5.6$	
12	B (330)	1.32 (s, 9H), 1.48 (m, 1H), 2.18 (m, 1H), 2.43 (s, 3H), 3.86 (m, 1H), 4.55 (m, 1H), 4.66 (m, 1H), 6.32 (dd, 1H), 6.50 (dd, 1H), 7.45 (d, 2H), 7.76 (d, 2H)	$J_{1,2} = 3.9$, $J_{1,4} < 1$, $J_{1,6} = 2.0$, $J_{2,3-exo} = 9$, $J_{2,3-endo} = 4.5$, $J_{3-exo-endo} = 11.9$, $J_{3-exo,4} = 3.6$, $J_{4,5} = 2.2$, $J_{5,6} = 5.8$	
(−)-**13**	B (410)	1.16 (s, 3H), 1.27 (s, 3H), 1.39 (bs, 9H), 1.64 (q, 1H), 2.00 (dt, 1H), 2.42 (s, 3H), 3.31 (dd, 1H), 4.16 (d, 1H), 4.18 (bm, 1H), 4.20 (d, 1H), 4.28 (bm, 1H), 7.42 (d, 2H), 7.75 (d, 2H)	$J_{2,3-exo} = 5.3$, $J_{2,3-endo} = 8.7$, $J_{3-exo,endo} = 13.3$, $J_{3-exo,4} = 5.3$, $J_{5,6} = 5.4$	2 ↔ 6, 2 ↔ 3-*endo*
(+)-**14**	A (330)	1.31 (s, 3H), 1.40 (s, 3H), 1.41 (s, 9H), 1.77 (dd, 1H), 2.01 (ddd, 1H), 2.45 (s, 3H), 3.47 (ddd, 1H), 4.30 (dd, 1H), 4.33 (d, 1H), 4.38 (dd, 1H), 5.13 (d, 1H), 7.36 (d, 2H), 2.77 (d, 2H)	$J_{1,2} = 4.9$, $J_{1,4} = 0.9$, $J_{2,3-exo} = 11.3$, $J_{2,3-endo} = 5.9$, $J_{3-exo-endo} = 13.0$, $J_{3-exo,4} = 5.4$, $J_{5,6} = 5.5$	1 ↔ 2, 1 ↔ 6, 2 ↔ 3-exo, 3-exo↔3-endo, 3-endo ↔ 4, 3-endo ↔ 5, 5 ↔ 6
(−)-**44a**	A (325)	1.26 (d, 3H), 1.39 (s, 9H), 2.45 (s, 3H), 3.52 (t, 1H), 3.74 (s, 3H), 3.99 (bd, 1H), 4.10 (m, 1H), 4.58 (bm, 1H), 4.83 (m, 1H), 6.37 (dd, 1H), 6.49 (dd, 1H), 7.36 (d, 2H), 7.75 (d, 2H)	$J_{1,2} = 3.6$, $J_{1,6} = 2.1$, $J_{2,3} = 2.9$, $J_{4,5} = 2.5$, $J_{5,6} = 5.8$	
(−)-**45a**	A (325)	1.39 (d, 3H), 1.40 (s, 9H), 2.45 (s, 3H), 3.72 (s, 3H), 3.74 (t, 1H), 4.15 (d, 1H), 4.20 (q, 1H), 4.65 (bm, 1H), 4.75 (bm, 1H), 6.36 (dd, 1H), 6.57 (dd, 1H), 7.34 (d, 2H), 7.79 (d, 2H)	$J_{1,2} \cong 3.3$, $J_{1,6} = 2.1$, $J_{2,3} = 2.7$, $J_{4,5} = 2.6$, $J_{5,6} = 5.9$	
(+)-**46**	A (330)	0.83 (bs, 3H), 1.41 (s, 9H), 2.44 (s, 3H), 3.38 (m, 1H), 3.46 (t, 3H), 4.04 (d, 1H), 4.75 (bt, 1H), 4.82 (bs, 1H), 6.34 (dd, 1H), 6.53 (dd, 1H), 7.37 (d, 2H), 7.77 (d, 2H)	$J_{1,2} \cong 3.3$, $J_{1,6} = 2.1$, $J_{2,3} = 2.7$, $J_{4,5} = 2.8$, $J_{5,6} = 5.9$, $J_{AB} = 12$ (CH_2O)	1 ↔ 2, 2 ↔ 3, 3 ↔ 4
(−)-**47**	A (330)	1.15 (d, 3H), 1.39 (s, 9H), 2.44 (s, 3H), 3.37 (dd, 1H), 3.49 (dd, 1H), 3.54 (t, 1H), 3.67 (m, 1H), 4.15 (d, 1H), 4.56 (bs, 1H), 4.65 (bs, 1H), 6.37 (dd, 1H), 6.48 (dd, 1H), 7.39 (d, 1H), 7.78 (d, 2H)	$J_{1,2} = 3.5$, $J_{1,6} = 1.6$, $J_{2,3} = 2.9$, $J_{4,5} = 2.2$, $J_{5,6} = 5.8$, $J_{AB} = 11.9$ (CH_2O), $J_{AX} = 6.7$, $J_{BX} = 3.4$	1 ↔ 2, 1 ↔ 6, 2 ↔ 3, 3 ↔ 4, 3 ↔ 5

[a] A = $CDCl_3$, B = DMSO-d_6. [b] Single rotamer at probe temperature. [c] Two rotamers at this temperature.

prepared bis-Boc compound **20** underwent exclusive cis-dihydroxylation trans to the exceedingly voluminous bis-Boc moiety to produce **21** in over 90% yield. This stereochemistry is assured by the ca. 11 Hz *J* value for the trans diaxial hydrogens at C-4,5 (Table 2). Reaction of **21** with 6% sodium amalgam in buffered methanol solution[21] effected reductive removal of the arylsulfonyl group and hydrolysis to the oily mono-Boc olefinic diol **22**. Completion of the synthesis of (±)-conduramine A-1 required the introduction of the third hydroxyl group. Therefore the diol **22** was converted into the acetonide **23** which ensured that peracid oxidation of the double bond occurred without allylic oxygen participation. The epoxide **24**, so obtained, was cleaved with lithium phenyl selenide, and the phenylselenyl compound **25** was converted into the conduramine A-1 derivative **26** by the selenoxide cycloelimination process.[22] Aqueous trifluoroacetic acid removed the protecting groups from **26**, and addition of aqueous ammonia to this solution liberated (±)-conduramine A-1 (**27a**) which was converted into the crystalline tetracetyl derivative **27b**. The ^{13}C NMR spectrum of **27b** was identical to that reported[8b] for the tetracetyl derivative of (+)-conduramine A-1.

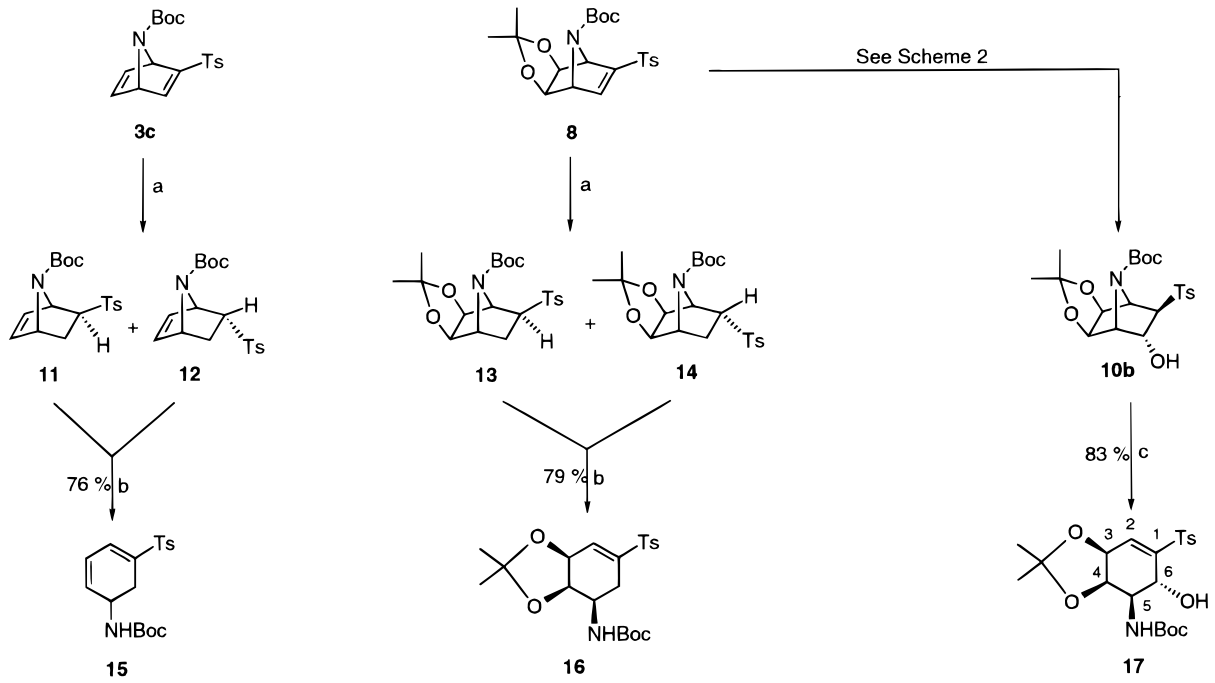
2. (±)-Conduramine F-1 (Scheme 5). Three of the four substituents in conduramine F-1 are oriented cis, and the C-5 hydroxyl group is trans disposed. It was expected that the necessary *cis*-3-amino-4-oxy stereochemistry would result on peroxycarboxylic acid epoxidation of the Boc-diene **15** because of hydrogen bonding of the peracid to the Boc moiety in the transition state for epoxidation.[23] Indeed, reaction of **15** with *m*-chloroperoxybenzoic acid in a dichloromethane solution gave a 9:1 mixture of epoxides (>90% yield), the major component of which was **28**, as judged from the small $J_{3,4}$ and $J_{4,5}$ values (Table 2). Sulfuric acid catalyzed hydrolysis of **28** gave a single diol (**29**) which was reductively

(21) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, 3477.

(22) (a) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697. (b) Reich, H. J.; Wollowitz, S.; Trend, J. E.; Chow, F.; Wendleborn, D. F. *J. Org. Chem.* **1978**, *43*, 1697.

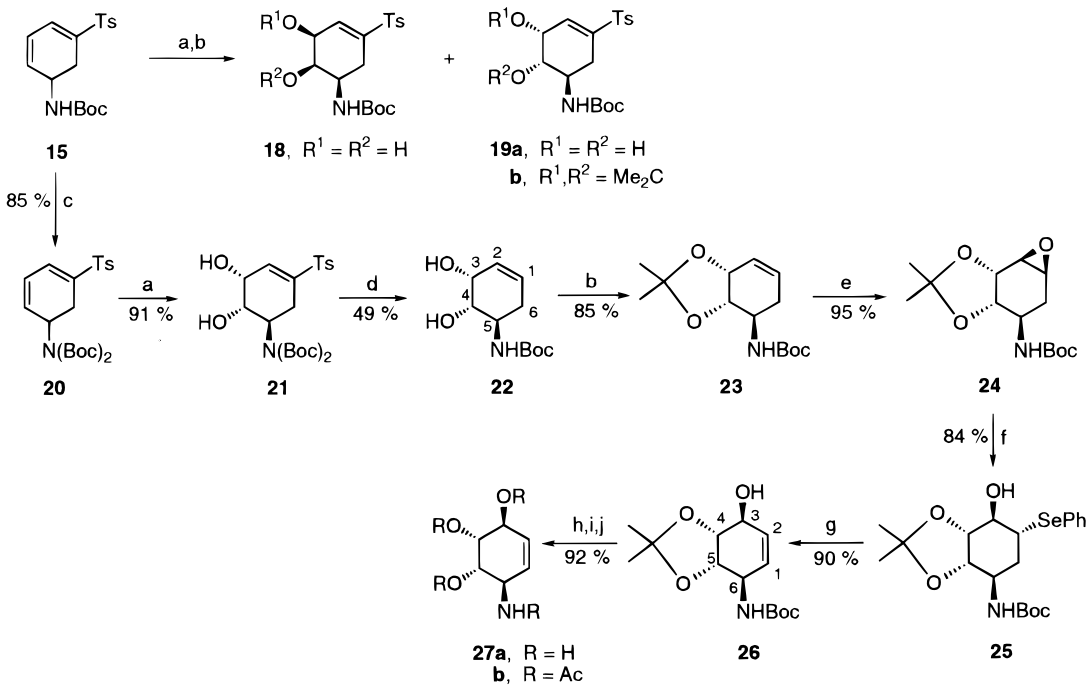
(23) Jenmalm, A.; Berts, W.; Luthman, K.; Csoregh, I.; Hacksell, U. *J. Org. Chem.* **1995**, *60*, 1026 and refs cited therein.

Scheme 3[a]



[a] Reagents and conditions: (a) $NaBH_4$/MeOH/0 °C; (b) $Li(NTMS)_2$/THF/−78 to 0 °C; (c) MeMgBr/THF/rt.

Scheme 4[a]



[a] Reagents and conditions: (a) OsO_4, NMO/$NaHCO_3$, *t*-BuOH, H_2O, THF/rt; (b) $Me_2C(OMe)_2$, Me_2CO/TsOH, rt; (c) $(Boc)_2O$/cat. 4-DMAP/MeCN; (d) 6% Na, Hg/Na_2HPO_4/MeOH, THF/−12 °C; (e) MCPBA/$NaHCO_3$/CH_2Cl_2; (f) $(PhSe)_2$/*n*-BuLi/THF; (g) H_2O_2/(*i*-Pr)$_2$NEt/CH_2Cl_2/0 °C then THF/Δ; (h) TFA, H_2O/CH_2Cl_2; (i) NH_3/MeOH; (j) Ac_2O/Py, cat. 4-DMAP.

desulfonylated (to **30a**) and then diacetylated to **30b**. The coupling constants $J_{3,4} = 4.7$ Hz and $J_{4,5} = 2.7$ Hz (Table 2) for **30b** leave no doubt that hydrolysis of **28** had occurred with the expected[24] regio- and stereochemical control. Compound **30b** was then converted into (±)-conduramine F-1 (**34a**) by a reaction sequence analogous to that used for the synthesis of (±)-conduramine A-1. It was fully characterized as the crystalline, known[3e] tetraacetate **34b**.

D. Synthesis of (±)-Conduramines from the (±)-Acetonide of *all-cis*-1-*tert*-Butoxycarbonylamino-2,3-dihydroxy-5-*p*-toluenesulfonylcyclohex-4-ene (16). 1. (±)-Conduramine C-1 (Scheme 6). The *all-cis*-acetonide **35b**, used for the synthesis of (±)-conduramine

(24) Carless, H. A. J. *Tetrahedron: Asymmetry* **1992**, *3*, 795 (See especially pp 805−809).

Table 2. NMR Spectral Data of Conduramines, Conduramine Derivatives, and Conduramine Precursors

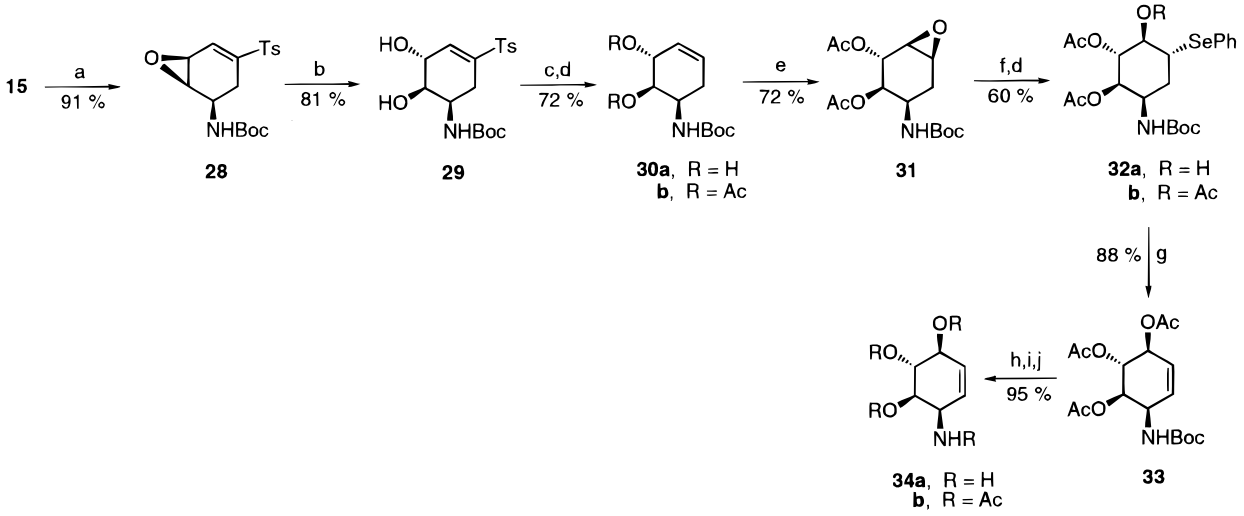
compd no.	solvent[a] (*T*, K)	δ (ppm)	J_{Values} (Hz)	NOE's
15	A (330)	1.38 (s, 9H), 2.43 (s, 1H), 2.52 (dq, 1H), 2.60 (dq, 1H), 4.35 (bq, 1H), 6.04 (dd, 1H), 6.18 (ddd, 1H), 7.03 (m, 1H), 7.31 (d, 2H), 7.74 (d, 2H)	$J_{2,3} = 5.6$, $J_{2,4} < 1$, $J_{2,6a} = 2.9$, $J_{2,6e} = 2.0$, $J_{3,4} = 9.4$, $J_{3,5}$=1.1, $J_{4,5} = 4.8$, $J_{5,6a} = 8.2$, $J_{5,6e} = 7.2$, $J_{6a,e} = 17.5$	
16	A (310)	1.20 (s, 3H), 1.36 (s, 3H), 1.42 (s, 9H), 2.10 (tdd, 1H), 2.44 (s, 3H), 2.55 (dd, 1H), 3.96 (bq, 1H), 4.28 (dd, 1H), 4.76 (m, 1H), 4.85 (bd, 1H), 6.75 (t, 1H), 7.34 (d, 2H), 7.73 (d, 2H)	$J_{2,3} = 2.8$, $J_{2,6a} = 3.0$, $J_{3,4} = 5.2$, $J_{3,6a} = 2.3$, $J_{4,5} = 2.2$, $J_{5,6a} = 10.4$, $J_{5,6e} = 5.5$, $J_{6a,e} = 16.3$	2 ↔ 3, 3 ↔ 4, 3 ↔ 5(w), 3 ↔ 6a, 4 ↔ 5, 5 ↔ 6e, 6a ↔ 6e, 6a ↔ NH
17	B (350)	1.28 (s, 3H), 1.31 (s, 3H), 1.35 (s, 9H), 2.40 (s, 3H), 3.76 (dd, 1H), 4.34 (bd, 1H), 4.39 (dd, 1H), 4.84 (ddd, 1H), 6.78 (bd, 1H), 7.38 (d, 2H), 7.73 (d, 2H)	$J_{2,3} = 3.0$, $J_{2,6} = 1.2$, $J_{3,4} = 5.3$, $J_{3,6} = 1.5$, $J_{4,5} = 3.1$, $J_{5,6}$= 7.5	2 ↔ 3, 3 ↔ 4, 3 ↔ 6, 4 ↔ 5, 5 ↔ 6 (w), 2 ↔ OH, 5 ↔ OH (w)
(+)-**18**	B (360)	1.35 (s, 9H), 2.14 (m, 1H), 2.23 (m, 1H), 2.40 (s, 3H), 3.58 (m, 1H), 3.76 (dd, 1H), 4.29 (m, 1H), 6.58 (m, 1H), 7.41 (d, 2H), 7.68 (d, 2H)	$J_{2,3} = 3.5$, $J_{2,6a} = 1.8$, $J_{2,6e} = 1.3$, $J_{3,4} = 3.7$, $J_{3,6a} = 3.3$, $J_{4,5} = 1.8$, $J_{5,6a} = 9.5$, $J_{5,6e} = 6.1$, $J_{6a,e} = 16.8$	
20	A (325)[b]	1.43 (s, 18H), 2.41 (s, 3H), 2.64 (ddd, 1H), 2.74 (ddd, 1H), 5.17 (ddt, 1H), 5.88 (dd), 5.98 (ddd, 1H), 6.94 (ddd, 1H), 7.30 (d, 2H), 7.74 (d, 2H)	$J_{2,3} = 5.5$, $J_{2,4} = 0.9$, $J_{2,6a} = 2.5$, $J_{2,6e} = 1.2$, $J_{3,4} = 9.8$, $J_{3,5} = 2.8$, $J_{4,5} = 2.8$, $J_{4,6a} = 0.8$, $J_{5,6a} = 14.4$, $J_{5,6e} = 11.4$, $J_{6a,e} = 17.2$	
21	A (probe)[c]	1.45 (s, 18H), 2.43 (s, 3H), 2.57 (dd, 1H), 2.72 (ddd, 1H), 4.12 (dd, 1H), 4.37 (dt, 1H), 4.44 (t, 1H), 6.91 (dd, 1H), 7.33 (d, 2H), 7.74 (d, 2H)	$J_{2,3} = 5.4$, $J_{2,6a} = 2.2$, $J_{3,4} = 4.2$, $J_{4,5} = 11.2$, $J_{5,6a} = 10.8$, $J_{5,6e} = 5.7$, $J_{6a,e} = 17.1$	
23	A (335)	1.38 (s, 3H), 1.45 (s, 9H), 1.93 (m, 2H), 2.56 (dt, 1H), 3.84 (dt, 1H), 4.05 (dd, 1H), 4.55 (m, 1H), 4.58 (b, 1H), 5.79−5.89 (m, 2H)	$J_{1,2} = 10.0$, $J_{1,6a} = 2.9$, $J_{1,6e} = 4.0$, $J_{2,3} = 3.2$, $J_{3,4} = 5.9$, $J_{3,6a} = 1.4$, $J_{4,5} = 7.7$, $J_{5,6a} = 7.6$, $J_{5,6e} = 4.9$, $J_{6a,e} = 17.4$	
24	A (probe)[c,d]	1.36, (s, 3H), 1.43 (s, 12H), 2.05 (dt, 1H), 2.40 (dd, 1H), 3.11 (dd, 1H), 3.33 (m, 1H), 4.13 (bm, 1H), 4.15 (bdd, 1H), 4.45 (d, 1H), 5.32 (bd, 1H)	$J_{1,2} = 3.9$, $J_{1,6a} = 2.8$, $J_{1.6e} < 1$, $J_{2,3} < 1$, $J_{2,4} = 1.2$, $J_{3,4} = 5.2$, $J_{4,5} = 3.6$, $J_{5,6a} = 5.1$, $J_{5,6e} = 2.3$, $J_{6a,e} = 15.5$	1 ↔ 2, 1 ↔ 6a, 1 ↔ 6e, 2 ↔ 3, 3 ↔ 4, 4 ↔ 6a, 4 ↔ 6e, 6a ↔ 6e
25	A (probe)[c]	1.33 (s, 3H), 1.38 (s, 3H), 1.44 (s, 9H), 1.94 (ddd, 1H), 2.12 (dt, 1H), 3.00 (td, 1H), 3.56 (dd, 1H), 4.02 (m, 1H), 4.05 (dd, 1H), 4.12 (dd, 1H), 4.56 (bd, 1H), 7.27−7.38 (m, 3H), 7.58−7.62 (m, 2H)	$J_{1,2} = 10.7$, $J_{1,6a} = 11.6$, $J_{1,6e} = 4.2$, $J_{2,3} = 6.7$, $J_{3,4} \cong 5.0$, $J_{4,5} \cong 4.0$, $J_{5,6a} \approx 4.3$, $J_{5,6e} = 4.3$, $J_{5,NH} \approx 7.5$, $J_{6a,e} = 14.3$	1 ↔ 3, 1 ↔ NH, 1 ↔ 6e, 2 ↔ 6a, 5 ↔ 6a, 5 ↔ 6e
26	A (probe)[c]	1.35 (s, 3H), 1.45 (s, 12H), 4.03 (m, 1H), 4.18 (m, 2H), 4.22 (m, 1H), 4.92 (bd, 1H), 5.80 (ddd, 1H), 5.91 (dt, 1H)	$J_{1,2} = 9.8$, $J_{1,3} = 1.8$, $J_{1,6} = 3.6$, $J_{2,3} = 3.0$, $J_{2,6} = 2.3$, $J_{5,6} = 7.8$, $J_{6,NH} = 6.9$	
28	A (320)	1.44 (s, 9H), 1.88 (ddd, 1H), 2.44 (s, 3H), 2.62 (ddd, 1H), 3.54 (m, 2H), 4.09 (bq, 1H), 7.12 (t, 1H), 7.30 (d, 2H), 7.71 (d, 2H)	$J_{2,3} = 4.0$, $J_{2,6a} = 3.2$, $J_{3,4} = 4.2$, $J_{3,6e} = 1.6$, $J_{4,5} < 1$, $J_{5,6a} = 10.9$, $J_{5,6e} = 6.6$, $J_{6a,e} = 16.3$	
29	B (330)[e]	1.36 (s, 9H), 2.11 (bq, 1H), 2.22 (bq, 1H), 2.42 (s, 3H), 3.62 (m, 1H), 3.68 (m, 1H), 4.12 (t, 1H), 6.72 (m, 1H), 7.44 (d, 2H), 7.69 (d, 2H)	$J_{2,3} = 4.6$, $J_{2,6a} = 2.6$, $J_{2,6e} = 1.8$, $J_{3,4} = 3.0$, $J_{3,6a} \approx 0.9$, $J_{4,5} \approx 3.0$, $J_{5,6a} = 9.8$, $J_{5,6e} = 5.7$, $J_{6a,e} = 17.0$	2 ↔ 3, 2 ↔ 6, 3 ↔ 4, 5 ↔ 6e, 6a ↔ 6e
30b	A (330)[e]	1.45 (s, 9H), 2.05 (s, 3H), 2.06 (s, 3H), 2.12 (m, 1H), 2.50 (m, 1H), 4.19 (bm, 1H), 4.63 (bs, 1H), 5.07 (dd, 1H), 5.28 (m, 1H), 5.70 (m, 1H), 5.90 (m, 1H)	$J_{1,2} = 10.3$, $J_{1,3} = 1.0$, $J_{1,6a} = 3.1$, $J_{1,6e} = 4.5$, $J_{2,3} = 3.5$, $J_{2,6a} \approx 2.2$, $J_{2,6e} \approx 2.2$, $J_{3,4} = 4.7$, $J_{4,5} = 2.7$, $J_{5,6a} \approx 7.7$, $J_{5,6e} = 5.5$, $J_{6a,e} \approx 17.4$	1 ↔ 2, 1 ↔ 6a, 1 ↔ 6e, 2 ↔ 3, 3 ↔ 4, 4 ↔ 5, 5 ↔ 6a, 5 ↔ 6e
31	A (probe)[c,f]	1.42 (s, 9H), 2.00 (s, 3H), 2.10 (s, 3H), 2.28 (m, 2H), 3.11 (d, 1H), 3.28 (m, 1H), 4.27 (m, 1H), 4.78 (dd, 1H), 5.19 (bs, 1H), 5.22 (d, 1H)	$J_{1,2} = 3.5$, $J_{3,4} = 8.9$, $J_{4,5} = 3.7$	1 ↔ 2, 1 ↔ 6, 2 ↔ 3, 4 ↔ 5, 5 ↔ 6, 3-OAc ↔ 2
32b	A (320)[g]	1.44 (s, 9H), 1.60 (ddd, 1H), 1.98 (s, 3H), 1.99 (s, 3H), 2.00 (s, 3H), 2.46 (dt, 1H), 3.25 (ddd, 1H), 4.16 (sex, 1H), 4.67 (bd, 1H), 4.83 (dd, 1H), 5.00 (dd, 1H), 5.18 (dd, 1H), 7.28−7.34 (m, 3H), 7.57−7.60 (m, 2H)	$J_{1,2} = 10.8$, $J_{1,6a} = 13.3$, $J_{1,6e} = 4.1$, $J_{2,3} = 9.0$, $J_{3,4} = 10.3$, $J_{4,5} = 4.4$, $J_{5,6a} = 3.4$, $J_{5,6e} \approx 3.9$, $J_{6a,e} = 14.6$, $J_{1,NH} = 7.0$	1 ↔ 3, 1 ↔ NH, 1 ↔ 6e, 2 ↔ 6a, 3 ↔ NH, 4 ↔ 5, 5 ↔ 6a, 5 ↔ 6e, 6a ↔ 6e
33	A (probe)[c]	1.45 (s, 9H), 2.03 (s, 3H), 2.06 (s, 3H), 2.07 (s, 3H), 4.55 (bm, 1H), 4.65 (m, 1H), 5.06 (dd, 1H), 5.35 (m, 2H), 5.71 (m, 1H), 5.84 (ddd, 1H)	$J_{1,2} = 10.0$, $J_{1,3} = 1.5$, $J_{1,6} = 4.8$, $J_{2,3} = 2.1$, $J_{3,4} = 7.0$, $J_{4,5} = 10.2$, $J_{5,6} = 4.8$	1 ↔ 2, 1 ↔ 6, 2 ↔ 3, 3 ↔ 5, 5 ↔ 6
34b	A (probe)[c]	2.01 (s, 3H), 2.02 (s, 3H), 2.05 (s, 3H), 2.06 (s, 3H), 5.02 (m, 1H), 5.09 (dd, 1H), 5.35 (m, 1H), 5.41 (dd, 1H), 5.36 (dd, 1H), 5.60 (bm, 1H), 5.76 (ddd, 1H), 5.84 (ddd, 1H)	$J_{1,2} = 9.8$, $J_{1,3} = 1.6$, $J_{1,6} = 4.6$, $J_{2,3} = 2.7$, $J_{3,4} = 6.7$, $J_{4,5} = 10.0$, $J_{5,6} = 4.6$	
(+)-**35a**	A (330)	1.44 (s, 9H), 2.18 (m, 1H), 2.28 (m, 1H), 2.68 (bs, 2H), 3.84 (bq, 1H), 3.97 (m, 1H), 4.31 (m, 1H), 5.26 (bs, 1H), 5.60 (m, 1H), 5.74 (m, 1H)	$J_{1,2} = 10.2$, $J_{1,3} = 1.7$, $J_{1,6a} = 3.1$, $J_{1,6e} = 4.1$, $J_{2,3}$= 4.4, $J_{2,6a} = 2.8$, $J_{2,6e} = 2.0$, $J_{3,4} = 4.1$, $J_{4,5} = 2.2$, $J_{5,6a} = 8.3$, $J_{5,6e} = 4.0$, $J_{6a,e} = 17.6$	
35b	A (335)[b]	1.37 (s, 3H), 1.38 (s, 3H), 1.45 (s, 9H), 2.12 (m, 1H), 2.23 (m, 1H), 3.94 (m, 1H), 4.32 (dd, 1H), 4.59 (m, 1H), 4.98 (bd, 1H), 5.65 (m, 1H), 5.77 (m, 1H)	$J_{1,2} = 10.1$, $J_{1,3} = 0.7$, $J_{1,6a} = 2.5$, $J_{1,6e} = 5.5$, $J_{2,3} = 3.1$, $J_{2,4} = 0.8$, $J_{2,6a} = 2.6$, $J_{2,6e} = 1.1$, $J_{3,4} = 5.7$, $J_{4,5} = 2.6$, $J_{5,6a} = 10.0$, $J_{5,6e} = 5.5$, $J_{6a,e} = 16.5$	
36	A (probe)[c]	1.37 (s, 3H), 1.43 (s, 3H), 1.44 (s, 9H), 1.95 (ddd, 1H), 2.24 (ddd, 1H), 2.98 (dt, 1H), 3.29 (m, 1H), 4.09 (bm, 1H), 4.19 (dt, 1H), 4.47 (d, 1H)	$J_{1,2} = 3.6$, $J_{1,6a} = 1.1$, $J_{1,6e} = 2.9$, $J_{2,3} < 0.5$, $J_{2,4} = 1.2$, $J_{3,4} = 5.7$, $J_{3,5} = 1.3$, $J_{4,5} = 2.4$, $J_{5,6a} = 11.6$, $J_{5,6e} = 5.1$, $J_{6a,e} = 14.1$	1 ↔ 2, 1 ↔ 6a, 1 ↔ 6e, 2 ↔ 3, 3 ↔ 5, 4 ↔ 5, 5 ↔ 6a, 5 ↔ 6e, 6a ↔ 6e
37	A (315)	1.32 (s, 3H), 1.35 (s, 3H), 1.43 (s, 9H), 1.60 (q, 1H), 2.23 (m, 1H), 2.86 (ddd, 1H), 3.41 (dd, 1H), 3.92 (bm, 1H), 3.97 (dd, 1H), 4.24 (t, 1H), 7.25−7.36 (m, 3H), 7.57−7.60 (m, 2H)	$J_{1,2} = 11.3$, $J_{1,6a} = 12.8$, $J_{1,6e} = 3.1$, $J_{2,3} = 7.1$, $J_{3,4} = 5.0$, $J_{4,5} = 3.8$, $J_{5,6a} \approx 12.6$, $J_{6a,e} \approx 12.9$	1 ↔ 6e, 1 ↔ 3, 1 ↔ 5, 2 ↔ 6a, 3 ↔ 4, 4 ↔ 5, 5 ↔ 6e, 6a ↔ 6e
38	A (325)[h]	1.33 (s, 3H), 1.35 (s, 3H), 1.46 (s, 9H), 4.24 (dd, 1H), 4.40 (ddd, 1H), 4.55 (m, 2H), 5.11 (bs, 1H), 5.83 (ddd, 1H), 6.02 (m, 2H)	$J_{1,2} = 9.9$, $J_{1,5} = 1.5$, $J_{1,6} = 2.3$, $J_{2,3} = 5.3$, $J_{2,4} = 0.9$, $J_{2,6} = 2.5$, $J_{3,4} = 2.7$, $J_{4,5} = 6.8$, $J_{5,6} = 4.4$	1 ↔ 2, 1 ↔ 3 (?), 1 ↔ 5, 2 ↔ 3, 2 ↔ 5 (?), 3 ↔ 4, 4 ↔ 5
40	B (335)	1.36 (s, 9H), 1.83 (dd, 1H), 2.03 (ddd, 1H), 3.17 (ddd, 1H), 3.23 (t, 1H), 3.42 (bm, 1H), 3.60 (bm, 1H), 3.90 (dd, 1H)	$J_{1,2} = 4.0$, $J_{1,6a} = 0.9$, $J_{1,6e} = 4.8$, $J_{2,3} = 2.2$, $J_{2,4} = 1.5$, $J_{3,4} = 4.4$, $J_{4,5} = 2.0$ $J_{4,6e} \leq 0.7$, $J_{5,6a} = 10.2$, $J_{5,6e} = 6.8$, $J_{6a,e} = 15.3$	1 ↔ 2, 1 ↔ 6e, 2 ↔ 3, 3 ↔ 4, 3 ↔ 5, 4 ↔ 5, 5 ↔ 6a, 5 ↔ 6e, 6a ↔ 6e

Table 2 (Continued)

compd no.	solvent[a] (*T*, K)	δ (ppm)	J_{Values} (Hz)	NOE's
41b	B (350)[i]	1.39 (s, 9H), 1.82 (ddd, 1H), 1.89 (s, 3H), 1.97 (s, 3H), 2.02 (s, 3H), 2.23 (ddd, 1H), 3.85 (sex, 1H), 4.00 (m, 1H), 5.03 (dd, 1H), 5.11 (t, 1H), 5.34 (t, 1H), 6.34 (bd, 1H), 7.32 (m, 3H), 7.57 (m, 2H)	$J_{1,2}$ = 7.7, $J_{1,6a}$ = 8.7, $J_{1,6e}$ = 4.0, $J_{2,3}$ = 3.2, $J_{3,4}$ = 2.3, $J_{4,5}$ = 3.5, $J_{5,6a}$ = 7.6, $J_{5,6e}$ = 3.8, $J_{6a,e}$ = 14.2	1 ↔ 2, 1 ↔ 6a, 2 ↔ 3, 3 ↔ 4, 3 ↔ 5, 4 ↔ 5, 6a ↔ 6e
42	B (350)	1.40 (s, 9H), 1.99 (s, 3H), 2.00 (s, 6H), 4.41 (bm, 1H), 5.23 (q, 1H), 5.47 (m, 1H), 5.71 (ddd, 1H), 5.79 (ddd, 1H)	$J_{1,2}$ = 10.2, $J_{1,3}$ = 1.4, $J_{1,6}$ = 3.0, $J_{2,3}$ = 3.2, $J_{2,6}$ = 2.0, $J_{3,4}$ = 2.1, $J_{4,5}$ = 2.1, $J_{5,6}$ = 2.1	1 ↔ 2, 1 ↔ 3, 1 ↔ 6, 2 ↔ 3, 2 ↔ 6, 3 ↔ 4, 5 ↔ 6
43a	B (380)	3.75 (bt, 1H), 2.09 (dd, 1H), 3.96 (m, 1H), 4.15 (dt, 1H), 5.79 (ddd, 1H), 5.90 (dddd, 1H)	$J_{1,2}$ = 10.2, $J_{1,3}$ = 1.8, $J_{1,6}$ = 4.1, $J_{2,3}$ = 2.3, $J_{2,4}$ = 1.2, $J_{2,6}$ = 1.5, $J_{3,4}$ = 4.1, $J_{4,5}$ = 1.8, $J_{5,6}$ = 5.1	1 ↔ 2, 1 ↔ 3, 1 ↔ 6, 2 ↔ 3, 2 ↔ 4, 3 ↔ 4, 3 ↔ 5, 4 ↔ 5, 5 ↔ 6
43b	A (330)	1.98 (s, 3H), 2.03 (s, 3H), 2.04 (s, 3H), 2.11 (s, 3H), 4.98 (bm, 1H), 5.23 (dd, 1H), 5.49 (m, 1H), 5.54 (dt, 1H), 5.71 (m, 1H), 5.86 (ddd, 1H)	$J_{1,2}$ = 10.1, $J_{1,3}$ = 3.0, $J_{1,6}$ = 4.0, $J_{2,3}$ = 2.6, $J_{2,4}$ = 1.1, $J_{2,6}$ = 0.9, $J_{3,4}$ = 4.4, $J_{4,5}$ = 1.9, $J_{5,6}$ = 5.6	1 ↔ 2, 1 ↔ 6, 2 ↔ 3, 3 ↔ 5, 4 ↔ 5, 5 ↔ 6

[a] A = $CDCl_3$, B = DMSO-d_6. [b] Identical *J* values for spectrum measured at probe temperature. [c] Single rotamer at probe temperature. [d] Nonchair conformation with H-6e at δ 2.05 and H-6a at δ 2.40. [e] Half chair conformation with OH or OAc groups axial. [f] Twisted chair or boat conformation with NHBoc axial. [g] Chair conformation with PhSe equatorial. [h] Twisted half chair or boat conformation. Note, $J_{3,4}$ and $J_{4,5}$. [i] Boat conformation with NHBoc equatorial and 2-OAc axial.

Scheme 5[a]



[a] Reagents and conditions: (a) MCPBA/CH_2Cl_2; (b) H_2O, H_2SO_4/THF/70 °C; (c) 6% Na, Hg/Na_2HPO_4/MeOH, THF/−23 °C; (d) Ac_2O/Py; (e) MCPBA/$NaHCO_3$/CH_2Cl_2/45 °C; (f) $(PhSe)_2$/*n*-BuLi/THF; (g) H_2O_2/(*i*-Pr)$_2$NEt/CH_2Cl_2, THF/50 °C; (h) 10% HCl/THF/reflux; (i) NH_3/MeOH; (j) Ac_2O/Py, cat. 4-DMAP.

C-1, was best prepared from **16** by conversion into the diol **18** (previously also obtained as one of the products of peracid oxidation of **15**; see Scheme 4), reductive desulfonylation to **35a** with sodium amalgam, and reprotection. Compound **35b** was then converted into (±)-conduramine C-1 (**39a**) and the tetraacetyl derivative **39b** by a procedure analogous to that described for (±)-conduramine A-1 and F-1. The melting points and spectroscopic properties of **39a** and **39b** were concordant with those reported in the literature[8e,f] for these substances.

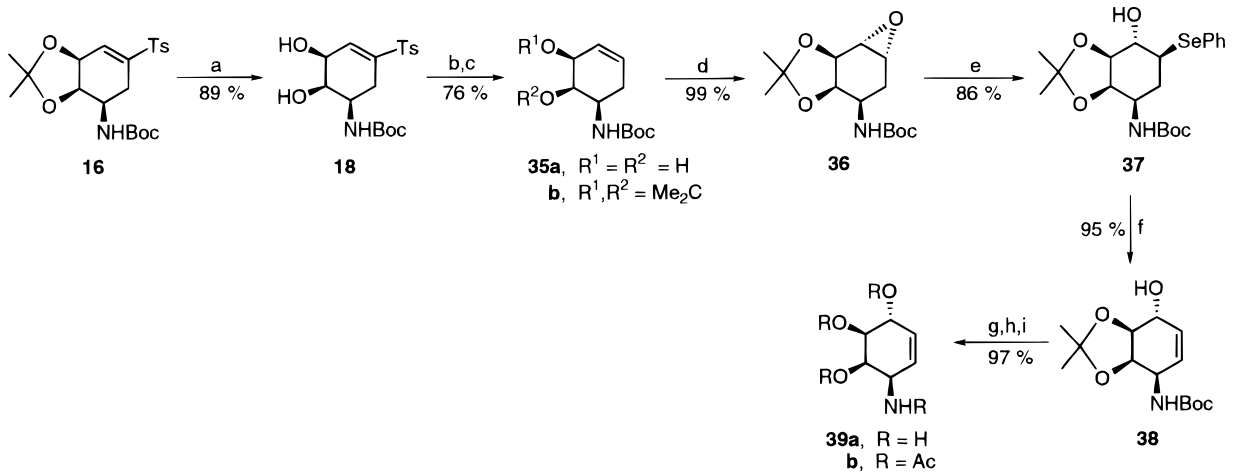
2. (±)-Conduramine D-1 (Scheme 7). This previously unknown conduramine was prepared from the unprotected *cis*-diol **35a**. (Note the arbitrary change of the absolute configuration of **35a** to correspond to the absolute configuration of (+)-**43a**. See also Scheme 8.) *m*-Chloroperoxybenzoic acid oxidation of **35a** gave the epoxide **40** with five contiguous cis substitutents exclusively, as expected for peracid epoxidation of cyclic allylic alcohols.[24,25] The transformation of **40** into (±)-conduramine D-1 (**43a**, oily HCl salt) and its crystalline tetraacetyl derivative **43b** was then effected by methodology similar to that used for the generation of several other conduramines. The small values of the H−H coupling constants (Table 2) for the tetrahedral carbons of conduramine D-1 and of its tetraacetyl derivative are fully consistent with the all-cis configuration of these compounds.

E. Generation of the Enantiomers of Azabicycloheptane 3c (Scheme 8). A most desirable route for the preparation of the enantiomers of **3c** would require the use of optically pure catalysts which could then be used to effect a catalytic, highly enantioselective, Diels−Alder reaction. Although this specific type of asymmetric cycloaddition is now known for propargylic aldehydes,[26] given the relatively vigorous conditions required to produce **3c** and its derivatives, we opted to study the preparation of the enantiomers by classical methodology. The facility with which conjugate additions to the unsaturated sulfone moiety in **3c** and its derivatives took place (Schemes 2 and 3) induced us to examine the base catalyzed reaction of **3c** with various optically pure

(25) Berti, G. *Top. Stereochem.* **1973**, *7*, 93 (See especially pp 130−152).

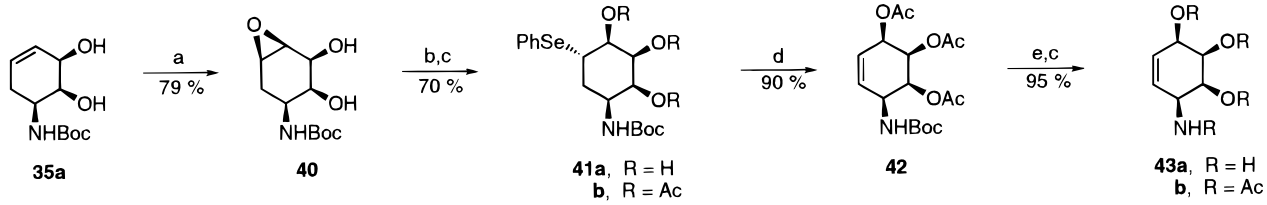
(26) Ishihara, K.; Kondo, S.; Kurihara, H.; Yamamoto, H. *J. Org. Chem.* **1997**, *62*, 3026.

Scheme 6[a]



[a] Reagents and conditions: (a) MeOH/cat. TsOH; (b) 6% Na, Hg/Na_2HPO_4/MeOH, THF/−23 °C; (c) $Me_2C(OMe)_2$, Me_2CO/cat. TsOH; (d) MCPBA/$NaHCO_3$/CH_2Cl_2; (e) $(PhSe)_2$/*n*-BuLi/THF; (f) H_2O_2/(*i*-Pr)$_2$NEt/CH_2Cl_2/0 °C, then THF/Δ; (g) TFA, H_2/CH_2Cl_2; (h) NH_3/MeOH; (i) Ac_2O/Py, cat. 4-DMAP.

Scheme 7[a]



[a] Reagents and conditions: (a) MCPBA/$NaHCO_3$/CH_2Cl_2; (b) $(PhSe)_2$/*n*-BuLi/THF; (c) Ac_2O/Py, cat. 4-DMAP; (d) H_2O_2/(*i*-Pr)$_2$NEt/CH_2Cl_2/0 °C, then THF/Δ; (e) 5 N HCl/reflux.

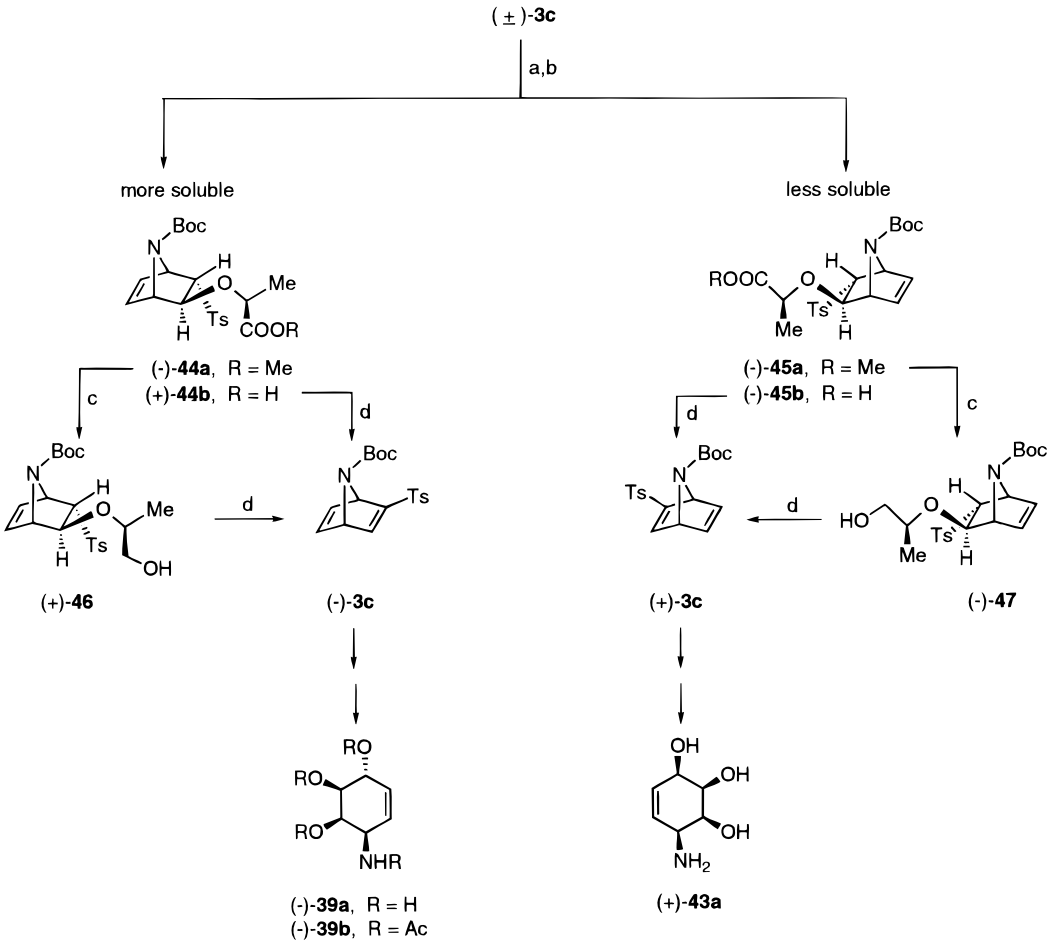
alcohols and amines. Adduct formation took place efficiently, with high exo selectivity, and in some cases the diastereomeric mixtures were separable. The most spectacularly successful example was the mixture obtained from inexpensive (−)(S)-methyl lactate (96% yield). Fractional crystallization of the mixture from hexanes−ethyl acetate (4:1) gave more and less soluble Michael adducts **44a** and **45a**, respectively (Scheme 8), each in nearly theoretical yield. Unfortunately, of all the reaction conditions studied,[27] only excess methylmagnesium bromide effected the conversion of the lactate adducts to enantiopure **3c**, albeit in poor yield (≤25%). As a consequence, a modified strategy was devised to regenerate the enantiomers of **3c** from **44a** and **45a**. Saponification of these esters on one hand and sodium trimethoxyborohydride reduction[28] on the other produced the carboxylic acids **44b** and **45b** and the primary alcohols **46** and **47**. It was hoped that, upon reaction with *n*-butyllithium, frank salt formation as well as chelation of Li^+ with the ethereal oxygen atom would facilitate anionic *β*-elimination. Addition of 2.5 equiv of *n*-butyllithium to a THF solution of either the carboxylic acids or the alcohols (−78 to −30 °C) caused the rapid appearance of **3c**, as judged by TLC. Quenching of these reaction mixtures and subsequent column chromatographic separation of the products produced enantiomerically pure (by chiral HPLC) (−)-**3c** from **44b** or **46** and (+)-**3c** from **45b** or **47**. These reactions could never, however, be forced to completion, and the yield of (−)- or (+)-**3c** never exceeded 60%, the remainder of the product being starting material. The inclusion of additives such as LiCl, $SnCl_4$, $TiCl_4$, (i-PrO)$_3$TiCl, (i-PrO)$_4$Ti, (i-PrO)$_3$B, and so forth in the above reaction mixtures did little to improve the situation. It was found, however, that the addition of incremental amounts (up to 2 equiv) of methylmagnesium bromide (THF) to the *n*-butyllithium reaction mixtures at room temperature caused rapid and complete consumption of the starting material. Then (−)- or (+)-**3c** were isolable in >80% yields from both the acids and the alcohols. In fact, *n*-butyllithium was not required; addition of 2.5 equiv of methylmagnesium bromide to THF solutions of **44b** or **46** and **45b** or **47** routinely produced (−)-**3c** and (+)-**3c** in yields exceeding 90%. In this way, the pure enantiomers (−)-**3c** and (+)-**3c** can be produced in 81−85% and 84−87% overall yields from (±)-**3c** via the carboxylic acid and alcohol routes, respectively.

F. Absolute Configuration of (−)- and (+)-3c. Synthesis of (−)-Conduramine C-1 and (+)-Conduramine (D-1). With (−)- and (+)-**3c** now available in quantity, it was a simple matter to determine their absolute stereochemistry. Since the absolute configuration of (−)- and (+)-conduramine C-1 has been established,[8e,f] we chose to find out which of these enantiomers would be obtained from (−)-**3c**. Therefore (−)-**3c** was converted into the bicyclic acetonide (−)-**8** (Scheme 2) which was transformed into the monocyclic

(27) Conditions which did not effect the reverse Michael reaction were (a) Δ/DMF, (b) Ac_2O/Py−DBU, (c) DBU/THF−reflux, (d) NaH/DMSO/70 °C, (e) KOtBu/THF−DMF/−78 °C, rt. (f) LDA−THF/−78 °C, rt. (g) *n*-BuLi−THF/−78 °C, rt.

(28) Soai, K.; Oyamada, H.; Takase, M.; Ookawa, A. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 1948.

Scheme 8[a]



[a] Reagents and conditions: (a) (−)-Methyl lactate/cat. NaH/THF, then fractional crystallization; (b) NaOH, MeOH, THF; (c) $NaBH_4$, MeOH/THF 70 °C; (d) 2.5 MeMgBr/THF.

acetonide (−)-**16** (Scheme 3), and this compound, when subjected to the sequence of reactions depicted in Scheme 6, gave rise to (−)-conduramine C-1 [(−)-**39a**, Scheme 8]. Therefore, (−)-**3c** and (+)-**3c** must have the absolute configurations shown in Scheme 8. In addition, (+)-**3c** led to (+)-**8** and (+)-**16**, and the latter compound was converted into (+)-conduramine D-1 by the reaction sequence shown in Scheme 7. This fixes the absolute configuration of (+)-conduramine D-1 as **43a** (Scheme 8).

Conclusion

The general methodological principles have been worked out for the conversion of the Boc-pyrrole-derived Diels−Alder adduct **3c** into racemic and optically pure conduramines. Two general strategies were devised for this purpose. One of these involves the regio- and stereoselective hydroxylation of **3c** to compounds such as **10b** (Scheme 2) and the exo−endo mixture **13**−**14** (Scheme 3), and subsequent anionic fragmenation (methylmagnesium bromide or lithium bis(trimethylsilylamide) to the highly functionalized cyclohexene derivatives **17** and **16**, respectively (Scheme 3). Compound **17** is an aminocyclitol with the stereochemistry of a conduramine C but with an altered substituent sequence. Compound **16** served as a precursor of (±)-conduramine C-1 (**39a**, Scheme 6) and the previously unknown, *all-cis*-(±)-conduramine D-1 (**43a**) (Scheme 7). In the second strategy, anionic fragmentation of the bicyclic system is effected before installation of the hydroxyl groups. Thus, fragmentation of the exo−endo mixture of azabicycloheptenes **11** and **12** efficiently produced the aminocyclohexadiene derivative **15** (Scheme 3) which was then transformed into (±)-tetraacetyl conduramine A-1 (**27b**, Scheme 4) and (±)-tetraacetyl conduramine F-1 (**34b**, Scheme 5).

Racemic **3c** was easily separated into enantiopure (−)-**3c** and (+)-**3c** via a process which involved fractional crystallization of the diastereomeric Michael adducts (−)-**44a** and (−)-**45a** prepared from (−)-methyl lactate (Scheme 8). Saponification or sodium trimethoxyborohydride reduction of (−)-**44a** produced (+)-**44b** or (+)-**46**, respectively. Reaction of either (+)-**44b** or (+)-**46** with excess methylmagnesium bromide generated optically pure (−)-**3c** in ca. 40% overall yield from racemic **3c**. Similarly, (−)-**45a** was transformed into (+)-**3c** via (−)-**45b** or (−)-**47** with comparable efficiency. Then (−)-**3c** and (+)-**3c** were converted into (−)-conduramine C-1 [(−)-**39a**] and (+)-conduramine D-1 [(+)-**43a**] (Scheme 8) by procedures which had previously been used for the synthesis of the corresponding racemates.

It is quite probable that the methodology disclosed herein could be applied to prepare any imaginable conduramine derivative in both the racemic and optically pure forms. In addition, the ready availability of (−)- and (+)-**3c** makes them attractive starting materials for

the synthesis of a number of natural products. The results of studies along these lines will be disclosed in due course.

Experimental Section

The terms "worked up in the usual manner", "the usual workup", and so forth signify that the organic phase was washed with saturated aqueous NaCl solution and then dried over anhydrous $MgSO_4$ or $NaSO_4$ after which the solvent was removed in vacuo. Unless stipulated otherwise, the terms "column chromatography" and "column chromatographic purification" signify purification by flash column chromatography on silica gel.

IR spectra were recorded as dispersions in KBr unless specified otherwise. NMR spectra (300 MHz) were measured in $CDCl_3$ solution at the probe temperature unless indicated otherwise.

(−)-1-Menthyloxycarbonylpyrrole (1d). A. Pyrrolylsodium. A solution of pyrrole (2.8 mL, 2.7 g, 40 mmol) in anhydrous THF (80 mL) was added to a stirred suspension of sodium hydride (1.6 g, 60% suspension in mineral oil, 40 mmol) (N_2 atmosphere) in anhydrous THF (20 mL), and then the mixture was stirred at reflux temperature for 3 h.

B. (−)-Menthyl chloroformate. Solutions of pyridine (3.3 mL, 3.2 g, 40 mmol) in dry dichloromethane (50 mL) and (−)-menthol (6.24 g, 40 mmol) in dry dichloromethane (50 mL) were added sequentially to a stirred and cooled (0 °C) solution of phosgene in toluene (23.3 mL of a 1.93 M solution, 45 mmol). Stirring at 0 °C was continued for 2 h, the mixture was filtered, and the filtrate was evaporated in vacuo to give the chloroformate as an oil.

To prepare compound **1d**, a solution of the above chloroformate in anhydrous THF (20 mL) was added to the stirred suspension of the above pyrrolylsodium cooled to 0 °C. The mixture was stirred at this temperature for 3 h, excess dilute aqueous NH_4Cl and ethyl acetate were added sequentially, and this was followed by the usual workup procedures. The crude product was purified by column chromatography, using hexane to elute pure **1d** as an oil (7.9 g, 79% yield): IR (neat) 1744 cm^{-1}; ^1H NMR δ 0.81 (3H, d, J = 7.0 Hz), 0.92 (d, 2H, J = 7.0 Hz), 0.93 (d, 2H, J = 7.0 Hz), 1.10−1.19 (m, 2H), 1.47−1.60 (m, 2H), 1.68−1.77 (m, 2H), 1.95 (sept, 0.5H, J = 7.0 Hz), 1.96 (sept, 0.5H, J = 7.0 Hz), 2.13−2.20 (m, 1H), 4.83 (dt, 1H, J = 4.4, 10.9 Hz), 6.23 (t, 2H), 7.27 (t, 2H); MS *m/z* (relative intensity) 249 (M^+, 5). Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.29; H, 9.43; N, 5.53. $[\alpha]_D$ −100.0° (*c* 0.121, $CHCl_3$).

Synthesis of the 2-Arylsulfonyl-7-alkoxycarbonyl-7-azabicyclo[2.2.1]heptadienes (3). (±)-2-*p*-Toluenesulfonyl-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]-heptadiene (3c). The synthesis of this compound was typical. A mixture of 1-*tert*-butoxycarbonylpyrrole (**1c**)[29] (33.4 g, 0.2 mol) and ethynyl *p*-tolyl sulfone[30] (**2a**) (18.0 g, 0.1 mol) was heated in an inert atmosphere at 80−85 °C for 48 h. The reaction mixture was separated into its components by column chromatography. Elution with hexanes−ethyl acetate (95:5) gave recovered **1c** (16.5 g), and a small amount of **2a** (0.2 g) was eluted with hexanes−ethyl acetate (9:1). The product was eluted with hexanes−ethyl acetate (4:1) as a solid which on crystallization from hexanes−ethyl acetate gave pure **3c** (29.5 g, 84% yield), mp 97−98 °C. A reaction carried out on triple this scale gave pure **3c** in 82% yield: IR 1707, 1595, 1372, 1345, 1316, 1152 cm^{-1}; ^{13}C NMR (DMSO-d_6; 340 K) δ 20.98, 27.54 (3C), 66.49, 67.86, 80.46, 127.57 (2C), 130.13 (2C), 135.64, 141.72 (2C), 142.78, 144.72, 153.12, 158.25; MS *m/z* (rel intensity) 347 (M^+, 2), 291 (6), 182 (18), 92 (23), 91 (24), 67 (51), 57 (100). Anal. Calcd for $C_{18}H_{21}NO_4S$: C, 62.23; H, 6.09; N, 4.03. Found: C, 62.25; H, 5.91; N, 4.27.

The enantiomers could be separated by HPLC on a Chiracel OD-H column using hexanes−ethyl acetate (9:1), a flow rate of 0.8 mL/min and scanning at 230 nm. Two equiintense peaks at 22.3 and 25.2 min corresponding to (+)- and (−)-**3c**, respectively, were observed (see below).

(±)-2-*p*-Toluenesulfonyl-7-ethoxycarbonyl-7-azabicyclo-[2.2.1]heptadiene (3b): obtained in 75% yield as an oil; MS *m/z* (rel intensity) 319 (M^+, 8), 164 (25), 139 (100), 92 (19), 91 (18), 67 (19). Anal. Calcd for $C_{16}H_{17}NO_4S$: C, 60.17; H, 5.37; N, 4.39. Found: C, 60.36; H, 5.05; N, 4.18.

(±)-2-*p*-Toluenesulfonyl-7-(−)-menthyloxycarbonyl-7-azabicyclo[2.2.1] heptadiene (3d): obtained in 75% yield as a foam; MS *m/z* (rel intensity) 429 (M^+, 5), 292 (14), 274 (12), 249 (30), 233 (24), 182 (18), 155 (17), 138 (45), 136 (21), 97 (25), 92 (33), 91 (50), 83 (100), 67 (44), 57 (47). Anal. Calcd for $C_{24}H_{31}NO_4S$: C, 67.10; H, 7.27; N, 3.26. Found: C, 66.89; H, 7.50; N, 3.21.

(±)-2-*p*-Toluenesulfonyl-5-*exo*-6-*exo*-dihydroxy-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]hept-2-ene (7). A. Direct Process. Solutions of compound **3c** (13.9 g, 40 mmol) in THF (50 mL), *N*-methylmorpholine-*N*-oxide (7.0 g, 60 mmol), and osmium tetroxide (4 mL of a 2.5 wt % solution in *tert*-butyl alcohol) were added in succession to a stirred solution of sodium bicarbonate (3.36 g, 40 mmol) in *tert*-butyl alcohol (320 mL) and water (80 mL). The reaction mixture was stirred at room temperature for 16 h (complete by TLC after 5 h), and then excess 10% aqueous $NaHSO_3$ solution was added. Stirring was continued for 30−45 min, and then the reaction mixture was diluted with a large volume of ethyl acetate and worked up in the usual manner. Compound **7** was isolated from the crude reaction product by column chromatography on silica gel, using hexanes−ethyl acetate (7:3) and then dichloromethane−methanol (98:2) to elute the solid product. Recrystallization of this material from hexanes−ethyl acetate gave **7** as a solid (11.5 g, 73%): mp 168−170 °C; IR 3443, 1713, 1688, 1590, 1387, 1317 cm^{-1}. Anal. Calcd for $C_{13}H_{23}NO_6S$: C, 56.68; H, 6.08; N, 3.67. Found: C, 56.71; H, 6.26; N, 3.18.

(−)-2-*p*-Toluenesulfonyl-5-*exo*,6-*exo*-dihydroxy-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]hept-2-ene [(−)-7]. This compound was prepared by the method used for (±)-**7** except that the reaction time was 2.5 h. Pure (−)-**7** was obtained in 89% yield: mp 152−153 °C; ^{13}C NMR (DMSO-d_6 + $CDCl_3$; 360 K) δ 21.42, 27.80 (3C), 66.92, 67.64, 68.27, 80.81, 128.02 (2C), 129.71 (2C), 136.44, 143.59, 145.03, 150.35, 155.98. Anal. Calcd for $C_{18}H_{23}NO_6S$: C, 56.68; H, 6.08; N, 3.67. Found: C, 56.78; H, 6.23; N, 3.76. $[\alpha]_D$ −24.7° (*c* 0.2185, $CHCl_3$).

(+)-2-*p*-Toluenesulfonyl-5-*exo*,6-*exo*-dihydroxy-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]hept-2-ene [(+)-7]. This compound was prepared by the method used for (±)-**7**, except that the reaction time was 6 h. Pure (+)-**7**, obtained in 84% yield after crystallization from ethyl acetate−hexane, had mp 150−151 °C. Anal. Calcd for $C_{18}H_{23}NO_6S$: C, 56.68; H, 6.08; N, 3.67. Found: C, 56.53; H, 6.18; N, 3.67. $[\alpha]_D$ +23.3° (*c* 0.245, $CHCl_3$).

B. Via Phenyl Boronic Acid Ester 6. A solution of **3c** (19.0 g, 55 mmol) was added to a stirred mixture of dichloromethane (150 mL), osmium tetroxide (18 mL of a 2.5 wt % solution in *tert*-butyl alcohol), *N*-methylmorpholine *N*-oxide (8.4 g, 71.5 mmol), and phenylboronic acid (8.72 g, 71.5 mmol). After 24 h, a 10% $NaHSO_3$ solution was added, and after 1 h, the mixture was filtered through Celite. The filtrate was concentrated in vacuo, and the phenyl boronate **6** was isolated from the residue by column chromatography, using dichloromethane−ethyl acetate (9:1) to elute the solid product (24.3 g). Crystallization of this material from dichloromethane−ethyl acetate gave pure **6** (23.6 g, 92% yield): mp 197−200 °C; IR 1709, 1372, 1325, 1157 cm^{-1}; ^{13}C NMR δ 21.70, 27.66 (3C), 65.48, 66.78, 79.2, 80.10, 81.57, 127.85, 128.71, 130.32, 131.82, 135.00, 135.9, 143.8, 145.58; MS *m/z* (rel intensity) 467 (M^+, 4). Anal. Calcd for $C_{24}H_{26}BNO_6S$: C, 61.68; H, 5.61; N, 3.00. Found: C, 61.76; H, 6.01; N, 3.16.

Aqueous hydrogen peroxide (30%, 50 mL) was added to a stirred solution of the above boronate (20.1 g, 43 mmol) in THF (200 mL) and dichloromethane (300 mL) at room temperature.

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After 1 h, water (250 mL) was added, and 0.5 h later the organic phase was separated and washed with 10% aqueous $NaHSO_3$ solution. After the usual workup, the crude product was purified by flash column chromatography on neutral alumina (Act II), using dichloromethane and then dichloromethane−methanol (9:1) to elute the pure crystalline diol **7** (14.5 g, 88% yield).

Acetonide of (±)-2-*p*-Toluenesulfonyl-5-*exo*,6-*exo*-dihydroxy-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]hept-2-ene (8). A solution of the diol **7** (18.0 g, 47.2 mmol) in acetone (75 mL) and 2,2-dimethoxypropane (75 mL) containing *p*-toluenesulfonic acid monohydrate (0.5 g) was stirred at room temperature for 3 h. The solution was made neutral with a few drops of triethylamine, and then the volatile materials were removed in vacuo. The residue was dissolved in ethyl acetate and washed with dilute HCl solution, and the organic phase was worked up in the usual way.

The residue was crystallized from ethyl acetate to give a solid (16.9 g, 85% yield): mp 121−122 °C; IR 1717, 1370, 1354, 1318, 1152 cm^{-1}; ^{13}C NMR (320 K) δ 21.68, 25.62, 26.23, 27.82 (3C), 64.25, 65.18, 78.90, 79.80, 80.86, 116.69, 128.16, 130.29, 135.8, 144.37, 145.41, 150.8, 155.1; MS *m/z* (CI/NH_3) (rel intensity) 439 (MH^+, 4), 383 (4), 322 (23), 299 (23), 297 (71), 280 (100), 161 (46). Anal. Calcd for $C_{21}H_{27}NO_6S$: C, 59.84; H, 6.46; N, 3.32. Found: C, 59.99; H, 6.42; N, 3.27.

If this acetonide was prepared without purification of the crude dihydroxy compound **7** (prepared by method a), the yield of **8** was 83%.

Acetonide of (−)-2-*p*-Toluenesulfonyl-5-*exo*,6-*exo*-dihydroxy-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]-heptene-2-ene [(−)-8]. This compound was prepared in 97% yield by the method used for (±)-**8**, except that the reaction time was 0.5 h, and the pure compound was obtained by column chromatography, using hexanes−ethyl acetate (4:1) as the eluant. Pure (−)-**8** had mp 148−149 °C. Anal. Calcd for $C_{21}H_{27}NO_6S$: C, 59.84; H, 6.46; N, 3.32. Found: C, 60.12; H, 6.53; N, 3.45. $[\alpha]_D$ −15.5° (*c* 1.1175, $CHCl_3$).

Acetonide of (+)-2-*p*-Toluenesulfonyl-5-*exo*,6-*exo*-dihydroxy-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]hepten-2-ene [(+)-8]. This compound was prepared by the method used for (±)-**8**. Pure (+)-**8** was obtained in 96% yield after column chromatography [hexanes−ethyl acetate mixtures (9:1 and then 4:1)] and crystallization from hexanes−ethyl acetate. It had mp 119−120 °C. Anal. Calcd for $C_{21}H_{27}NO_6S$: C, 59.84; H, 6.46; N, 3.32. Found: C, 59.76; H, 6.63; N, 3.47. $[\alpha]_D$ +15.3° (*c* 1.06, $CHCl_3$).

Synthesis of Benzaldoxime Adducts (±)-9a and (±)-10a from (±)-8. A solution of sodium methylsulfinylmethide in DMSO (3 mL of a 0.1 M solution, 0.3 mmol) was added to a stirred solution of benzaldoxime (0.36 g, 3 mmol) in anhydrous DMSO (40 mL), and this solution was heated at 70 °C for 0.5 h. To this solution, at room temperature, was added a solution of **8** (1.26 g, 3 mmol) in dry DMSO (15 mL), and the resulting solution was stirred at room temperature for 16 h. The solution was poured onto ice, acidified with dilute HCl, and extracted with ethyl acetate. The extract was washed with a 10% NaOH solution and then worked up in the usual manner.

The solvent was removed in vacuo, and the residue was separated into its components by column chromatography, using hexanes−ethyl acetate mixtures (9:1 and then 85:15) as eluants. The 2-endo-3-exo compound **9** was eluted first (0.18 g, 11%), followed by the 2-exo-3-endo adduct **10a** (1.34 g, 82%). Compound **9**: mp 78−80 °C (hexanes−ethyl acetate); IR (KBr) 1705, 1638, 1383, 1152 cm^{-1}. Anal. Calcd for $C_{28}H_{34}N_2O_7S$: C, 61.97; H, 6.32; N, 5.16. Found: C, 61.97; H, 6.55; N, 4.95.

Compound **10a**: mp 171 °C (hexanes−ethyl acetate); IR 1709, 1630, 1597, 1392, 1370, 1150 cm^{-1}. Anal. Calcd for $C_{28}H_{34}N_2O_7S$: C, 61.97; H, 6.32; N, 5.16. Found: C, 61.92; H, 6.28; N, 5.15.

Acetonide of (±)-2-*exo*-*p*-Toluenesulfonyl-3-*endo*-hydroxy-5-*exo*,6-*exo*-dihydroxy-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]heptane (10b). A solution of trifluoroacetic acid (1.9 mL, 2.85 g, 25 mmol) in THF (5 mL) was added to a stirred suspension of sodium borohydride (0.95 g, 25 mmol) in THF (75 mL) at room temperature. When gas evolution had ceased, a solution of the oximate **10a** (1.7 g, 3.1 mmol) in THF (25 mL) was added, and the reaction mixture was stirred for 2 h at room temperature, followed by stirring for 2 h at reflux temperature. Dilute hydrochloric acid was added to the reaction mixture at room temperature, and then it was evaporated to dryness in vacuo. Dichloromethane was added to the residue and the organic phase was washed successively with dilute NH_4Cl solution and saturated NaCl solution and then was dried ($MgSO_4$). The solvent was evaporated in vacuo, and the residue was subjected to column chromatographic purification. Elution with hexanes−ethyl acetate mixtures (4:1 and then 1:1) gave the *endo*-hydroxy compound **10b** as a solid (1.15 g, 85% yield): mp 208−209 °C (ethyl acetate−hexane); IR (KBr) 3434, 1707, 1676, 1152 cm^{-1}. Anal. Calcd for $C_{21}H_{29}NO_7S$: C, 57.39; H, 6.65; N, 3.19. Found: C, 57.38; H, 6.72; N, 3.36.

(±)-2-*exo*- and (±)-2-*endo*-*p*-Toluenesulfonyl-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]hept-5-ene (11 and 12). A mixture of the diene **3c** (1.39 g, 4 mmol) and sodium borohydride (1.20 g, 32 mmol) in methanol (80 mL) was stirred at room temperature for 3 h. The reaction mixture was made acidic with dilute HCl solution, the volatile materials were removed in vacuo, and ethyl acetate was added to the residue. After the usual workup the product mixture was separated into its components by column chromatography, using hexanes−ethyl acetate mixtures (4:1 and then 1:1) to elute the less polar *endo*-sulfone **12** and then the *exo*-sulfone **11**. Crystallization of the exo isomer from dichloromethane−pentane gave pure **11** (0.12 g, 9%): mp 95−96 °C; IR 1715, 1370, 1165, 1150 cm^{-1}; ^{13}C NMR (DMSO-d_6, 330 K) δ 20.65, 27.25, 27.55 (3C), 58.82, 60.72, 62.74, 79.09, 127.05, 128.22 (2C), 129.38 (2C), 129.69, 135.26, 143.94, 152.61. Anal. Calcd for $C_{18}H_{23}NO_4S$: C, 61.87; H, 6.63; N, 4.01. Found: C, 61.63; H, 6.55; N, 3.88. Crystallization of the endo isomer from hexanes−ethyl acetate gave pure **12** (1.20 g, 86%): mp 101−102 °C; IR 1717, 1370, 1350, 1150 cm^{-1}; ^{13}C NMR (DMSO-d_6, 330 K) δ 20.74, 27.46 (3C), 28.25, 60.50 (2C), 61.30, 79.74, 127.15, 127.42 (2C), 129.70 (2C), 131.00, 136.65, 144.19, 153.20. Anal. Calcd for $C_{18}H_{23}NO_4S$: C, 61.87; H, 6.63; N, 4.01. Found: C, 62.09; H. 6.60; N, 4.22.

Both **11** and **12** readily undergo fragmentation to 1-*tert*-butoxycarbonylpyrrole and *p*-toluenesulfonylethylene at ca. 60 °C.

Acetonides of (±)-2-*exo*- and (±)-2-*endo*-*p*-Toluenesulfonyl-5-*exo*,6-*exo*-dihydroxy-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]heptane (13 and 14). A mixture of compound **8** (8.4 g, 20 mmol) and sodium borohydride (6.1 g, 160 mmol) in methanol (300 mL) was stirred at 0 °C for 2 h, and then the reaction mixture was worked up as above for **11** and **12**. The crude product was separated into its components by column chromatography exactly as described for **11** and **12**. The endo isomer **14** (0.80 g, 9%) was eluted first. The major, more polar, exo isomer **13** (7.62 g, 90%): mp 169−171 °C (ethyl acetate−hexane); IR 1701, 1368, 1152 cm^{-1}; MS *m/e* (CI/NH_3) (rel intensity) 441 [$(MNH_4)^+$, 20], 384 (100), 324 (44), 168 (33). Anal. Calcd for $C_{21}H_{29}NO_6S$: C, 59.55; H, 6.90; N, 3.31. Found: C, 59.83; H, 6.66; N, 2.98. The endo isomer **14**: mp 134−136 °C (ethyl acetate−hexane); IR 1705, 1371, 1146 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 21.33, 24.20, 25.34, 28.05 (3C), 59.64, 59.99, 61.60, 80.74, 81.15, 110.59, 127.62 (2C), 130.15 (2C), 136.06, 145.02, 153.81. Anal. Calcd for $C_{21}H_{29}NO_6S$: C, 59.55; H, 6.90; N, 3.31. Found: C, 59.65; H, 6.94; N, 3.46.

Acetonides of (−)-2(*S*)-*exo*- and (+)-2(*R*)-*endo*-*p*-Toluenesulfonyl-5-*exo*,6-*exo*-dihydroxy-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]heptane [(−)-2(*S*)-13 and (+)-2(*R*)-14]. These were prepared by the method used for the racemates except that hexanes−ethyl acetate (4:1) was used as the eluant for the chromatographic separation of the exo and endo isomers. The exo compound (−)-2-(S)-**13** was obtained in 85% yield and had mp 179−180 °C. Anal. Calcd for $C_{21}H_{29}NO_6S$: C, 59.55; H, 6.90; N, 3.31. Found: C, 59.70; H, 6.97; N, 3.43. $[\alpha]_D$ −39.8° (*c* 1.0225, $CHCl_3$).

The endo compound (+)-2-(R)-**14** was isolated in 11% yield and had mp 134−136 °C. Anal. Calcd for $C_{21}H_{29}NO_6S$: C, 59.55; H, 6.90; N, 3.31. Found: C, 59.65; H, 6.94; N, 3.46. $[\alpha]_D$ +20.0° (*c* 0.545, $CHCl_3$).

Acetonides of (+)-2(*R*)-*exo*- and (−)-2(*S*)-*endo*-*p*-Toluenesulfonyl-5-*exo*,6-*exo*-dihydroxy-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]heptane [(+)-2(*R*)-13 and (−)-2(*S*)-14]. These compounds were prepared by the method used for the racemates except that the chromatographic separation was effected, using hexanes−ethyl acetate mixtures (4:1 and then 1:1) as the eluting solvents. (+)-2(*R*)-*exo*-**13** was obtained in 88% and had mp 167−169 °C. Anal. Calcd for $C_{21}H_{29}NO_6S$: C, 59.55; H, 6.90; N, 3.31. Found: C, 59.81; H, 6.97; N, 3.32. $[\alpha]_D$ +39.9° (*c* 1.055, $CHCl_3$).

The (−)-2(*S*)-*endo*-**14** was obtained in 9.5% yield and had mp 129−131 °C. Anal. Calcd for $C_{21}H_{29}NO_6S$: C, 59.55; H, 6.90; N, 3.31. Found: C, 59.53; H, 7.00; N, 3.25. $[\alpha]_D$ −20.2° (*c* 0.535, $CHCl_3$).

(±)-1-*p*-Toluenesulfonyl-5-*tert*-butoxycarbonylamino-1,3-cyclohexadiene (15). A solution of a mixture of the *exo*- and *endo*-sulfones **11** and **12** (13.0 g, 37.5 mmol) in dry THF (50 mL) was added dropwise to a stirred solution of lithium bis(trimethylsilyl)amide (56.2 mmol) in THF (450 mL) at −78 °C (inert atmosphere). After the solution was added, the reaction mixture was left to warm to −20 °C at which temperature stirring was continued for 45 min. The reaction mixture was quenched with excess dilute NH_4Cl solution, ethyl acetate was added, and after the usual workup, the product was obtained pure by column chromatography. It was eluted from the column with hexanes−ethyl acetate (4:1), and on crystallization of the material so obtained from hexanes−ethyl acetate, **15** was isolated as a white solid (10.4 g, 76%): mp 130−132 °C; IR 3428, 3328, 1701, 1676, 1366, 1151 cm^{-1}; ^{13}C NMR (330 K) δ 21.49, 28.01, 28.08 (3C), 42.80, 79.65, 123.85, 127.92, 129.59, 129.82, 131.86, 135.76, 136.20, 144.29, 154.34. Anal. Calcd for $C_{18}H_{23}NO_4S$: C, 61.87; H, 6.63; N, 4.01. Found: C, 61.97; H, 6.70; N, 4.15.

Acetonide of (±)-1-*p*-Toluenesulfonyl-3,4-*cis*-dihydroxy-5-*cis*-*tert*-butoxycarbonylaminocyclohexene (16). A solution of a mixture of the *exo*- and *endo*-sulfones **13** and **14** (6.1 g, 14.4 mmol) in dry THF (50 mL) was added dropwise at −78 °C (inert atmosphere) to a stirred solution of lithium bis(trimethylsilyl)amide (21 mmol) in THF (250 mL). The reaction mixture was left to reach room temperature (1 h), and after an additional hour, it was worked up exactly as described for the synthesis of **15**. After crystallization of the crude product from hexanes−ethyl acetate, **16** was obtained as a white solid (4.8 g, 79%): mp 181−182 °C; IR 3437, 3374, 1713, 1696, 1522, 1370, 1152 cm^{-1}; ^{13}C NMR δ 21.67, 24.56, 26.47, 27.73, 28.33 (3C), 72.78, 74.44, 80.15, 110.28, 128.30 (2C), 130.02 (2C), 132.76, 135.26, 140.04, 144.87, 155.00. Anal. Calcd for $C_{21}H_{29}NO_6S$: C, 59.55; H, 6.90; N, 3.30. Found: C, 59.95; H, 6.69; N, 2.97.

Acetonide of (−)-1-*p*-Toluenesulfonyl-3,4-*cis*-dihydroxy-5-*cis*-*tert*-butoxycarbonylaminocyclohexene [(−)-16]. This compound was prepared in the manner described for (±)-**16** except that pure (−)-2(*S*)-*exo*-**13** was used and hexanes−ethyl acetate (85:15) was the solvent system utilized in the column chromatographic purification. Pure (−)-**16** was obtained in 80% yield and had mp 132−134 °C. Anal. Calcd for $C_{21}H_{29}NO_6S$: C, 59.55; H, 6.90; N, 3.31. Found: C, 59.70; H, 6.70; N, 3.17. $[\alpha]_D$ −26.3° (*c* 0.6465, $CHCl_3$).

Acetonide of (+)-1-*p*-Toluenesulfonyl-3,4-*cis*-dihydroxy-5-*cis*-*tert*-butoxycarbonylaminocyclohexene [(+)-16]. This compound was prepared in the manner used for (±)-**16** except that (+)-2(*R*)-**13** was used, and (+)-**16** was eluted from the column with hexanes−ethyl acetate (4:1). After crystallization from hexanes−ethyl acetate, pure (+)-**16** was obtained in 75% yield and had mp 173−175 °C. Anal. Calcd for $C_{21}H_{29}NO_6S$: C, 59.55; H, 6.90; N, 3.31. Found: C, 59.70; H, 6.64; N, 3.39. $[\alpha]_D$ +25.5° (*c* 0.710, $CHCl_3$).

Acetonide of (±)-1-*p*-Toluenesulfonyl-*cis*-3,4-dihydroxy-*cis*-5-*tert*-butoxycarbonylamino-*trans*-6-hydroxycyclohexene (17). All solutions were degassed by passing a slow stream of argon through them for 5−10 min while they were being sonicated. A THF−toluene solution of methylmagnesium bromide (8.8 mL of a 1.4 M solution, 12.3 mmol) was added in six equal portions at 5 min intervals to a stirred solution of **10b** (0.90 g, 2.05 mmol) in dry THF (75 mL) under an argon atmosphere. The reaction mixture was then stirred for an additional 1.5 h and quenched with dilute HCl solution. After the usual workup, the crude product was purified by column chromatography. Elution with hexanes−ethyl acetate (7:3) gave **17** (0.75 g, 83%), and further elution with 1:1 hexanes−ethyl acetate gave a small amount (0.052 g, 6%) of the starting material. Compound **17**: mp 185 °C (ethyl acetate−hexane); IR 3441, 1713, 1676, 1597, 1370, 1150 cm^{-1}; ^{13}C NMR (DMSO-d_6, 350 K) δ 20.97, 25.82, 27.25, 28.02 (3C), 53.54, 63.62, 71.25, 74.45, 109.18, 127.98 (2C), 129.34 (2C), 135.91, 137.65, 142.65, 143.81, 155.15. Anal. Calcd for $C_{21}H_{29}NO_7S$: C, 57.39; H, 6.65; N, 3.19. Found: C, 57.45; H, 6.73; N, 3.35.

(±)-1-*p*-Toluenesulfonyl-*cis*-3,4-dihydroxy-5-*cis*-*tert*-butoxycarbonylaminocyclohexene (18). A solution of compound **16** (2.12 g, 5.0 mmol) in methanol (150 mL) containing *p*-toluenesulfonic acid monohydrate (0.2 g) was stirred at room temperature for 6 h. A few drops of triethylamine was added, and the solvent was removed in vacuo. The residue was dissolved in ethyl acetate, washed with dilute HCl, and dried, and the solvent was eliminated in vacuo. Crude **18** was purified by column chromatography, using hexanes−ethyl acetate (4:1), followed by dichloromethane−methanol (99:1) as the eluant. Compound **18** was obtained as a solid (1.71 g, 89%): mp 189−189.5 °C (ethyl acetate−hexane); IR 3430, 3373, 1709, 1663, 1534, 1146 cm^{-1}; ^{13}C NMR (DMSO-d_6, 315 K) δ 21.64, 26.47, 28.81 (3C), 50.53, 69.33, 70.28, 80.55, 129.26 (2C), 131.08 (2C), 136.98, 138.74, 140.32, 146.27, 157.50. Anal. Calcd for $C_{18}H_{25}NO_6S$: C, 56.38; H, 6.57; N, 3.62. Found: C, 56.53; H, 6.72; N, 3.52.

This compound could also be obtained as one component of the 1:1 mixture produced upon osmate catalyzed cis dihydroxylation of the diene **15**.

(+)-1-*p*-Toluenesulfonyl-*cis*-3(*S*),4(*R*)-Dihydroxy-5(*R*)-*cis*-*tert*-butoxycarbonylaminocyclohexene [(+)-3(*S*),4(*R*),5(*R*)-18]. This compound was prepared from (−)-**16** by the method used to prepare (±)-**18** except that the column chromatographic purification was effected with ethyl acetate−hexane (4:1) and dichloromethane−methanol (98:2) as the eluting solvents. Pure (+)-**18** was obtained in 95% yield and had mp 207 °C. Anal. Calcd for $C_{18}H_{25}NO_6S$: C, 56.38; H, 6.57; N, 3.62. Found: C, 56.28; H, 6.70; N, 3.45. $[\alpha]_D$ +39.1° (*c* 0.2325, $CHCl_3$). The specific rotation was identical in methanol solution.

(−)-1-*p*-Toluenesulfonyl-*cis*-3(*R*),4(*S*)-Dihydroxy-5(*R*)-*cis*-*tert*-butoxycarbonylaminocyclohexene [(−)-3(*R*),4(*S*),5(*R*)-18]. This compound was prepared from (+)-**16** in the same manner that was used to obtain the racemate except that the chromatographic purification was effected with hexanes−ethyl acetate mixtures (4:1 and then 98:2) as the eluting solvents. Pure (−)-**18** was obtained in 92% yield as a solid and had mp 188−189 °C. Anal. Calcd for $C_{18}H_{25}NO_6S$: C, 56.38; H, 6.57; N, 3.62. Found: C, 56.34; H, 6.65; N, 3.48. $[\alpha]_D$ -40.0° (*c* 0.355, $CHCl_3$).

***N*,*N*-Bis-*tert*-butoxy Derivative of (±)-1-*p*-Toluenesulfonyl-5-aminocyclohex-1,3-diene (20).** A solution of the diene **15** (2.1 g, 6 mmol) in acetonitrile (100 mL) containing di-*tert*-butyldicarbonate (2.6 g, 12 mmol) and 4-(dimethylamino)pyridine (0.250 g) was stirred at room temperature for 16 h. The reaction mixture was diluted with ethyl acetate, and the resulting solution was washed with dilute aqueous HCl and then worked up in the usual way. The pure bis-Boc derivative **20** (2.25 g, 85%) was obtained by column chromatography of the crude product, using hexanes−ethyl acetate (4:1) as the eluant. Pure **20** had mp 121−122 °C (hexanes−ethyl acetate); IR 1755, 1707, 1370, 1152 cm^{-1}; ^{13}C NMR δ 21.61, 25.72, 27.96 (6C), 52.92, 80.30 (2C), 120.18, 128.07 (2C), 129.87 (2C), 130.18, 135.00, 136.31, 136.76, 144.36, 152.01 (2C). Anal. Calcd for $C_{23}H_{31}NO_6S$: C, 61.45; H, 6.95; N, 3.12. Found: C, 61.54; H, 7.02; N, 3.21.

***N,N*-Bis-*tert*-butoxycarbonyl Derivative of (±)-1-*p*-Toluenesulfonyl-3,4-*cis*-dihydroxy-*trans*-5-aminocyclohexene (21).** Compound **20** was converted into the *cis*-diol **21** by the same method which was used to convert **3c** into **7**. Purification of the crude product by column chromatography, using hexanes−ethyl acetate mixtures (3:1 and then 1:1), eluted pure **21** in 91% yield: mp 156−159 °C (ethyl acetate−hexane); IR 3445, 1740, 1701, 1653, 1647, 1635, 1370, 1152 cm^{-1}; ^{13}C NMR δ 21.63, 27.62, 27.79 (6C), 52.93, 65.86, 68.80, 83.18 (2C), 128.38 (2C), 130.05 (2C), 133.79, 135.07, 142.81, 144.94, 153.37 (2C). Anal. Calcd for $C_{23}H_{33}NO_8S$: C, 57.13; H, 6.88; N, 2.90. Found: C, 57.01; H, 6.93; N, 2.49.

(±)-3,4-*cis*-Dihydroxy-5-*trans*-*tert*-butoxycarbonylaminocyclohexene (22). Sodium amalgam (6%, 8 g) was added in 2 g portions over a 30 min period to a stirred and cooled (−12 °C) solution of compound **21** (1.00 g, 2.1 mmol) in a 1:1 THF−MeOH mixture (40 mL) containing disodium hydrogen phosphate (8.5 g, 60 mmol) (inert atmosphere). The reaction mixture was stirred at −12 °C for 1 h and then quenched with dilute aqueous HCl. After being partitioned with ethyl acetate, the organic phase was worked up in the usual manner, and crude product was purified by column chromatography, using hexanes−ethyl acetate (1:1), followed by dichloromethane−methanol (99:1) to elute **22** as an oil (0.230 g, 49%): IR (neat) 3301, 1708 (w), 1682, 1545 cm^{-1}; MS *m/z* (CI/NH_3) (rel intensity) 247 [$(MNH_4)^+$, 100], 230 (MH^+, 71), 191 (42); ^{13}C NMR (330 K) δ 28.39 (3C), 32.22, 48.20, 66.65, 69.35, 80.25, 126.93, 129.57, 157.20. This compound was directly converted into the crystalline acetonide **23**.

Acetonide of (±)-3,4-*cis*-Dihydroxy-5-*trans*-*tert*-butoxycarbonylaminocyclohexene (23). This compound was synthesized in the same manner as described for compound **8** except that the reaction time was 4 h. The crude product was purified by column chromatography, using hexanes−ethyl acetate (3:1) to elute pure **23** (85% yield): mp 110−112 °C (hexanes−ethyl acetate); IR 3378, 3345, 1700 (sh), 1682 cm^{-1}; ^{13}C NMR (315 K) δ 26.24, 28.15, 28.34 (3C), 28.94, 48.86, 71.86, 75.98, 79.80, 109.27, 125.04, 129.15, 155.59. Anal. Calcd for $C_{11}H_{23}NO_4$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.49; H, 8.61; N, 5.09.

Acetonide of (±)-1,2-Epoxy-*anti*-3,4-*cis*-dihydroxy-5-*trans*-*tert*-butyoxycarbonylaminocyclohexane (24). A mixture of **23** (0.035 g, 0.13 mmol), *m*-chloroperoxybenzoic acid (0.053 g, 0.26 mmol), and sodium bicarbonate (0.022 g, 0.26 mmol) in dichloromethane (10 mL) was stirred at room temperature for 16 h. The organic phase was separated and then worked up in the usual manner. Purification of the crude product by column chromatography, using hexanes−ethyl acetate mixtures (95:5, 9:1 and 85:15), gave **24** as a solid (0.035 g, 95% yield) which, after crystallization from ethyl acetate−hexane, had mp 66−68 °C (hexanes−ethyl acetate); IR (neat) 3436, 1717 cm^{-1}; ^{13}C NMR δ 23.93, 25.79, 27.74, 28.40 (3C), 42.59, 52.30, 52.45, 70.05, 73.11, 79.51, 109.76, 155.12. Anal. Calcd for $C_{14}H_{23}NO_5$: C, 58.93; H, 8.13; N, 4.91. Found: C, 59.11; H, 7.99; N, 4.57.

Acetonide of (±)-1-Phenylseleno-*trans*-2-hydroxy-*anti*-3,4-*cis*-dihydroxy-5-*trans*-*tert*-butoxycarbonylaminocyclohexane (25). A solution of *n*-butyllithium in hexane (56 μL, 2.5 M, 0.14 mmol) was added to a stirred solution of diphenyl diselenide (0.044 g, 0.14 mmol) in anhydrous THF (5 mL, inert atmosphere). After 5 min, a solution of the epoxide **24** (0.020 g, 0.07 mmol) in THF (2 mL) was added, and stirring at room temperature was continued for 16 h. Dilute hydrochloride acid was added to the reaction mixture, followed by ethyl acetate. The organic phase was worked up as usual. The crude product was purified by preparative TLC on silica gel, using hexanes−ethyl acetate (1:1) as the developing solvent. Compound **25** was obtained as a solid (0.026 g, 84% yield): mp 55−58 °C (hexanes−ethyl acetate); IR 3428, 1686 cm^{-1}; ^{13}C NMR δ 26.17, 27.95, 28.39 (3C), 32.73, 42.56, 48.49, 74.01, 77.20, 78.96, 109.59, 128.64, 129.25, 136.31, 148.9; HRMS calcd for $C_{20}H_{29}NO_5{}^{78}Se$ 441.1219, found 441.1198.

Acetonide of (±)-*N*-*tert*-Butoxycarbonyl Conduramine A-1 (26). To a stirred and cooled (0 °C) solution of the phenylseleno compound **25** (0.040 g, 0.090 mmol) in dichloromethane (5 mL) was added 30% aqueous hydrogen peroxide (0.1 mL) and diisopropylethylamine (0.1 mL). After 15 min, THF (5 mL) was added, and the mixture was heated at 50 °C for 1.5 h. The mixture was cooled to room temperature, ethyl acetate was added, and the organic phase was washed successively with dilute sodium carbonate solution, dilute hydrochloric acid, and saturated NaCl solution. The dried organic phase was evaporated in vacuo, and the residue was subjected to column chromatographic purification, using hexanes−ethyl acetate mixtures (4:1 and then 7:3) to elute **26** as a solid (0.023 g, 90% yield): mp 93−95 °C (hexanes−ethyl acetate); IR (neat) 3451, 3406, 1717, 1699, 1501 cm^{-1}; ^{13}C NMR δ 24.79, 27.02, 28.38 (3C), 51.04, 69.11, 79.32 (2C), 82.2, 109.11, 130.02, 130.65, 155.43; HRMS calcd for $C_{14}H_{23}NO_5$ 286.1654, found 286.1631.

(±)-Tetraacetyl Conduramine A-1 (27b). Trifluoroacetic acid (0.5 mL) was added to a stirred solution of compound **26** (0.023 g, 0.08 mmol) in dichloromethane (0.5 mL). After 1 h, water (0.5 mL) was added, and after an additional 1 h period, the solvent was removed in vacuo. The residue was dissolved in 2 M methanolic ammonia solution (10 mL), and after being stirred for 2−3 h, the solvent was removed in vacuo to give a residue which contained (±)-conduramine A-1 (**27a**). To this material were added pyridine (1.5 mL), acetic anhydride (1.5 mL), and 4-(dimethylamino)pyridine (0.005 g), and after stirring for 16 h, ethyl acetate was added to the reaction mixture. The solution thus obtained was washed successively with dilute HCl, saturated sodium carbonate solution, and saturated NaCl solution and then dried. The solvent was removed in vacuo, and pure (±)-tetracetyl conduramine A-1 was isolated from the residue by column chromatography, using hexanes−ethyl acetate (3:1) and dichloromethane−methanol (99:1) as the eluants. Compound **27b** was obtained as a solid (0.023 g, 92% yield), which on crystallization from hexanes−ethyl acetate, had mp 156−159 °C (reported[3a] mp 156−157 °C): ^{13}C NMR δ 20.89, 20.95, 23.28, 47.78, 68.24, 69.59, 124.94, 131.32, 169.75, 170.01, 170.10, 170.88 (identical to that published[8b] for (+)-conduramine A-1). Anal. Calcd for $C_{14}H_{19}NO_7$: C, 53.67; H, 6.11; N, 4.47. Found: C, 53.40; H, 6.00; N, 4.23.

(±)-1-*p*-Toluenesulfonyl-3,4-epoxy-5-*cis*-*tert*-butoxycarbonylaminocyclohexene (28). A solution of the diene **15** (1.50 g, 4.3 mmol) in dichloromethane (25 mL) containing *m*-chloroperoxybenzoic acid (1.3 g, 6.4 mmol) was stirred at room temperature for 16 h. Saturated aqueous sodium carbonate solution was added, and after thorough agitation, the organic phase was worked up in the usual manner. The crude product upon purification by column chromatography (hexanes−ethyl acetate, 7:3) gave **28** as a solid (1.50 g, 91% yield): mp 73−76 °C, after crystallization from hexanes−ethyl acetate; IR 3432, 1709, 1636, 1597, 1520, 1154 cm^{-1}; ^{13}C NMR (320 K) δ 21.66, 26.31, 28.30, 46.24, 47.98, 57.25, 83.0, 128.27, 130.12, 131.63, 135.20, 143.61, 145.02, 155.0. Anal. Calcd for $C_{18}H_{23}NO_5S$: C, 59.16; H, 6.31; N, 3.83. Found: C, 59.18; H, 6.37; N, 3.77.

(±)-1-*p*-Toluenesulfonyl-*trans*-3,4-dihydroxy-*syn*-5-*tert*-butoxycarbonylaminocyclohexene (29). A stirred solution of compound **28** (0.45 g, 1.23 mmol) in THF (5 mL) containing water (1 mL), and concentrated sulfuric acid (3 drops) was heated at 80 °C for 3 h with periodic additions of small amounts of THF to keep the reaction mixture homogeneous. Ethyl acetate was added to the cooled reaction mixture, and after the usual workup, pure **29** was isolated by column chromatography, using dichloromethane−methanol (99:1) as the eluting solvent. Compound **29** was obtained as a solid (0.38 g, 81% yield): mp 172−173 °C (ethyl acetate−hexane); IR 3411, 1682, 1597, 1516, 1291, 1150 cm^{-1}; ^{13}C NMR (DMSO-d_6, 330 K) δ 21.09, 24.90, 28.17 (3C), 46.24, 67.91, 70.43, 77.92, 127.75 (2C), 130.07 (2C), 135.13, 135.53, 139.53, 144.46, 154.90. Anal. Calcd for $C_{18}H_{25}NO_6S$: C, 56.38; H, 6.57; N, 3.65. Found: C, 56.27; H, 6.67; N, 3.47.

(±)-*trans*-3,4,-Dihydroxy-*syn*-5-*tert*-butoxycarbonylaminocyclohexene (30a). This compound was prepared by the method used for **22** except that 10 g of 6% sodium amalgam/g of **29** was used, and the reaction temperature was

−23 °C. After chromatographic purification, compound **30a** was obtained as a solid (76% yield) with mp 41−43 °C; IR 3418, 1686 cm^{-1}; ^{13}C NMR (325 K) δ 28.41 (3C), 48.02, 69.79, 73.56, 80.12, 126.94, 127.56, 156.75; HRMS calcd for $[C_{11}H_{19}NO_4]H^+$ 230.1392, found 230.1372.

(±)-*trans*-3,4,-Diacetoxy-*syn*-5-*tert*-butoxycarbonylaminocyclohexene (30b). This compound was prepared in exactly the same manner as described for **27b**. Compound **30b** was obtained pure by column chromatography, using hexanes−ethyl acetate (7:3) as the eluant. Pure **30b** was obtained as a solid (95% yield): mp 92−94 °C (hexanes−ethyl acetate); IR (neat) 3366, 1740, 1713 cm^{-1}; ^{13}C NMR (330 K) δ 21.04, 21.09, 28.35 (3C), 28.99, 45.73, 68.61, 72.08, 82.35, 123.07, 130.14, 155.2, 170.0, 170.4. Anal. Calcd for $C_{15}H_{23}NO_6$: C, 57.50; H, 7.40; N, 4.47. Found: C, 57.67; H, 7.36; N, 4.37.

(±)-1,2-Epoxy-*trans*-*anti*-3,4-diacetoxy-*cis*-5-*tert*-butoxycarbonylaminocyclohexane (31). This compound was prepared by the method described for the synthesis of **24** except that the reaction was carried out at 45 °C for 7 h. Compound **31** was obtained pure (72% yield) by column chromatography, using hexanes−ethyl acetate mixtures (4:1 and then 7:3) as the eluant. **31**: mp 44−47 °C (hexanes−ethyl acetate); IR 1750, 1717 cm^{-1}; ^{13}C NMR δ 20.95, 28.30 (3C), 43.66, 52.48, 54.09, 68.12, 72.04, 79.39, 155.6, 160.2, 160.8. HRMS calcd for $[C_{15}H_{23}NO_7C_4H_8]H^+$ 274.0927, found 274.0925.

(±)-1-Phenylselenyl-*trans*-*anti*-*trans*-2,3,4-triacetoxy-*cis*-5-*tert*-butoxycarbonylaminocyclohexane (32b). Compound **32a** was first prepared by the method used to synthesize **25** except that a 5:1 molar ratio of lithium phenylselenide to **31** was used. Compound **32a** was purified by column chromatography using hexanes−ethyl acetate (9:1) followed by dichloromethane−methanol (99:1) as the eluting solvents. This material was then converted into the triacetate **32b** by the method which had been used to convert compound **27a** into (±)-tetraacetyl conduramine A-1 (**27b**). Crude **32b** was obtained pure by column chromatography, using hexanes−ethyl acetate (85:15) as the eluant. Pure **32b** was isolated as a solid (60% yield): mp 163−166 °C (hexanes−ethyl acetate); IR 1751, 1716 cm^{-1}; ^{13}C NMR (320 K) δ 20.67, 20.74 (2C), 28.28 (3C), 32.92, 37.52, 71.11, 71.61, 74.15, 80.2, 128.78, 129.27, 136.42, 155.30, 169.77, 169.85; MS *m*/*z* (rel intensity) 529 (MH^+, 5), 351 (12), 316 (14), 292 (73), 290 (40), 274 (31), 256 (15), 249 (14), 196 (25), 154 (41), 110 (27), 57 (72), 43 (100). Anal. Calcd for $C_{23}H_{31}NO_8Se$: C, 52.28; H, 5.91; N, 2.65. Found: C, 52.72; H, 6.02; N, 2.65.

(±)-Triacetoxy-*N*-*tert*-butoxycarbonyl Conduramine F-1 (33). This compound was prepared in the same manner as **26**. Pure **33** was obtained as a solid (88% yield) after column chromatography, using hexanes−ethyl acetate (3:1) as the eluting solvent. Upon crystallization from hexanes−ethyl acetate, it had the following properties: mp 110−112 °C; ^{13}C NMR δ 20.74, 20.82, 20.93, 28.26 (3C), 46.57, 68.69, 68.98, 71.58, 80.01, 127.56, 127.82, 155.15, 170.06, 170.20 (2C); HRMS (FAB^+) calcd for $[C_{17}H_{26}NO_8]^+$ 372.1658, found 372.1678.

(±)-Tetracetyl Conduramine F-1 (34b). A mixture of compound **33** (0.025 g, 0.067 mmol), THF (0.5 mL), and 10% HCl (1.5 mL) was heated at reflux temperature for 3 h. The mixture was evaporated to dryness, and the residue was sequentially reacted with methanolic ammonia and acetic anhydride−pyridine−4-DMAP, as described for the preparation of (±)-tetraacetyl conduramine A-1 (**27b**). Pure **34b** was obtained as a solid (0.020 g, 95% yield) by column chromatography, using hexanes−ethyl acetate (7:3) and dichloromethane−methanol (99:1) as the eluting solvents, and after crystallization from hexanes−ethyl acetate, it had the following properties: mp 139−141 °C (reported[3e] mp 142 °C); ^{13}C NMR δ 20.67, 20.76, 20.94, 23.26, 45.35, 68.54, 68.60 71.73, 127.44, 127.99, 169.89, 169.96, 170.18. Anal. Calcd for $C_{14}H_{19}NO_7$: C, 53.67; H, 6.11; N, 4.47. Found: C, 53.41; H, 6.25; N, 4.30.

(±)-*cis*-3,4-Dihydroxy-*syn*-5-*tert*-butoxycarbonylaminocyclohexene (35a). This compound was prepared by the method used for **22** except that the reaction was effected at −22 °C, using 5 g of 6% sodium amalgam/g of **18**. Pure **35a** was obtained as a clear glass (78% yield) by column chromatography, using hexanes−ethyl acetate (4:1) and dichloromethane−methanol (99:1) as the eluants; IR 3395, 1690, 1510 cm^{-1}; ^{13}C NMR (330 K) δ 28.21, 28.44 (3C), 48.94, 67.96, 70.15, 79.74, 127.22, 127.44, 155.94; HRMS calcd for $C_{11}H_{19}NO_4-C_3H_8$ 173.0688, found 173.0688.

(+)-*cis*-3(*S*),4(*R*)-Dihydroxy-*syn*-5(*R*)-*tert*-butoxycarbonylaminocyclohexene [(+)-3(*S*),4(*R*),5(*R*)-35a]. This compound was prepared by the same method as used for (±)-**35a** except that a 12.5:1 g/g ratio of 6% sodium to (+)-**18** was used. Pure (+)-**35a** was obtained as an oil in 84% yield: MS *m*/*z* (CI/NH_3) 247 [$(MNH_4)^+$, 24], 230 [$(MH)^+$, 100], 191 (85), 174 (26), 130 (94). Anal. Calcd for $C_{11}H_{19}NO_4$: C, 57.62; H, 8.35; N, 6.11. Found: C, 57.03; H, 8.36; N, 6.02. $[\alpha]_D$ +34.0° (*c* 0.52, $CHCl_3$).

(−)-*cis*-3(*R*),4(*S*)-Dihydroxy-*syn*-5(*S*)-*tert*-butoxycarbonylaminocyclohexene [(−)-3(*R*),4(*S*),5(*S*)-35a]. This compound was prepared in the same manner as the dextrorotatory enantiomer in 70% yield. Pure (−)-**35a** was an oil: MS *m*/*z* (CI/NH_3) 247 [$(MNH_4)^+$, 5], 230 [$(MH)^+$, 100], 191 (39), 174 (53), 130 (29); $[\alpha]_D$ −33.7° (*c* 0.415, $CHCl_3$).

Acetonide of (±)-*cis*-3,4-Dihydroxy-*syn*-5-*tert*-butoxycarbonylcyclohexene (35b). This compound was prepared from **35a** by the method used to obtain compound **8** except that the reaction time was 0.5 h. It was obtained pure (97% yield) by column chromatography, using hexanes−ethyl acetate (85:15) as the eluant, and had mp 72−74 °C after crystallization from hexanes−ethyl acetate: IR 3383, 1717, 1518 cm^{-1}; ^{13}C NMR δ 26.56, 26.63, 27.51, 28.36, 47.52, 73.34, 75.20, 79.50, 109.32, 126.15, 127.48, 155.31. Anal. Calcd for $C_{14}H_{23}NO_4$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.32; H, 8.48; N, 5.12.

Acetonide of (+)-*cis*-3(*S*),4(*R*)-Dihydroxy-*syn*-5(*R*)-*tert*-butoxycarbonylaminocyclohexene [(+)-3(*S*),4(*R*),5(*R*)-35b]. This compound was prepared from (+)-3(*S*),4(*R*),5(*R*)-**35a** by the same method which was used to prepare the racemate. It was obtained in 94% yield and had mp 72−74 °C. Anal. Calcd for $C_{14}H_{23}NO_4$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.83; H, 8.76; N, 5.18. $[\alpha]_D$ +61.5° (*c*, 0.522 $CHCl_3$).

Acetonide of (±)-1,2-Epoxy-*anti*-*cis*-3,4-dihydroxy-*syn*-5-*tert*-butoxycarbonylaminocyclohexane (36). This compound was prepared by the method used to synthesize compound **24**. The crude product was obtained pure by column chromatography, using hexanes−ethyl acetate mixtures (9:1 and then 4:1) to elute **36** as a thick clear oil (99% yield): IR (neat) 3455, 3359, 1717, 1514 cm^{-1}; ^{13}C NMR δ 25.11, 25.84, 27.59, 28.33 (3C), 41.94, 51.22, 53.10, 72.21, 74.27, 79.65, 109.81, 155.01; MS *m*/*z* (CI/NH_3) (rel intensity) 303 [$(MNH_4)^+$, 11], 286 [$(MH)^+$, 100], 247 (25), 230 (54), 171 (15), 127 (25). Anal. Calcd for $C_{14}H_{23}NO_5$: C, 58.93; H, 8.13; N, 4.91. Found: C, 58.83; H, 8.13; N, 4.11.

Acetonide of (+)-1,2-Epoxy-*anti*-*cis*-3,4-dihydroxy-*syn*-5-*tert*-butoxycarbonylaminocyclohexane [(+)-36]. This compound was prepared by the method used for (±)-**36** except that the product was eluted from the column with hexanes−ethyl acetate (4:1). The compound (+)-**36** was obtained as a glass in 97% yield. Anal. Calcd for $C_{14}H_{23}NO_5$: C, 58.93; H, 8.13; N, 4.91. Found: C, 59.13; H, 8.11; N, 4.53. $[\alpha]_D$ +57.2° (*c* 0.495, $CHCl_3$).

Acetonide of (±)-1-Phenylselenyl-*trans*-2-hydroxy-*anti*-*cis*-3,4-dihydroxy-*syn*-5-*tert*-butoxycarbonylaminocyclohexane (37). This compound was prepared by the method used to synthesize **25**. Compound **37** was obtained pure by column chromatography, using hexanes−ethyl acetate mixtures (9:1, 4:1, and 7:3 in succession) as the eluants. It was isolated as a solid (86% yield) which, after crystallization from hexanes−ethyl acetate, had the following properties: mp 140−141 °C; IR 3470, 3252, 1703, 1501 cm^{-1}; ^{13}C NMR δ 26.43; 28.14, 28.37 (3C), 33.38, 44.49, 48.46, 74.12, 75.79, 79.94 (2C), 109.79, 125.27, 128.71, 129.20 (2C), 136.58 (2C), 155.02; HRMS calcd for $C_{20}H_{29}NO_5{}^{78}Se$ 441.1219, found 441.1203.

Acetonide of (−)-1-Phenylselenyl-*trans*-2-hydroxy-*anti*-*cis*-3,4-dihydroxy-*syn*-5-*tert*-butoxycarbonylaminocyclohexane [(−)-37]. This compound was prepared by the method used to prepare the racemate except that the product was eluted from the column with hexanes−ethyl acetate (7:3). Pure (−)-**37** was obtained in 85% yield and had mp 139−

140 °C. Anal. Calcd for $C_{20}H_{29}NO_5Se$: C, 54.30; H, 6.61; N, 3.17. Found: C, 54.59; H, 6.63; N, 3.08. $[\alpha]_D$ −69.9° (*c* 0.475, $CHCl_3$).

Acetonide of (±)-3-Hydroxy-*anti*-*cis*-4,5-dihydroxy-*syn*-6-*tert*-butoxycarbonylaminocyclohexene (38). This compound was prepared by the method used for the synthesis of **26**. After purification by column chromatography with hexanes−ethyl acetate mixtures (4:1 and then 1:1) as the eluents, compound **38** was obtained as a solid (95% yield) which, on crystallization from hexanes−ethyl acetate, had mp 104−106 °C; ^{13}C NMR δ 24.50, 26.21, 28.40 (3C), 46.92, 65.22, 75.20, 77.88, 79.79, 108.59, 128.98, 134.62, 155.60; MS *m*/*z* (CI/NH_3) (rel intensity) 303 [$(MNH_4)^+$, 4], 288 (19), 286 (80), 247 (57), 232 (16), 230 (100), 186 (23), 171 (20), 127 (31). This compound was not characterized further.

Acetonide of (−)-3-Hydroxy-*anti*-*cis*-4,5-dihydroxy-*syn*-6-*tert*-butoxycarbonylaminocyclohexene [(−)-38]. This compound was prepared by the method used for the racemate in 97% yield. Pure (−)-**38** had mp 95−99 °C. Anal. Calcd for $C_{14}H_{23}NO_5$: C, 58.93; H, 8.12; N, 4.91. Found: C, 59.19; H, 8.22; N, 5.04. $[\alpha]_D$ −56.0° (*c* 0.470, $CHCl_3$).

(±)-Conduramine C-1 (39a). A solution of compound **38** (0.407 g, 1.43 mmol) in trifluoroacetic acid (10 mL) and dichloromethane (10 mL) was stirred at room temperature for 1 h, water (4 mL) was added, and stirring was continued for another 1 h. The volatile materials were removed in vacuo, the residue was dissolved in 2 M methanolic ammonia solution (30 mL), and the solution was stirred at room temperature for 16 h. The solvent was evaporated in vacuo, and the residue was purified by column chromatography on Act II neutral alumina using dichloromethane−methanol−concentrated ammonium hydroxide (60:10:1) to elute (±)-conduramine C-1 as a white solid (0.134 g, 65% yield): mp 147−149 °C (hexanes−ethyl acetate) (reported[8e] for (+)- or (−)-conduramine C-1, mp 148−150 °C); ^{13}C NMR (D_2O) δ 50.76, 68.86, 70.35, 73.78, 124.78, 131.06. This spectrum is similar, but not identical, to a spectrum of (±)-conduramine C-1 reported by Alleman and Vogel[8f] in MeOD. The differences probably are of solvent origin since the properties of the tetraacetate **39b** (see below) are perfectly concordant with those reported.[8f]

(−)-Conduramine C-1 [(−)-39a]. A mixture of (−)-**38** (0.083 g, 0.29 mmol) in THF (1 mL) and 5% hydrochloric acid (5 mL) was heated at reflux temperature for 3 h. The solution was evaporated to dryness in vacuo, and the residue was dissolved in 2 M methanolic ammonia solution (10 mL). After 3 h, the solvent was removed in vacuo, and the residue was purified in the manner described for the racemate. Pure (−)-conduramine C-1 was obtained in 88% yield: mp 142−145 °C (reported[8e] mp 148−150 °C); $[\alpha]_D$ −205° (*c* 0.490, MeOH) (reported[8e] $[\alpha]_D$ −221° (*c* 6.79, MeOH).

(±)-Tetraacetyl Conduramine C-1 (39b). This compound was prepared directly from **38** by the method that was used to obtain (±)-tetraacetyl conduramine A-1 (**27b**) from **26**. It was obtained as a solid (97% yield) by preparative TLC on silica gel, using hexanes−ethyl acetate as the developing solvent. After crystallization from ethyl acetate−hexane, it had mp 142−143 °C (reported[8f] mp 143−145 °C for (−)-tetraacetyl conduramine C-1). The ^{13}C NMR spectrum was completely identical to that reported[8f] for this compound. Anal. Calcd for $C_{14}H_{19}NO_7$: C, 53.67; H, 6.11; N, 4.47. Found: C, 53.39; H, 5.93; N, 4.22.

(−)-Tetraacetyl Conduramine C-1 [(−)-39b]. A solution of (−)-**38** (0.053 g, 0.19 mmol) in THF (1 mL) was mixed with 5% hydrochloric acid (5 mL), and the mixture was heated at reflux temperature for 3 h. The solution was evaporated to dryness in vacuo, and pyridine (2 mL) and acetic anhydride (2 mL) were added to the residue. The mixture was stirred for 16 h and evaporated to dryness, toluene was added, and the mixture was evaporated in vacuo (a total of three times). Pure (−)-**39b** was obtained from the residue by column chromatography, using ethyl acetate as the eluant. It was obtained in 95% yield as a solid mp 140−142 °C (reported[8f] mp 143−145 °C); $[\alpha]_D$ −178° (*c* 0.995, CH_2Cl) [reported[8f] $[\alpha]_D$ −181° (*c* 1.0, CH_2Cl_2). The ^{13}C NMR spectrum was identical to that reported for this compound by Allemann and Vogel.[8f]

(±)-1,2-Epoxy-*cis*-*syn*-3,4-dihydroxy-*cis*-5-*tert*-butoxycarbonylaminocyclohexane (40). Prepared by the method used for the synthesis of compound **24**. Purification of the crude product by column chromatography, using hexanes−ethyl acetate (4:1), followed by dichloromethane−methanol (98:2) as the eluants gave **40** as a solid (79% yield) which had mp 153−154 °C after crystallization from ethyl acetate−hexane: IR 3420, 3347, 1694, 1532 cm^{-1}; ^{13}C NMR (DMSO-d_6, 315 K) δ 24.90, 28.12, 48.65, 51.53, 55.23, 66.73, 70.49, 79.07, 154.60. Anal. Calcd for $C_{11}H_{19}NO_5$: C, 53.87; H, 7.81; N, 5.71. Found: C, 54.05; H, 7.80; N, 5.67.

(−)-1,2-Epoxy-*cis*-*syn*-3,4-dihydroxy-*cis*-5-*tert*-butoxycarbonylaminocyclohexane [(−)-40]. This compound was prepared by the method used for **24** except that pure (−)-**40** was eluted from the column as an oil in 75% yield, using dichloromethane−methanol mixtures (99:1 then 96:4) as the eluting solvents. Anal. Calcd for $C_{11}H_{19}NO_5$: C, 53.87; H, 7.81; N, 5.71. Found: C, 53.49; H, 7.77; N, 5.73. $[\alpha]_D$ −26.2° (*c* 0.625, $CHCl_3$).

(±)-1-Phenylselenyl-*anti*-*cis*-*syn*-2,3,4-trihydroxy-*cis*-5-*tert*-butoxycarbonylaminocyclohexane (41a). This compound was prepared by the method used to synthesize **25** except that the ratio of lithium phenylselenide to **40** was 4:1, and the reaction time was 1.5 h. Pure **41a** was obtained as a solid (72% yield) by column chromatography, using hexanes−ethyl acetate (4:1 then 98:2), followed by dichloromethane−methanol (96:4) as the eluting solvents. Compound **41a**: mp 55−59 °C; IR 3414, 1713 (sh), 1682, 1578 cm^{-1}; ^{1}H NMR δ 1.44 (s, 9H), 1.57−1.65 (m, 1H), 2.27 (ddd, 1H, J = 4.0, 6.8, 14.3 Hz), 3.46 (m, 1H), 3.57 (bm, 1H), 3.68 (bt, 1H), 3.98 (bm, 1H), 4.14 (t, 1H), 5.54 (bd, 1H), 7.26−7.36 (m, 3H), 7.57 (m, 2H). MS *m*/*z* (rel intensity) 403 (M^+, 9), 385 (13), 293 (39), 291 (18), 173 (14), 154 (12), 111 (14), 110 (17), 57 (100). Anal. Calcd for $C_{17}H_{25}NO_5Se$: C, 50.75; H, 6.26; N, 3.48. Found: C, 50.28; H, 6.31; N, 3.70.

(±)-1-Phenylselenyl-*anti*-*cis*-*syn*-2,3,4-triacetoxy-*cis*-5-*tert*-butoxycarbonylaminocyclohexane (41b). Chromatographically pure **41a**, prepared as described above, was peracetylated by the method that was used to prepare (±)-tetraacetyl conduramine A-1 (**27b**). The crude tetraacetyl compound **41b** was purified by column chromatography, using hexanes−ethyl acetate mixtures (85:15 and then 7:3) as the eluting solvents. Compound **41b** was obtained as a solid (70% yield from **40**): mp 65−68 °C (hexanes−ethyl acetate); IR 3451, 1752, 1722, 1634 cm^{-1}; ^{13}C NMR δ 20.64 (2C), 20.80, 28.38 (3C), 33.71, 35.16, 48.07, 68.32, 70.98, 71.78, 79.66, 128.72, 129.25, 155.37, 169.09, 169.37, 169.53. Anal. Calcd for $C_{23}H_{31}NO_8Se$: C, 52.27; H, 5.91; N, 2.65. Found: C, 51.96; H, 5.95; N, 2.54.

(+)-1-Phenylselenyl-*anti*-*cis*-*syn*-2,3,4-triacetoxy-*cis*-5-*tert*-butoxycarbonylaminocyclohexane [(+)-41b]. The epoxy compound (−)-**40** was first converted into the phenylselenyl compound (+)-**41a** by the method used to prepare (±)-**37**, and (+)-**41a** was then peracetylated by the method used to prepare (±)-tetraacetyl conduramine A-1 (**27b**). Pure (+)-**41b** was eluted from the column using hexanes−ethyl acetate mixtures (9:1 and then 7:3). The purified solid (69% yield) had mp 130−132 °C. Anal. Calcd for $C_{23}H_{31}NO_8Se$: C, 52.27; H, 5.91; N, 2.65. Found: C, 52.51; H, 6.00; N, 2.53. $[\alpha]_D$ +84.5° (*c* 0.620, $CHCl_3$).

(±)-Triacetoxy-*N*-*tert*-butoxycarbonyl Conduramine D-1 (42). Compound **42** was prepared by the technique used to prepare **26**. It was obtained pure as a solid (90% yield) by column chromatography, using hexanes−ethyl acetate mixtures (9:1 then 7:3) as the eluting solvents. **42**: mp 45−49 °C (hexanes−ethyl acetate); IR (neat) 3461, 3376, 1707 cm^{-1}; ^{13}C NMR δ 20.73 (2C), 20.67, 28.36 (3C), 46.09, 67.08, 67.28, 68.84, 79.73, 126.06, 129.02, 155.3, 169.65, 169.9. Anal. Calcd for $C_{17}H_{25}NO_8$: C, 54.98; H, 6.78; N, 3.77. Found: C, 54.65; H, 6.68; N, 3.60.

(+)-Triacetoxy-*N*-*tert*-butoxycarbonyl Conduramine D-1 [(+)-42]. This compound was prepared in 91% yield by the method used to prepare the racemate. (+)-**42**): mp 47−50 °C; HRMS calcd for $C_{17}H_{25}NO_8$ 371.1580, found 371.1558; $[\alpha]_D$ +124° (*c* 0.525, $CHCl_3$).

(±)-Conduramine D-1 Hydrochloride (43a). A mixture of **42** (0.090 g, 0.24 mmol) and 5 N hydrochloric acid (5 mL) was heated at reflux temperature for 3 h. The cooled solution was washed with ethyl acetate, and the aqueous phase was evaporated in vacuo to give **43a** as a glass (0.042 g, 95% yield): ^{13}C NMR (CD_3OD) δ 49.86, 66.77, 68.89, 72.93, 122.37, 136.51; HRMS (FAB^+) calcd for $[C_6H_{11}NO_3H]^+$ 146.0817, found 146.0821.

(+)-Conduramine D-1 Hydrochloride [(+)-43a]. This compound was prepared by the method used to prepare the racemate and obtained in 82% yield as a very hygroscopic solid: mp 156−161 °C; MS *m/z* (FAB^+, relative intensity) 146 (MH^+, 100); $[\alpha]_D$ +120.3° (*c* 0.600, MeOH).

(±)-Tetracetyl Conduramine D-1 (43b). A solution of **42** (0.200 g, 0.54 mmol) in THF (2 mL) and 5 N HCl (7 mL) was heated at reflux temperature for 3 h. The solution was evaporated in vacuo, acetic anhydride (5 mL) and pyridine (5 mL) were added to the residue, and the mixture was stirred for 16 h. The solvent was removed in vacuo, toluene was added, and the mixture was evaporated in vacuo. The addition and removal of toluene was carried out a total of three times, and the residue was taken up in ethyl acetate and filtered through silica gel. A solid (0.161 g, 95% yield) was obtained which, on crystallization from ethyl acetate−hexane, had the following properties: mp 147−149 °C; IR 3395, 3272, 1748, 1651, 1545 cm^{-1}; ^{13}C NMR δ 20.70, 20.91, 23.32, 44.66, 66.62, 67.05, 126.26, 128.73, 169.27, 169.57. Anal. Calcd for $C_{14}H_{19}NO_7$: C, 53.67; H, 6.11; N, 4.47. Found: C, 53.36; H, 6.26; N, 4.25.

Generation of (−)-3c-and (+)-3c from (±)-2-*p*-Toluenesulfonyl-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]-heptadiene (3c). A. Formation of Diasteriomeric Adducts 44a and 45a with (−)-Methyl Lactate. A solution of (−)-methyl lactate (10.4 g, 100 mmol) in dry THF (15 mL) was added to a stirred suspension of sodium hydride (0.300 g, 60% dispersion in mineral oil, 7.5 mmol) in dry THF (300 mL). After ca. 10 min, a solution of (±)-**3c** (34.7 g, 100 mmol) in dry THF (100 mL) was added, and the reaction mixture was stirred for 2 h. Ethyl acetate and a dilute aqueous ammonium chloride solution were added, and the organic phase was separated and worked up as usual. Removal of the solvent in vacuo gave a residue which was subjected to column chromatographic purification, using hexanes−ethyl acetate (4:1) to elute a mixture of **44a** and **45a** (43.3 g, 96% yield). This material was dissolved in the minimum amount of hot 4:1 hexanes−ethyl acetate, and the solution was left to cool (finally in the refrigerator).

Diastereomer **45a** (21.3 g, 47%) was collected by filtration. The filtrate was concentrated in vacuo, and the residue on crystallization from hexanes−ethyl acetate gave diastereomer **44a** (21.6 g, 48% yield).

Diastereomer **44a**: mp 81−82 °C; IR 3440, 1752, 1707, 1638, 1597, 1370, 1152 cm^{-1}; ^{13}C NMR δ 18.63, 21.51, 27.99 (3C), 51.92, 59.98, 67.72, 70.18, 74.72, 80.86, 81.60, 127.88 (2C), 130.06 (2C), 133.2, 135.61, 136.20, 145.08, 154.9, 172.2. Anal. Calcd for $C_{22}H_{29}NO_7S$: C, 58.52; H, 6.47; N, 3.10. Found: C, 58.71; H, 6.55; N, 3.03. $[\alpha]_D$ − 25.1° (*c* 0.1035, $CHCl_3$).

Diastereomer **45a**: mp 126−127 °C; IR 3440, 1752, 1690, 1368, 1156 cm^{-1}; ^{13}C NMR δ 18.61, 21.51, 28.00, 51.87, 59.79, 64.59, 66.30, 73.75, 80.80, 81.85, 127.81 (2C), 129.87 (2C), 132.58, 135.8, 136.20, 144.72, 154.06, 172.64. Anal. Calcd for $C_{22}H_{29}NO_7S$: C, 58.52; H, 6.47; N, 3.10. Found: C, 58.76; H, 6.52; N, 3.05. $[\alpha]_D$ −50.4° (*c* 0.113, $CHCl_3$).

B. Saponification of the Diastereomeric Esters (−)-44a and (−)-45a to the Carboxylic Acids (+)-44b and (−)-45b, Respectively. A solution of ester (−)-**44a** (4.51 g, 10 mmol) in tetrahydrofuran (20 mL) was added to a solution of sodium hydroxide (1.20 g, 30 mmol) in methanol (50 mL), and the reaction mixture was stirred at room temperature for 16 h. The volatile material was removed in vacuo, and the residue was partitioned between ethyl acetate and water. The aqueous phase was made acidic with concentrated hydrochloric acid, and the liberated carboxylic acid (+)-**44b** was extracted into the ethyl acetate. After the usual workup the crude acid was crystallized from ethyl acetate−hexane to give pure (+)-**44b** (4.05 g, 93% yield): mp 112−115 °C; IR 3428, 1744, 1709, 1597, 1370, 1154 cm^{-1}; ^{13}C NMR δ 17.75, 21.59, 28.17, 60.32, 65.05, 70.91, 75.06, 82.57, 128.01, 130.02, 132.88, 135.80, 136.61, 145.40, 154.97, 172.97. Anal. Calcd for $C_{21}H_{27}NO_7S$: C, 57.65; H, 6.22; N, 3.20. Found: C, 57.25; H, 6.18; N, 3.13. $[\alpha]_D$ +12.5° (*c* 0.998, $CHCl_3$).

In the same manner as (+)-**44b**, compound (−)-**45b** was obtained as a solid (94% yield): mp 110−112 °C after crystallization from ethyl acetate−hexane; IR 3391, 3227, 1737, 1709, 1597, 1370, 1152 cm^{-1}; ^{13}C NMR δ 18.35, 21.54, 28.19, 60.24, 65.69, 70.26, 74.07, 81.31, 128.14, 129.94, 133.24, 136.18, 136.72, 145.21, 154.08, 174.75. Anal. Calcd for $C_{21}H_{27}NO_7S$: C, 57.65; H, 6.22; N, 3.20. Found: C, 57.23; H, 6.22; N, 3.31. $[\alpha]_D$ −36.35° (*c* 0.985, $CHCl_3$).

C. Synthesis of the Diastereomeric Hydroxymethyl Compounds (+)-46 and (−)-47 from the Esters (−)-44a and (−)-45a, Respectively. A mixture of powdered sodium borohydride (12.8 g, 340 mmol) and tetrahydrofuran (500 mL) containing (−)-**44a** (19.0 g, 42.1 mmol) and methanol (34 mL) was stirred at 70 °C for 2 h. The cooled solution was made acidic with dilute hydrochloric acid, the volatile materials were removed in vacuo, and the residue was partitioned between water and ethyl acetate. The organic phase was worked up as usual and the crude product was purified by column chromatography using hexanes−ethyl acetate mixtures (9:1 and then 3:2) to elute solid (+)-**46** (16.9 g, 95% yield) which, on crystallization from ethyl acetate−hexane, had the following properties: mp 105−107 °C; IR 3428, 1682, 1593, 1381, 1370, 1163, 1146 cm^{-1}; ^{13}C NMR δ 15.31, 21.49, 28.02 (3C), 59.77, 64.86, 66.52, 70.33, 78.01, 81.54 (2C), 127.9 (2C), 129.92 (2C), 132.67, 134.99, 136.80, 144.91, 153.94. Anal. Calcd for $C_{21}H_{29}NO_6S$: C, 59.55; H, 6.90; N, 3.31. Found: C, 59.61; H, 6.97; N, 3.23. $[\alpha]_D$ +63.5° (*c* 0.104, $CHCl_3$).

The diastereomeric alcohol (−)-**47** was prepared exactly as described for (+)-**46** and was obtained as a solid (94% yield) which, after crystallization from ethyl acetate−hexane, had the following properties: mp 99−100 °C; IR 3513, 3440, 1707, 1618, 1599, 1367, 1165, 1150 cm^{-1}; ^{13}C NMR δ 16.99, 21.51, 27.85, 59.37, 66.20, 66.91, 69.62, 77.0, 80.88, 81.12, 127.84 (2C), 130.09 (2C), 133.06, 135.47, 136.07, 145.17, 154.27. Anal. Calcd for $C_{21}H_{29}NO_6S$: C, 59.55; H, 6.90; N, 3.31. Found: C, 59.47; H, 6.92; N, 3.51. $[\alpha]_D$ −38.3° (*c* 0.107, $CHCl_3$).

(−)-2-*p*-Toluenesulfonyl-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]heptadiene [(−)-3c] from (+)-44b or (+)-46. The method used was identical for both precursors of (−)-**3c**, and a typical procedure using (+)-**44b** follows. All solvents were degassed prior to use by bubbling a slow stream of argon through the ultrasonically irradiated solvent for 5−10 min. A solution of methylmagnesium bromide in 3:1 toluene−THF (1.57 mL of a 1.4 M solution, 2.2 mmol) was added dropwise over ca. 5 min to a stirred solution of (+)-**44b** (0.437 g, 1 mmol) in dry THF (10 mL, argon atmosphere) at room temperature. Stirring was continued for an additional 5 min, and then the reaction was quenched by the addition of excess dilute hydrochloric acid. The mixture was extracted with ethyl acetate, the extract was washed successively with dilute aqueous NaOH and saturated aqueous NaCl solution, and then it was dried and evaporated in vacuo. Pure (−)-**3c** was obtained as a solid (0.323 g, 93% yield) by column chromatography using hexanes−ethyl acetate (85:15) as the eluting solvent. It had mp 105−106 °C, was pure by HPLC (see synthesis of (±)-**3c**), and had the longer retention time (∼25 min). Anal. Calcd for $C_{18}H_{21}NO_4S$: C, 62.23; H, 6.09; N, 4.03. Found: C, 62.43; H, 6.14; N, 3.96. $[\alpha]_D$ −93.5° (*c* 1.0015, $CHCl_3$).

When (+)-**46** was used as the starting material, (−)-**3c** was obtained in 95% yield.

(+)-2-*p*-Toluenesulfonyl-7-*tert*-butoxycarbonyl-7-azabicyclo[2.2.1]heptadiene [(+)-3c] from (−)-45b or (−)-47. Using the methodology described above (+)-**3c** was obtained in 92% and 95% yields from (−)-**45b** and (−)-**47**, respectively. The compound (+)-**3c** had mp 107−108 °C, was pure by HPLC, and had a retention time of ca. 22 min. Anal. Calcd for $C_{18}H_{21}NO_4S$: C, 62.23; H, 6.09; N, 4.03. Found: C, 62.49; H, 6.12; N, 4.02. $[\alpha]_D$ +95.6° (*c* 0.967, $CHCl_3$).

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