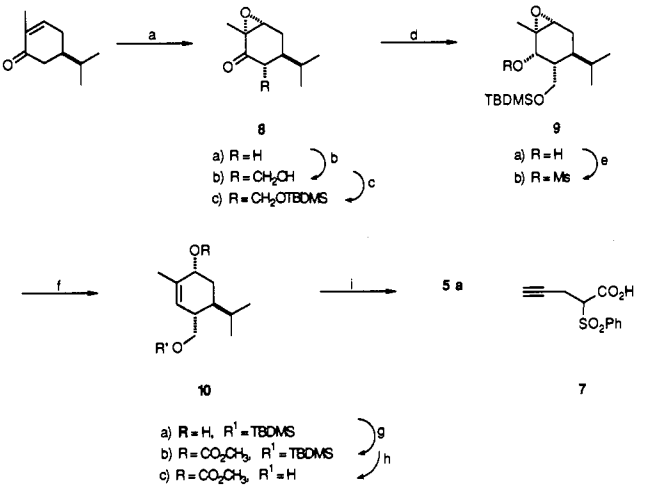
Scheme I. Synthesis of Pd(0) Substrate **5**[a]



[a](a) H_2O_2, NaOH, CH_3OH, 93%; (b) LDA, THF, CH_2O, -78 °C, 68%; (c) TBDMS-Cl, $(C_2H_5)_3N$, DMAP, CH_2Cl_2, 95%; (d) L-Selectride, THF, -78 °C, 91%; (e) CH_3SO_2Cl, $(C_2H_5)_3N$, CH_2Cl_2, 0 °C, 85%; (f) $NaC_{10}H_8$, THF, room temperature, 90%; (g) nC_4H_9Li, $ClCO_2CH_3$, 70-30 ether-hexane, 0 °C, 98%; (h) TBAF, THF, room temperature, 90%; (i) **7**, DCC, CH_2Cl_2, 0 °C, room temperature, 98%.

evolve an effective asymmetric synthesis of this alkaloid family.

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Supplementary Material Available: Analytical details including melting points, specific rotations, and IR, ^1H NMR, and ^{13}C NMR spectral data for compounds **2**, **3**, **5**, **8b**, **9a**, **10a,c**, **11b**, **12a,b**, **13a,d**, and **14a,b** (5 pages). Ordering information is given on any current masthead page.

New Trialkylsilyl Enol Ether Chemistry. Synthesis of the Benzomorphanone Core Structure Using a Stereoelectronic Conformational Lock

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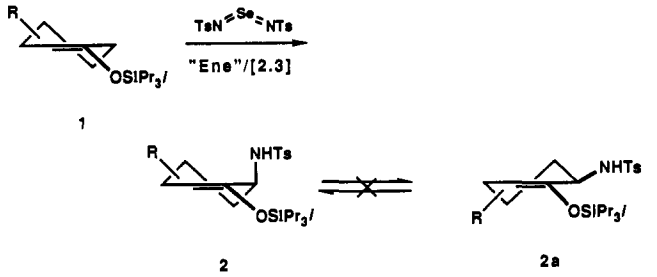
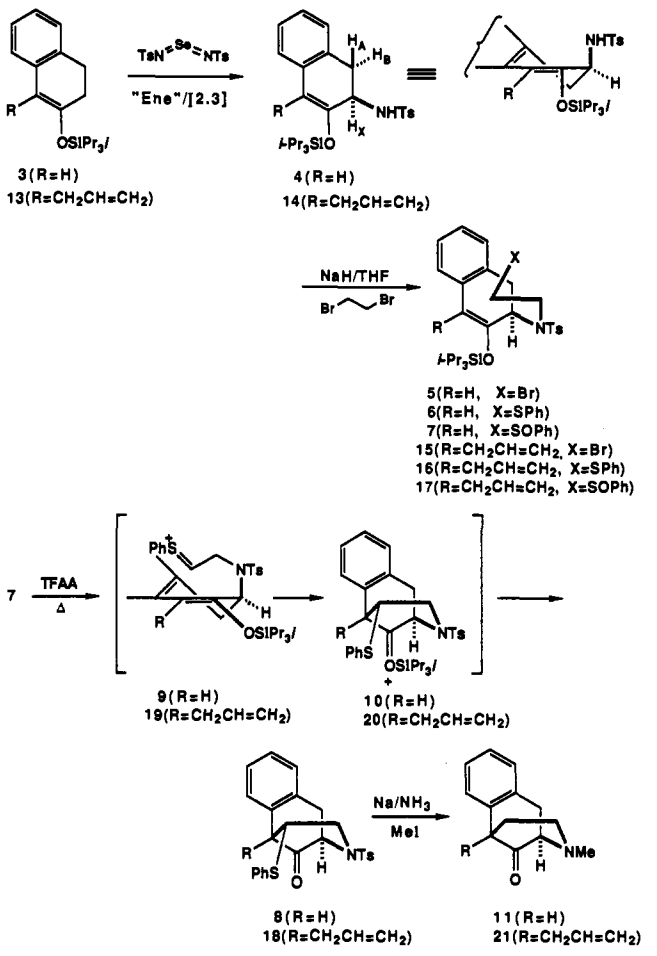
Triisopropylsilyl enol ethers **1** derived from cyclohexanones react with the Sharpless aminating reagent TsN=Se=NTs[1] at 0-20 °C to give the *axially aminated* adducts **2**.[2] We believe that the origin of the thermodynamically preferred axial conformation is the result of π-σ^* stabilization combined with $A^{1,3}$ strain.[3] The

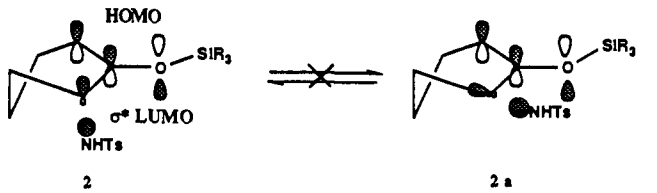
Scheme I



Scheme II



reaction depicted in Scheme I is ideally suited for the construction of the morphine alkaloids, in particular 9-ketobenzomorphans, since the axial nitrogen functionality is correctly oriented to direct intramolecular transformations.[4]



(1) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 7154. Sharpless, K. B.; Hori, T.; Truesdale, L. K.; Dietrich, C. O. *J. Am. Chem. Soc.* **1976**, *98*, 269. Sharpless, K. B.; Singer, S. P. *J. Org. Chem.* **1976**, *41*, 2504; **1978**, *43*, 1448. For a recent review of aza analogues of organic and inorganic compounds of selenium, and the suggestion that TsN=Se=NTs is in fact $(TsNNa)_2SeCl_2$, see: Derkach, N. Y.; Levchenko, E. S. *Russ. Chem. Rev.* **1989**, *58*(5), 507.

(2) Magnus, P.; Mugrage, B. *J. Am. Chem. Soc.* **1990**, *112*, 462.

(3) Magnus, P.; Lacour, J.; Mugrage, B.; Bauta, W., manuscript in preparation.

(4) For the most recent synthesis of *d*-morphine and a comprehensive list of references to prior synthetic endeavors, see: Toth, J. E.; Hamann, P. R.; Fuchs, P. L. *J. Org. Chem.* **1988**, *53*, 4694. Broka, C. A.; Gerlits, J. F. *J. Org. Chem.* **1988**, *53*, 2144. Sdassi, H.; Revial, G.; Pfau, M.; d'Andelo, J. *Tetrahedron Lett.* **1990**, *31*, 875. 9-Ketobenzomorphans: May, E. L.; Murphy, J. G. *J. Org. Chem.* **1955**, *20*, 257. Murphy, J. G.; Ager, J. H.; May, E. L. *J. Org. Chem.* **1960**, *25*, 1386. Takeda, M.; Inoue, H.; Saito, S.; Kugita, H. *J. Org. Chem.* **1972**, *37*, 2677. Kavadias, G.; Velkof, S.; Belleau, B. *Can. J. Chem.* **1979**, *57*, 1852, 1866. Kanematsu, K.; Parfitt, R. T.; Jacobsen, A. E.; Ager, J. H.; May, E. L. *J. Am. Chem. Soc.* **1968**, *90*, 1064.

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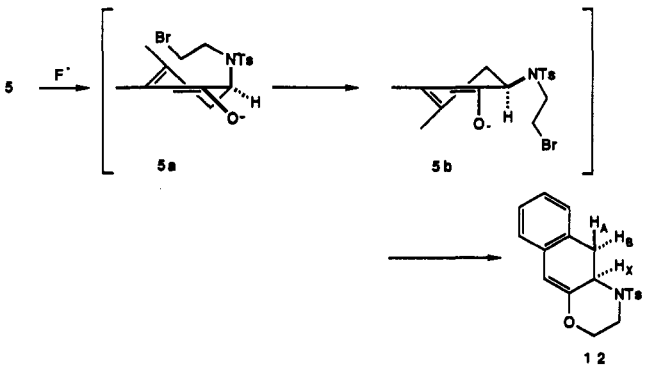
Scheme III

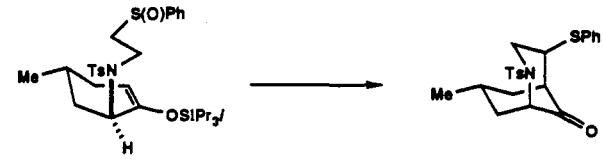


β-Tetralone was converted into the triisopropylsilyl enol ether **3** (94%) by treatment with KHMDS/*i*-Pr_3SiCl/THF/0 °C. Exposure of **3** to $(TsN)_2Se$ at 25 °C for 40 h gave the axially aminated adduct **4** (71%). Remarkably, this reaction did not result in any aromatization products, which suggests that there is little or no charge buildup in the "ene"/[2.3] sigmatropic rearrangement process. The NHTs group was assigned an axial (pseudo)[5] configuration on the basis of the methine couplings (ABX, J_{AX} = 6.0 Hz, J_{BX} = 6.0 Hz). Treatment of **4** with NaH/$BrCH_2CH_2Br$/THF/80 °C gave the N-alkylated compound **5** (84%), which was directly converted into the sulfide **6** (NaSPh/THF/80 °C (94%). When the derived sulfoxides **7** (MCPBA/CH_2CH_2/-78 °C (97%) were treated with trifluoroacetic acid anhydride/2,6-di-*tert*-butyl-4-methylpyridine/CH_2Cl_2/0 °C,[6] followed by addition of chlorobenzene and rapid heating to 130 °C, the benzomorphanone **8** was isolated in 50% yield (Scheme II).

The overall structure of **8** and the stereochemistry of the SPh substituent were determined by single-crystal X-ray crystallography.[7] The sulfonium ion **9** is ideally aligned with respect to the π-system of the triisopropylsilyl enol ether to give the oxonium ion **10**. For the case **9** (R = H), only the axial-SPh (synclinal attack) diastereomer was formed. This stereochemical outcome appears to be a consequence of aligning the $=SPh^+$ group away from the benzo portion of **9** (R = H). Removal of the SPh and Ts groups and concomitant N-methylation of **8** to give **11** (60%) were accomplished by treatment of **8** with Na/NH_3/THF, followed by methyl iodide (quenching with NH_4Cl gave the N-nor analogue, 59%).

To further demonstrate conformational immobilization of **4**-**7**, we treated **5** with $Bu_4N^+F^-$/THF/25 °C and isolated the O-alkylated derivative **12** (88%). The methine proton H_x is now in an axial configuration (J_{AX} = 15.0 Hz, J_{BX} = 6.3 Hz). Fluoride ion desilylation of **5** gives the enolate **5a**, which is now able to conformationally relax to the equatorial conformation **5b** more rapidly than undergo C-alkylation.[8] Once **5b** is formed it can only undergo O-alkylation resulting in **12** since the geometry of **5b** does not permit C-alkylation (Scheme III).

Starting with the 1-allyl derivative of β-tetralone, its triisopropylsilyl enol ether derivative **13** (97%) was converted into **14** (59%), **15** (87%), **16** (87%), and **17** (99%) as described for **3**. When **17** was exposed to the Pummerer reaction conditions (TFAA/2,6-di-*tert*-butyl-4-methylpyridine/CH_2Cl_2 at 0 °C and then PhCl at 130 °C, the benzomorphanone adduct **18** was isolated as a mixture of epimers (1.7:1, 79% yield) at the C-SPh bond. Treatment of **18** with Na/NH_3/THF, followed by methyl iodide, gave **21** (57%). This method for making azabicyclo[3.3.1] systems is equally applicable to simple cyclohexane derivatives. For example, when **22** was exposed to the above Pummerer-type conditions, the 2-azabicyclo[3.3.1]nonan-9-one **23** was isolated in 54% yield.



Acknowledgment. The National Institutes of Health are thanked for their support of this research (GM 32718). The Fulbright Commission is thanked for a travel award to I.C. Dr. John C. Huffman (Molecular Structure Center, Indiana University, Bloomington, IN 47405) is thanked for the X-ray structure determination of **8**. Bret Frost is thanked for carrying out the conversion of **22** into **23**.

Supplementary Material Available: General spectral details for compounds **4**-**6**, **8**, **11**-**16**, **18**, **21**, and **23**, details of the X-ray structure determination of **8**, and tables of fractional coordinates, isotropic thermal parameters, anisotropic thermal parameters, bond lengths, and bond angles for $C_{25}H_{23}S_2O_3N$ (21 pages). Ordering information is given on any current masthead page.

(5) In 1,3-cyclohexadienes it is a moot point as to whether or not an allylic substituent can be designated as axial or even pseudoaxial. Rabideau, P. W.; Sygula, A. Conformational Analysis of 1,3-Cyclohexadienes and Related Hydroaromatics. In *The Conformational Analysis of Cyclohexenes, Cyclohexadienes, and Related Hydroaromatic Compounds*; Rabideau, P. W., Ed.; VCH Inc.: Weinheim, 1989; Chapter 4, p 89.

(6) Gallagher, T.; Magnus, P.; Huffman, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 4750.

(7) Complete details of the single-crystal X-ray crystallographic structure determination of **8** are available from Dr. John C. Huffman (Molecular Structure Center, Indiana University, Bloomington, IN 47405). Please ask for Report No. 90901.

(8) We cannot exclude the possibility that the axial conformer **5a** undergoes exclusive O-alkylation to give, after conformational relation, **12**. In view of the pronounced tendency for cyclohexanone formation (Baldwin, J. E.; Kruse, L. I. *J. Chem. Soc., Chem. Commun.* **1977**, 77), this alternative seems less likely.

Metallobiochemistry of a Ribosomal RNA. A Possible Role for Na^+ and K^+ in the Regulation of Mg^{2+} Binding Sites on *Escherichia coli* 5S rRNA: Implications for Activity

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Although alkali and alkaline-earth metal ions are essential cofactors in the structural and catalytic chemistry of RNA,[1-5] there

(1) Latham, J. A.; Cech, T. R. *Science* **1989**, *245*, 276. Been, M. D.; Cech, T. R. *Science* **1988**, *239*, 1412. Altman, S.; Guerrier-Takada, C.; Frankfort, H. M.; Robertson, H. D. In *Nucleases*; Linn, S. M., Roberts, R. J., Eds.; Cold Spring Harbor Laboratory: 1985; pp 243 and 311.

(2) Moore, P. B. *Nature* **1988**, *331*, 223-227. Tang, R. S.; Draper, D. E. *Biochemistry* **1990**, *29*, 5232-5237. Ryan, P. C.; Draper, D. E. *Biochemistry* **1989**, *28*, 9949-9956. Wittmann, H. G. *Annu. Rev. Biochem.* **1982**, *51*, 155-183.

(3) Leontis, N. B.; Moore, P. B. *Biochemistry* **1986**, *25*, 5736-5744. Leontis, N. B.; Ghosh, P.; Moore, P. B. *Biochemistry* **1986**, *25*, 7386-7392. Kime, M. J.; Ratcliffe, R. G.; Moore, P. B.; Williams, R. J. P. *Eur. J. Biochem.* **1981**, *116*, 169-276. Kime, M. J.; Moore, P. B. *Nucleic Acids Res.* **1982**, *10*, 4973-4983.

(4) A large body of literature exists on DNA-cation interactions, e.g.: Record, M. T.; Woodbury, C. P.; Lohman, T. M. *Biopolymers* **1976**, *15*, 893-915. Record, M. T. *Biopolymers* **1975**, *14*, 2137-2138. Record, M. T.; Lohman, T. M.; de Haseth, P. *J. Mol. Biol.* **1976**, *107*, 145-158. Manning, G. S. *Biopolymers* **1972**, *11*, 937-949. Manning, G. S. *J. Chem. Phys.* **1969**, *51*, 924-938. Krakauer, H. *Biopolymers* **1971**, *10*, 2459-2490. Krakauer, H. *Biochemistry* **1974**, *13*, 2579-2589. However, these do not account for the more complex tertiary structure of RNA relative to DNA, while the theoretical analyses were based on considerations of the electrostatic interaction of cations with a phosphate backbone, and do not account for the possibility of H-bonding interactions with nucleotide bases and sugar hydroxyls. Further work in this area is therefore called for.

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