Further work along these lines is in progress.

Experimental Section

Melting points are uncorrected. IR spectra were recorded with a Hitachi 260-10 spectrometer with KBr pellets unless otherwise stated. Proton NMR were obtained with a Varian CFT-80 apparatus with $CDCl_3$ as solvent and Me_4Si as internal standard. Mass spectra were recorded with a Kratos MS-25 or a Hewlett-Packard 5985 B instrument at a 70-eV ionizing energy.

All commercial phenols were directly used without purification. Cyanohydrins **7** were prepared according to the literature methods.[27] Allylvanillin (**9f**) was prepared as previously described.[22]

Sodium phosphate buffers (0.2 M, pH 6, 7, or 10) were prepared by the literature methods.[28]

General Procedure for Fremy's Salt Promoted Degradative Oxidation of 7–10. Fremy's salt was dissolved in 0.2 M sodium phosphate buffer (pH 6) to give a 0.3 M solution. This was then added to a 0.1 M solution of the phenolic substrate in either $CHCl_3$ or Et_2O. The resulting two-phase mixture was then vigorously stirred until the starting material disappeared (TLC). The organic phase was separated and the aqueous solution extracted, at least three times, with $CHCl_3$. The combined extracts were then washed with H_2O and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure usually led to a solid residue which crystallized as indicated.

4b: mp 128–129 °C (EtOH) (lit.[29] mp 130–131 °C); IR 1690, 1660 cm^{-1}; ^1H NMR 7.32 (s) ppm.

4c: mp 138–139 °C (H_2O) (lit.[30] mp 138–139 °C); IR 1675, 1650 cm^{-1}; ^1H NMR 3.85 (s, 3 H), 5.95 (s, 1 H), 6.72 (s, 2 H) ppm.

4d: mp 162–163 °C (lit.[31] mp 161–162 °C); IR 1680, 1640 cm^{-1}; ^1H NMR 3.85 (s, 3 H), 5.95 (d, 1 H, J = 2 Hz), 7.19 (d, 1 H, J = 2 Hz).

4e: mp 252–254 °C (C_6H_6) (lit.[32] mp 249 °C); IR 1690, 1640 cm^{-1}; ^1H NMR 3.82 (s, 6 H), 5.85 (s, 2 H).

4f: mp 80–82 °C (hexane) (lit.[33]); IR 3050, 1675, 1645 cm^{-1}; ^1H NMR 3.19 (dd, 2 H, J = 6.5, 1.2 Hz), 3.82 s, 3 H), 5.04–6.1 (m, 3 H), 5.88 (d, 1 H, J = 2.3 Hz), 6.50 (m, 1 H) ppm; MS, m/e (relative intensity) 178 (M^+, 21), 163 (46), 150 (11), 135 (24), 107 (29), 94 (85), 69 (100).

11a: mp. 182–183 °C (sublimed) (lit.[34] mp 184–186 °C); IR 1665, 1655 cm^{-1}; ^1H NMR 4.00 (s, 3 H), 6.86 (s, 2 H), 7.24–7.74 (m, 3 H) ppm; MS, m/e relative intensity 188 (M^+, 100), 159 (21).

11b: mp 128–130 °C (sublimed) (lit.[35] mp 128 °C); IR 1660 cm^{-1}; ^1H NMR 6.97 (s, 2 H), 8.15–7.69 (m, 4 H) ppm.

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Registry No. **5a**, 106-51-4; **5b**, 19643-45-9; **5c**, 2880-58-2; **5d**, 23030-47-9; **5e**, 530-55-2; **5f**, 31788-37-1; **7a**, 13093-65-7; **7b**, 104266-79-7; **7c**, 33630-46-5; **7d**, 54246-09-2; **7e**, 102742-10-9; **8a**, 99-96-7; **8b**, 3337-62-0; **8c**, 121-34-6; **8d**, 6324-52-3; **8e**, 530-57-4; **9a**, 123-08-0; **9b**, 2973-77-5; **9e**, 134-96-3; **9f**, 20240-58-8; **10a**, 69833-14-3; **10b**, 7770-45-8; **11a**, 4923-61-9; **11b**, 130-15-4; $(KSO_3)_2NO$, 14293-70-0.

(27) Anhoury, M. L.; Crooy, P.; Eliaers J. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1015. Ladenburg, K.; Major, R T.; Folkers, K. *J. Am. Chem. Soc.* **1936**, *58*, 1992.

(28) Perrin, D. D.; Dempsey, B. *Buffers for pH and metal Ion Control*; Chapman and Hall: London, 1974.

(29) Grinev, A. N.; Terentev, A. P. *Vest. Mat., Mekh., Astron., Fix., Khim. Mosk. Univ. Ser.* **1957**, *12*, 147; *Chem. Abstr.* **1959**, *53*, 3187.

(30) Beilsteins Handbuch; Springer–Verlag: Berlin, 1934; Band VIII p 234.

(31) Blatchly, J. M.; Green, R J. S.; McOmie, J. F. W.; Searle, J. B. *J. Chem. Soc. C* **1969**, 1353.

(32) Teuber, H. J.; Rau, W. *Chem. Ber.* **1953**, *,6*, 1036.

(33) Giménez, F. G.; Almanza, R. C. *Rev. Lat. Quim.* **1970**, *1*, 16; *Chem. Abstr.* **1971**, *74*, 141410.

(34) Bossard, P.; Fumagalli, S.; Grod, R.; Trueb, W.; Philipsborn, W. V.; Eugster, G. H. *Helv. Chim. Acta* **1964**, *47*, 769.

(35) Teuber, H. J.; Götz, N. *Chem Ber.* **1954**, *87*, 1236.

2,2,2-Triphenyl-4,5-(2′,2″-biphenylene)-1,3,2-dioxaphospholane: An Effective Reagent for Converting Diols, Amino Alcohols, and Especially Mercapto Alcohols to the Corresponding Heterocycles

Jeffery W. Kelly, Philip L. Robinson, and Slayton A. Evans, Jr.*

The William Rand Kenan, Jr., Laboratories of Chemistry, The University of North Carolina, Chapel Hill, North Carolina 27514

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The successful application of diethoxytriphenylphosphorane [$Ph_3P(OEt)_2$; DTPP] for cyclodehydration[1,2] and oxidative cleavage[3] of diols to cyclic ethers and ketones, respectively, prompted an investigation to determine the efficiency with which DTPP would effect cyclodehydration of α,ω-mercapto alcohols to cyclic sulfides.[4] We subsequently established that in cases where the rates of DTPP-promoted chain closure of mercapto alcohols to cyclic sulfides are low, the rates of competitive S-ethylations affording the ethyl thio alcohols dominate the course of the reaction.[4]

Our choice of 2,2,2-triphenyl-4,5-(2′,2″-biphenylene)-1,3,2-dioxaphospholene (TDP)[5] as a cyclodehydrating reagent especially for α,ω-mercapto alcohols reflects an attempt to eliminate competitive S-alkylations, a process which impedes the desired ring closure reaction using DTPP. With TDP, the competitive side reaction involving thiolate displacement of triphenylphosphine oxide (TPPO) would require thiolate attack on an sp^2 carbon which should be energetically prohibitive.

TDP, arising from the equivalent of a concerted [4 + 2] cycloaddition of phenanthrenequinone and triphenylphosphine (70 °C),[6] is hydrolytically labile but otherwise quite stable in dry toluene solvent. The ^{13}C and ^{31}P (δ −16.8 in toluene) NMR parameters[7] are consistent with the expected structure and the ^{31}P NMR shift corroborates that previously reported by Ramirez et al. (δ −15.6).[5a]

TDP is best prepared and used under an argon or nitrogen atmosphere since exposure to oxygen slowly leads to formation of TPPO and phenanthrenequinone 1.[9] Presumably, a retro [4 + 2] collapse of TDP, followed by slow oxidation of triphenylphosphine with molecular oxygen adequately accounts for this observation. One further note may be useful. 1,2-Dihydroquinone **2** is immediately

(1) (a) Bass, S. W.; Barry, C. N.; Robinson, P. L.; Evans, S. A., Jr. *ACS Symp. Ser.* **1981**, *No. 171*, 165. (b) Robinson, P. L.; Barry, C. N.; Bass, S. W.; Jarvis, S. E.; Evans, S. A., Jr. *J. Org. Chem.* **1983**, *48*, 5396–5398. (c) Robinson, P. L.; Barry, C. N.; Kelly, J. W.; Evans, S. A., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 5210. (d) Kelly, J. W.; Robinson, P. L.; Evans, S. A., Jr. *J. Org. Chem.* **1985**, *50*, 5007–5009.

(2) Robinson, P. L.; Kelly, J. W.; Evans, S. A., Jr. *Phosphorus Sulfur* **1986**, *26*, 15–24.

(3) Robinson, P. L.; Evans, S. A., Jr. *J. Org. Chem.* **1985**, *50*, 3860–3863.

(4) (a) Robinson, P. L.; Kelly, J. W.; Evans, S. A., Jr. *Phosphorus Sulfur*, in press. (b) Robinson, P. L. Ph.D. Thesis, University of North Carolina, Chapel Hill, NC, 1985.

(5) (a) Ramirez, F.; Smith, C. P.; Gulati, A. S.; Patwardhan, A. V. *Tetrahedron Lett.* **1966**, *19*, 2151–2158. (b) Ramirez, F. *Acc. Chem. Res.* **1968**, *1*, 168–174.

(6) Abdou, W. M.; Mahran, M. R. *Phosphorus Sulfur* **1986**, *26*, 119–127.

(7) The ^{13}P NMR shift for TDP is solvent and phase dependent: ^{31}P δ −16.45 in benzene-d_6, δ −16.05 in $CDCl_3$, and δ −1.5 in the solid state.[8]

(8) Dennis, L. W.; Bartuska, V. J.; Maciel, G. E. *J. Am. Chem. Soc.* **1982**, *104*, 230–235.

(9) (a) We have determined using ^{13}C and ^{31}P NMR that TDP slowly reacts with molecular oxygen (40 °C, 80 h) to afford triphenylphosphine oxide and phenanthrenequinone. (b) Buckler has also shown that triphenylphosphine reacts slowly with molecular oxygen affording TPPO in benzene solvent. See: Buckler, S. A. *J. Am. Chem. Soc.* **1962**, *84*, 3093.

0022-3263/86/1951-4473$01.50/0

Scheme I

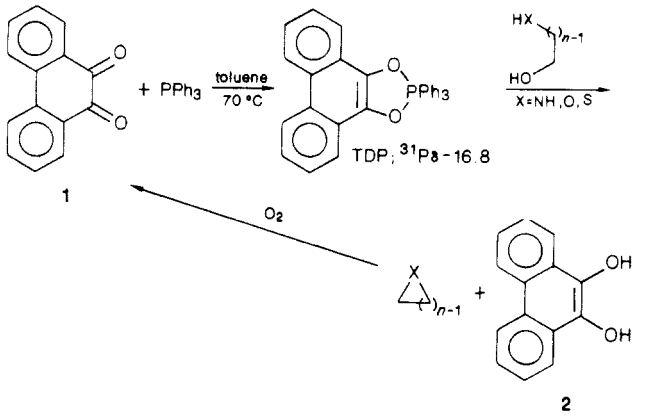
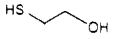
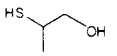
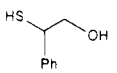
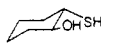
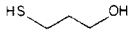
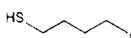


Table I. Cyclodehydration of Mercapto Alcohols with TDP[a]

mercapto alcohols	sulfides	yield, %
		98
		85
		98
		71
		80
		85
		84

[a] See Experimental Section for details.

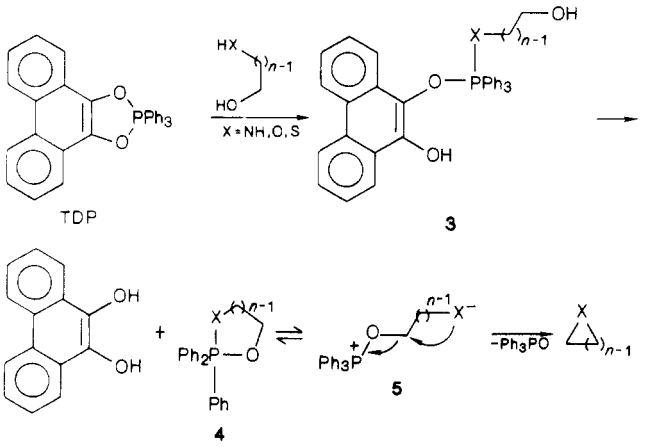
oxidized to phenanthrenequinone 1 when exposed to oxygen and since quinone 1 is only slightly soluble in toluene solvent this property facilitates its removal by filtration (Scheme I).

The efficiency of TDP in promoting the cyclodehydration of 1,4-butanediol and 1,2-propanediol to tetrahydrofuran (95%) and propylene oxide (93%), respectively, mirrors the results obtained with DTPP.[1c] Tetrahydropyran is formed in >95% from reaction of TDP with 1,5-pentanediol, which is a considerable improvement compared to the 72% yield of tetrahydropyran obtained with DTPP.[1c]

The effectiveness of TDP in converting amino alcohols to aziridines is underscored by the conversion of 2-benzyl-2-aminoethanol and *trans*-2-aminocyclohexanol to the corresponding aziridines (60% and 71%, respectively). Also, the possibility for N-alkylation using TDP is eliminated as demonstrated in the exclusive synthesis of cyclohexenimine (71%) with TDP in contrast to the attempted cyclodehydration of *trans*-2-aminocyclohexanol with DTPP which affords *trans*-2-(*N*-ethylamino)cyclohexanol.[10]

The versatility of TDP in preparing cyclic sulfides is dramatic and clearly demonstrated in the conversion of several mercapto alcohols to the cyclic sulfides in moderate to excellent yields (Scheme I). This methodology is superior to the current literature methods including DTPP which affords predominantly S-ethylated alcohols especially with substituted 1,2-mercapto alcohols.[4] With TDP,

Scheme II. Mechanistic Rationale for Formation of Heterocycles with TDP and $HX(CH_2)_nOH$



formation of episulfides occur in excellent yields (85–98%), while the yields of four-, five-, and six-membered ring sulfides are also good (70–85%).

A resonable mechanistic rational for these transformations involves initial phosphoranylation of $HX(CH_2)_nOH$ (where X = NH, O, S) by TDP through proton transfer to unsymmetrical dioxyphosphorane **3**. Loss of 1,2-dihydroquinone **2** through bisphosphoranylation of $HX(CH_2)_nOH$ gives the prerequisite 1,3,2-heteraoxaphosphorane **4**. Phosphorane **4** is in equilibrium with the requisite betaine **5**, and this undergoes cyclization to the desired heterocycle with expulsion of TPPO[1c] (Scheme II).

Experimental Section

^{13}C and ^{31}P nuclear magnetic resonance spectra were recorded on the IBM-Bruker 200 and the Bruker Model WM-250 NMR spectrometers. Chemical shift parameters are presented in parts per million (δ) downfield from internal tetramethylsilane (Me_4Si) for ^{13}C spectra and relative to external 85% H_3PO_4 for ^{31}P spectra.

Gas–liquid chromatographic (GLC) analyses were obtained on the Hewlett-Packard Model 5754B research gas chromatograph using a stainless steel column [0.125 in. (i.d.) × 10 ft] packed with 15% Carbowax DC-550 on Chromosorb W-HP-AW-DMCS, 80–100 mesh. Thin-layer chromatography (TLC) analyses were performed on plastic sheets coated with silica gel (Baker-Flex) and used for confirmation of sample homogeneity.

Toluene solvent was distilled from benzophenone ketyl, formed by addition of sodium to benzophenone in toluene solvent.[11]

The synthesis of all the mercapto alcohols and cyclic sulfides employed here have been described previously.[4]

Preparation of TDP. Triphenylphosphine (1.57 g, 0.006 mol) and phenanthrenequinone (1; 1.24 g, 0.006 mol) were heated (70 °C, 48 h) in anhydrous toluene solvent (7 mL) under an argon atmosphere for 48 h with magnetic stirring to afford in situ TDP (>95% by ^{31}P NMR): ^{13}C NMR (0.58 M in CD_2Cl_2) δ 142.8 (d, J = 118.1 Hz, Cl),[a] 128.2 (d, J = 13.2 Hz, C2),[b] 131.8 (d, J = 10.4 Hz, C3),[b] 129.8 (s, C4),[a] 136.4 (s, C5),[c] 123.6 (d, J = 9.4 Hz, C6),[a] 126.9 (s, C10),[a,b] 124.3 (s, C9),[a,d] 123.5 (s, C8),[a,d] 121.0 (s, C7),[a,d] and 126.4 (s, C11).[c,d] [During the off-resonance decoupling experiment, a = doublet, b = doublet of doublets, and c = singlet, while d indicates that the assignments of these ^{13}C resonances may be interchangeable.

General Procedure for Reaction of TDP with Mercapto Alcohols: 4-Mercaptobutanol (460 mg, 50.0 mmol) and anhydrous K_2CO_3 (1.0 g) were dissolved in a toluene solution (7 mL) containing TDP (ca. 60 mmol), and the resulting mixture was heated (45 °C) for 24 h. The yield (85%) and identity of tetramethylene sulfide was ascertained by coincidence of its ^{13}C NMR spectrum and GLC retention time with authentic material. Purification of the product was accomplished by rapid chromatography or

(10) Kelly, J. W.; Eskew, N. A.; Evans, S. A., Jr. *J. Org. Chem.* **1986**, *51*, 94–97.

(11) Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; Wiley-Interscience: New York, 1972; p 439.

distillation. The yields reported in Table I were ascertained by ^{13}C NMR and GLC analyses.

Acknowledgment. We are grateful to the Rohm & Haas Company for sponsoring the American Chemical Society's Organic Divisional Fellowship for J.W.K. (1985–1986). We also thank the National Research Council's Senior Postdoctoral Fellows Program (Ford Foundation), the Fulbright-Hays Scholar Program (to S.A.E.), and the Department of Energy for support of this research.

Registry No. 1, 84-11-7; 2, 604-84-2; TDP, 6546-78-7; $HO(CH_2)_4OH$, 110-63-4; $HOCH_2CH(OH)CH_3$, 57-55-6; $HO(CH_2)_5OH$, 111-30-8; $HOCH_2CH(NH_2)CH_2Ph$, 16088-07-6; $HO(CH_2)_2SH$, 60-24-2; $HOCH_2CH(CH_3)SH$, 3001-64-7; $HOCH_2CH(Ph)SH$, 60615-96-5; $HO(CH_2)_3SH$, 19721-22-3; $HO(CH_2)_4SH$, 14970-83-3; $HO(CH_2)_5SH$, 1633-79-0; PPh_3, 603-35-0; tetrahydrofuran, 109-99-9; propylene oxide, 75-56-9; tetrahydropyran, 142-68-7; *trans*-2-aminohexanol, 6982-39-4; 2-benzylaziridine, 13906-90-6; 7-azabicyclo[4.1.0]heptane, 286-18-0; thiirane, 420-12-2; phenylthiirane, 1498-99-3; methylthiirone, 1072-43-1; 7-thiabicyclo-[4.1.0]heptane, 286-28-2; thietane, 287-27-4; tetrahydrothiophene, 110-01-0; tetrahydro-2*H*-thiopyran, 1613-51-0; *trans*-2-mercaptocyclohexanol, 60861-06-5.

Asymmetric Synthesis. 6.[1] Practical Synthesis of (+)-Solenopsin A[2]

David S. Grierson, Jacques Royer, Luc Guerrier, and Henri-Philippe Husson*

Institut de Chimie des Substances Naturelles, CNRS, 91190 Gif-sur-Yvette, France

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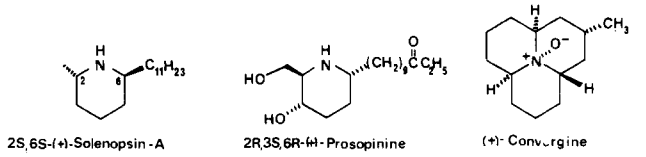
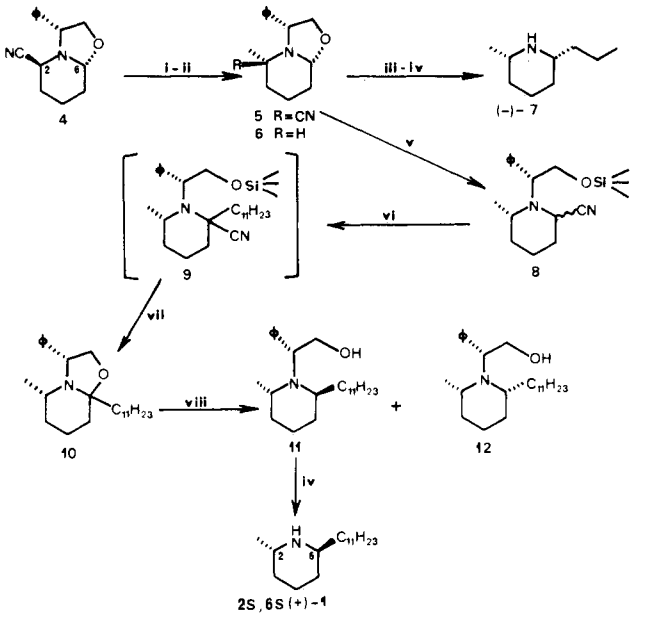
In a recent publication[3] we described the preparation of the (−)-2-cyano-6-oxazolopiperidine synthon **4**, a new chiral 1,4-dihydropyridine equivalent, and showed that selective functionalization of either the C-2 (α-amino nitrile) or C-6 (α-amino ether) centers could be achieved. In particular, it was shown that introduction of a second alkyl substituent at C-6 of intermediate **6** by reaction with PrMgBr was highly stereoselective producing the 2,6-cis substitution pattern typical to the piperidine alkaloid (−)-dihydropinidine (**7**) (Scheme I).

We have now extended our study of synthon **4** to the synthesis of the alternate and generally less accessible 2,6-trans relative configuration which is indigenous to piperidine alkaloids of both animal [i.e., solenopsin A (**1**) and the ladybug alkaloid convergine (**3**)] and plant [i.e., prosopinine (**2**)] origin (Chart I). Our strategy is based upon observations made during earlier work on the stereoselective reductive decyanation of 2-cyanopiperidines[4] and is illustrated by the first enantiospecific synthesis of the fire ant venom solenopsin A (**1**).[5]

Chart I



Scheme I[a]



[a] Reagents: (i) LDA, CH_3I, THF, −78 °C, 2.5 h; (ii) $Zn(BH_4)_2$, $AgBF_4$, THF, −78 °C, 1 h; (iii) PrMgBr, Et_2O, −60 °C, 20 h; (iv) H_2, Pd–C, MeOH; (v) Me_3SiCN, $ZnBr_2$ (catalyst), CH_2Cl_2, Δ, 15 h; (vi) LDA, THF–HMPA, $C_{11}H_{23}Br$, −20 °C, 15 h; (vii) 5% HFaq, CH_3CN; (viii) $NaBH_4$, MeOH, −10 °C, 2 h.

A key step (Scheme I) involved the reaction of intermediate **6** with trimethylsilyl cyanide in the presence of a catalytic amount of $ZnBr_2$ in refluxing CH_2Cl_2 (15 h). Under these conditions the oxazolidine ring was opened, which transformed the C-6 amino ether center to an α-amino nitrile system and converted the liberated hydroxyl group to its *O*-Me_3Si derivative. On rapid filtration of the crude reaction mixture through a short column of silica gel [hexane–ether (8/2)] compound **8** was obtained as a (7:3) mixture of epimers in nearly quantitative yield.

The possibility then existed to generate an anion at C-6 of **8**. Treatment of **8** with lithium diisopropylamide (LDA) in THF proved to be inefficient. However anion formation was readily achieved by reaction with 3 equiv of LDA in THF–HMPA (5 equiv) at −20 °C (30 min). Subsequent reaction of the orange anion solution with undecyl bromide (−20 °C, 15 h) gave **9**. As the crude product mixture invariably contained significant quantities of the recyclized compound **10** a solution of 5% aqueous HF in CH_3CN was generally added to the reaction before extractive workup in order to liberate the alcohol function and effect complete cyclization of **9** to **10**.[6] Compound **10** was isolated in 58% yield as a colorless low-melting crystalline solid after flash chromatography on silica gel.

Reductive cleavage of the oxazolidine ring of **10** was studied under a variety of conditions. In analogy with our earlier results[4] reaction of **10** with $NaBH_4$ in methanol (−10 °C, 2 h) led to formation of a 70:30 mixture of the trans

(1) For Part 5, see: Ratovelomanana, V.; Royer, J.; Husson, H.-P. *Tetrahedron Lett.* **1985**, *26*, 3803.

(2) Preliminary communication at the International Research Congress on Natural Products, University of North Carolina, Chapel Hill, July 1985.

(3) Guerrier, L.; Royer, J.; Grierson, D. S.; Husson, H.-P. *J. Am. Chem. Soc.* **1983**, *105*, 7754.

(4) Bonin, M.; Romero, J. R.; Grierson, D. S.; Husson H.-P. *Tetrahedron Lett.* **1982**, *23*, 3369. A synthesis of (±)-solenopsin A based upon the same mechanistic considerations has recently appeared.[5e]

(5) For the most recent syntheses of (±)-solenopsin A and analogues, see: (a) Sakane, S.; Matsumura, Y.; Yamamura, Y.; Ishida, Y.; Maruska, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1983**, *105*, 672. (b) Carruthers, W.; Williams, M. J.; Cox, M. T. *J. Chem. Soc., Chem. Commun.* **1984**, 1235. (c) Nakazono, Y.; Yamagushi, R.; Kawanisi, M. *Chem. Lett.* **1984**, 1129. (d) Mundy, B. P.; Bjorklund, M. *Tetrahedron Lett.* **1985**, *26*, 3899. (e) Takahashi, K. K.; Kurita, H.; Ogura, K.; Iida, H. *J. Org. Chem.* **1985**, *50*, 4368.

(6) Newton, R. F.; Reynolds, D. P.; Zinch, M. A. W.; Kelly, D. R.; Roberts, S. M. *Synth. Commun.* **1981**, *11*, 545.

0022-3263/86/1951-4475$01.50/0