Table IV. Reaction of Hexanal with $Me_3SiNCSe$[a]

solvent	catalyst	time, h	temp, °C	yield,[b] %
CH_3CN	–	48	RT[c]	<1
	$ZnCl_2$[d]	24	40	~15
hexane	–	48	40	<1
	$ZnCl_2$[d]	24	40	~85

[a] Reactions were carried out with $Me_3SiNCSe$ (5 mmol), hexanal (5 mmol), and a solvent (10 mL). [b] Determined by GLC with *n*-tridecane as an internal standard. [c] Room temperature. [d] 0.3 mmol.

Table V. One-Pot Reaction of Hexanal with $Me_3SiNCSe$ in Various Solvents[a]

solvent	catalyst	time, h	temp, °C	yield,[b] %
CH_3CN	$ZnCl_2$[c]	48	RT[e]	~5
	$ZnCl_2$[c]	24	40	17
CH_2Cl_2	–	24	40	42
	$ZnCl_2$[c]	24	40	69
	KSeCN/XAD-4[d]	24	40	61
benzene	–	24	40	55
	$ZnCl_2$[c]	24	40	60
hexane	–	24	40	78
	$ZnCl_2$[c]	20	40	>95
	KSeCN/XAD-4[d]	24	40	>95
	18-crown-6[c]	24	40	70

[a] All reactions were carried out with KSeCN (9 mmol), Me_3SiCl (5 mmol), hexanal (5 mmol), and a solvent (10 mL). [b] Determined by GLC. [c] 0.3 mmol. [d] KSeCN (9 mmol)/XAD-4 (2.0 g) was used in place of KSeCN (9 mmol). [e] Room temperature.

m/z 270 (M^+, ^{80}Se, ^{80}Se), 268 (M^+, ^{80}Se, ^{78}Se), 266 (M^+, ^{78}Se, ^{78}Se), 190 (M^+ – Se, ^{80}Se), 188 (M^+ – Se, ^{78}Se). Anal. Calcd for $C_4H_6N_2SeSi$: Se, 58.96. Found: Se, 57.8.

One-Pot Reaction of $Me_3SiNCSe$ with Hexanal in Various Solvents. After a mixture of KSeCN (1.3 g, 9 mmol), Me_3SiCl (0.54 g, 5 mmol), and a solvent (10 mL) was stirred for 7 h at room temperature, hexanal (0.50 g, 5 mmol) and tridecane (as an internal standard) were added to the mixture. The resulting mixture was stirred for the indicated time at 40 °C and analyzed by GLC (silicone SE-30, 10%, 1 m × 3 mm, 60 and 120 °C).

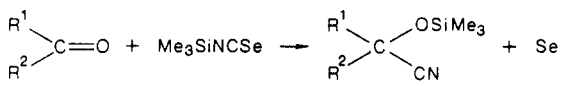
One-Pot Reaction of $Me_3SiNCSe$ with Carbonyl Compounds. GLC retention times and/or IR spectra of all the products were in agreement with those of the corresponding products obtained from the reaction with Me_3SiCN.[6]

Hexanal Cyanohydrin Trimethylsilyl Ether. After a mixture of KSeCN (4.32 g, 27 mmol), Me_3SiCl (2.43 g, 22.5 mmol), and hexane (30 mL) was stirred for 7 h at room temperature, hexanal (2.46 g, 24.6 mmol) and $ZnCl_2$ (0.08 g) were added to the mixture. The resulting mixture was stirred for 24 h at 40 °C. After the mixture had been cooled to room temperature, the solid material was filtered and washed with CH_2Cl_2. After removal of the solvent, the residue (4.63 g, ca. 100% yield) was distilled under reduced pressure, giving 4.09 g (91% yield) of product, bp 90–91 °C (10 mmHg). Redistillation, using a 70-mm column (with 5 mm × 5 mm rasching rings), gave the pure cyanohydrin ether: bp 89.0–89.5 °C (8 mmHg); IR (neat) 1256, 1128, 1100, 876, 848, 752 cm^{-1}, no CN; ^1H NMR ($CDCl_3$) δ 0.208 (s, 9 H), 0.906 (t, 3 H, *J* = 6 Hz), 1.1–1.9 (m, 8 H), 4.386 (t, 3 H, *J* = 6 Hz); MS, *m/z* 199 (M^+), 184 ($M^+ - CH_3$), 157.

Isobutyraldehyde Cyanohydrin Trimethylsilyl Ether. After a mixture of KSeCN (4.32 g, 27 mmol), Me_3SiCl (2.43 g, 22.5 mmol), and hexane (30 mL) was stirred for 7 h at room temperature, isobutyraldehyde (1.77 g, 24.6 mmol) and $ZnCl_2$ (0.08 g) were added. The resulting mixture was stirred for 48 h at 40 °C. The same treatment for hexanal gave 3.81 g (99% yield) of the crude product. The residue was distilled under reduced pressure to give 3.36 g (87% yield) of the cyanohydrin ether. Redistillation, using a 70-mm column (with 5 mm × 5 mm rasching rings), afforded the pure compound: bp 65.5–66.0 °C (14 mmHg); IR (neat) 1256, 1104, 872, 848, 752 cm^{-1}, no CN; ^1H NMR ($CDCl_3$) δ 0.208 (s, 9 H), 1.033 (dd, 6 H, *J* = 6.5, 1.8 Hz), 1.5–2.3 (m, 1 H), 4.158 (d, 1 H, *J* = 5.6 Hz); MS, *m/z* 171 (M^+), 156 ($M^+ - CH_3$), 129.

Trimethylacetaldehyde Cyanohydrin Trimethylsilyl Ether. This compound was isolated in 84% yield: bp 69–70 °C (15 mmHg); IR (neat) 1256, 1108, 868, 848, 752 cm^{-1}, no CN; ^1H NMR ($CDCl_3$) δ 0.208 (s, 9 H), 1.014 (s, 9 H), 3.982 (s, 1 H); MS, *m/z* 185 (M^+), 170 ($M^+ - CH_3$), 143.

Table VI. One-Pot Cyanosilylation Using $Me_3SiNCSe$[a]



R^1	R^2	solvent	time, h	temp, °C	yield,[b] %
CH_3CH_2	H	CH_2Cl_2	48	40	>95
		hexane	20	40	>95
$CH_3(CH_2)_4$	H	CH_2Cl_2	24	40	69
		hexane	24	40	~100 (91)[c]
$CH_3CH=CH$	H	hexane	72	60	22
$(CH_3)_2CH$	H	CH_2Cl_2	24	40	57
		hexane	24	40	86
		hexane	48	40	~99 (87)[c]
$(CH_3)_3C$	H	hexane	24	40	75
		hexane	48	40	>97 (84)[c]
C_6H_5	H	benzene	48	40	8
		hexane	40	60	30
CH_3CH_2	CH_3	hexane	24	40	0
$CH_3(CH_2)_4$	CH_3	hexane	24	40	0
$(CH_3)_2C=CH$	CH_3	hexane	72	40	0
C_6H_5	CH_3	benzene	48	40	0
		hexane	48	40	0

[a] Unless otherwise noted, reactions were carried out with KSeCN (9 mmol), Me_3SiCl (5 mmol), a carbonyl compound (5 mmol), $ZnCl_2$ (0.3 mmol), and a solvent (10 mL). [b] Determined by GLC. [c] Isolated yields. Reactions were carried out with KSeCN (27 mmol), Me_3SiCl (22.5 mmol), a carbonyl compound (24.6 mmol), $ZnCl_2$ (0.6 mmol), and a solvent (30 mL).

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Registry No. **1**, 16966-40-8; **2**, 119336-64-0; **3**, 119336-65-1; **4**, 16966-42-0; **5**, 119336-66-2; **6**, 119336-67-3; **7**, 119336-68-4; KSeCN, 3425-46-5; Me_3SiCl, 75-77-4; $Me_2PhSiCl$, 768-33-2; *t*-$BuMe_2SiCl$, 18162-48-6; Et_3SiCl, 994-30-9; $MePh_2SiCl$, 144-79-6; Ph_2HSiCl, 1631-83-0; Me_2SiCl_2, 75-78-5; $Ph_2HSiSeCN$, 119336-69-5; CH_3CH_2CHO, 123-38-6; $CH_3(CH_2)_4CHO$, 66-25-1; $CH_3CH=CHCHO$, 4170-30-3; $(CH_3)_2CHCHO$, 78-84-2; $(CH_3)_3CCHO$, 630-19-3; C_6H_5CHO, 100-52-7; $CH_3CH_2COCH_3$, 78-94-4; $CH_3(CH_2)_4COCH_3$, 110-43-0; $(CH_3)_2C=CHCOCH_3$, 141-79-7; $C_6H_5COCH_3$, 98-86-2; $CH_3CH_2CH(CN)OSiMe_3$, 24731-32-6; $CH_3(CH_2)_4CH(CN)OSiMe_3$, 40326-17-8; $CH_3CH=CHCH(CN)OSiMe_3$, 40326-20-3; $(CH_3)_2CHCH(CN)OSiMe_3$, 40326-16-7; $(CH_3)_3CCH(CN)OSiMe_3$, 88522-73-0; $C_6H_5CH(CN)OSiMe_3$, 25438-37-3; $ZnCl_2$, 7646-85-7; 18-crown-6, 17455-13-9; amberlite XAD-4, 37380-42-0.

Supplementary Material Available: Table III containing physical and spectral properties of silyl isoselenocyanates 1–7 (1 page). Ordering information is given on any current masthead page.

Pressure Effects in a Solvolysis Involving Extended π Participation

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Introduction

Knowledge and understanding of the effect of pressure on the rate and equilibrium constants of chemical reactions in solution have become increasingly widespread in recent

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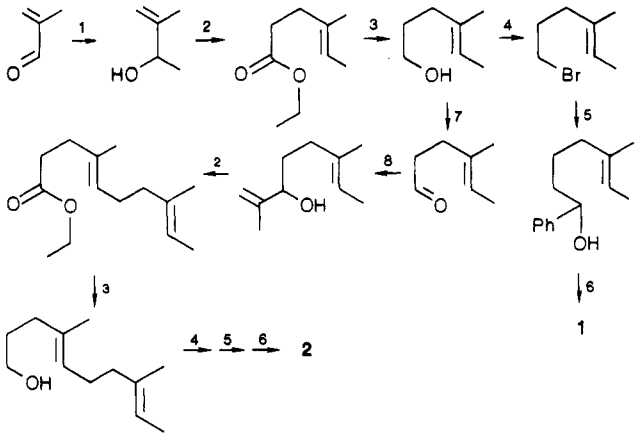
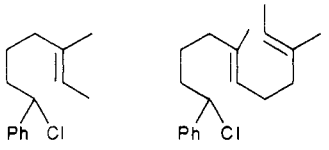
Scheme I[a]



[a] (1) MeLi in Et_2O at 0 °C; (2) $MeC(OEt)_3$, 180 °C, trace acid, 1 h; (3) $LiAlH_4$; (4) TsCl in pyr; LiBr in $(CH_2OMe)_2$; (5) Li in THF; PhCHO; (6) MeLi; MsCl at 0 °C; LiCl in HMPA/Et_2O at 0 °C; (7) CrO_3in CH_2Cl_2; (8) CH_2=$C(CH_3)MgBr$.

years, and chemists in numerous laboratories have acquired the equipment necessary to exploit the synthetic possibilities opened thereby.[1] One of the more intriguing questions not yet considered in the literature is the volume profile of the cyclization process that takes place in biomimetic pathways to steroid derivatives.[2] It is known that ionogenic reactions are invariably strongly accelerated by pressure, particularly when π participation is operative in the process.[3,4] It is less clear whether the several steps leading to polycyclic products occur successively[5-7] or in concert;[8,9] however, pressure-mediated yield improvements are conceivable either way.

Sunko and co-workers[9] have studied the solvolysis of a number of compounds such as **1**, in which π participation is indicated by small rate increases compared to saturated analogues, in spite of the levelling effect expected of the α phenyl group.[10] A claim has even been made for extended participation, i.e., by both double bonds, in substrate **2**.[11] We were interested in the question whether pressure could contribute evidence for such extended assistance, and hence we have determined the activation volumes for the solvolysis of compounds **1** and **2**.



1 **2**

Results and Discussion

These compounds were prepared according to Scheme I. It is similar to that used but not described in detail by Sunko;[9] the Experimental Section records details of this scheme that are not available in the literature.

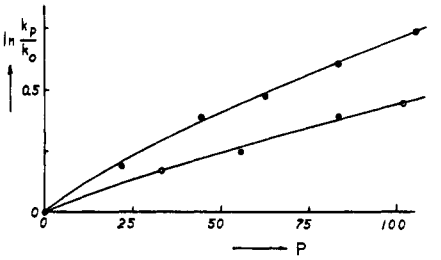
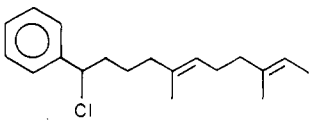


Figure 1. Solvolysis rates of **1** (open circles) and **2** (closed circles) at high pressure; k_P is the rate at high pressure and k_o is the rate at ambient pressure; P is given in MPa.

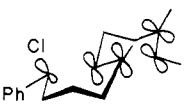
The rates of chloride ion formation in 80% aqueous ethanol at 45.0 °C were followed by means of conductance to at least 99% completion; the Guggenheim plots were nicely linear throughout, and the first-order rate constants were obtained with correlation coefficients averaging 0.998. At atmospheric pressure, they are 1.55 and 1.03×10^{-4} for **1** and **2**, respectively, in reasonable agreement with data published by Borcic et al. (measured under somewhat different conditions).[11] The activation volumes were computed in the usual way[12] from the rate constants at various pressures (see Figure 1); the values of -13.3 ± 1.0 and -24.0 ± 0.5 cm^3/mol for **1** and **2**, respectively.

In all previous reports[13] of the volume profile of solvolysis, "initial" volume contractions (i.e., at ambient pressure) have been noted and attributed to the process of electrostriction: the local increase in solvent density that accompanies the introduction and solvation of charge. These reports included one instance[4] (a 7-norbornenyl derivative) in which an enormously fast rate reveals π participation; in that case, the volume contraction was somewhat larger than normal (by perhaps 2–4 cm^3/mol). We have attributed this to the extra bond that is formed between the charged center and the olefinic bridge. In the present case, we therefore expected to see a similar difference between **1** and **2**; but as noted, the difference is substantially larger than that.

We tentatively suggest that this larger contraction may be the result of the conformational changes that must occur in order to achieve the prealignment of double bonds required for extended π participation. Such a change was not required in the norbornenyl case.



extended **2**



prealigned **2**

There is support for such an effect in the literature: in several instances in which IR spectra of 1,1-disubstituted ethanes have been determined at high pressure, intensity changes have been noted that could be attributed to increases in the relative populations of the gauche isomers as compared to the *anti* conformers.[14] This agrees with the general phenomenon that increased crowding leads to increased densities.[13]

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In order to gain some insight into the product-forming steps, we carried out methanolysis of **1** and **2** at 1 atm and at pressures of 600–800 MPa (1 MPa = 10 bar). It was ascertained that no significant reaction occurred before the final pressure was reached. The crude reaction mixtures were reduced by means of hydrogen and 5% palladium on carbon; GCMS data then allowed us to evaluate to what extent both open chain and cyclic olefins and methyl ethers had formed. The formation of cyclic chlorides (i.e., products resulting from rearrangement followed by return) was also detected in **1**.

The chromatograms resulting from the low- and high-pressure reactions of **1** are remarkably similar (83% cyclic product at atmospheric pressure, 84% at 600 MPa), but for **2**, there was a noticeable increase in the GC peak corresponding to a parent ion mass of 256 (phenyltrimethyldecalins) between 0.1 and 800 MPa. Unfortunately, overlapping peaks made it impossible to assess the pressure effect on the product distribution more precisely.

We tentatively conclude from the unusually large volume contraction that extended π participation does occur in the solvolysis of **2**. If our interpretation is correct, this contraction raises hopes that the application of pressure may improve yields in the multiple cyclization reactions characteristic of the biomimetic approach in steroid synthesis.

Experimental Section

3-Methylbut-3-en-2-ol. Methacrolein (20 g, 0.285 mol) dissolved in 100 mL of anhydrous ether was treated dropwise with methyllithium (210 mL, 0.3 mol) in ether under nitrogen at 0 °C. Saturated aqueous NH_4Cl solution was added; the organic layer was washed several times with water. After solvent evaporation the yellow liquid obtained was distilled at reduced pressure; the fraction at 118–120 °C was collected (35%). IR (neat): 3400 cm^{-1} (b, –OH). ^1H NMR ($CDCl_3$): δ 4.9–4.7 (m, 2 H, vinyl), 4.2 (q, 1 H, CHOH), 1.22 (d, 3 H, CH_3), 1.70 (s, 3 H, CH_3).

Ethyl 4-Methylhex-4-enoate. The procedure of Johnson et al. was used.[15] A mixture of the alcohol (10 g, 0.65 mol), ethyl orthoacetate (105 g, 0.8 mol), and propionic acid (0.1 mL) was heated, and the ethanol formed was collected; then, the distillation was continued at 0.5 Torr to yield the ester as colorless liquid boiling at 90 °C. The yield was 98%. ^1H NMR ($CDCl_3$): δ 1.24 (t, 3 H, CH_2CH_3), 1.6 (m, 6 H, CH_3), 2.34 (m, 4 H, CH_2CH_2), 4.11 (q, 2 H, OCH_2), 5.27 (q, 1 H, C=CH).

4-Methylhex-4-en-1-ol. The procedure of Borcic et al. was used.[11] The ester (5 g, 0.032 mol) was added dropwise and with magnetic stirring to a mixture of $LiAlH_4$ (1.21 g, 0.032 mol) and anhydrous ether (100 mL) under nitrogen at 0 °C. After the addition was complete, stirring was continued for about 2 h at room temperature, 10 mL of saturated aqueous Na_2SO_4 was added, and after filtration and evaporation of the solvent, the crude product was distilled at 9 Torr and 78 °C; the yield was 92%. IR (neat): 3400 cm^{-1} (b, –OH). ^1H NMR ($CDCl_3$): δ 5.27 (q, 1 H, C=CH), 3.62 (t, 2 H, $HOCH_2$), 1.95 (m, 4 H, CH_2), 1.55 (m, 6 H, CH_3). The CH_2OH proton is seen as a quartet in dry solution evidently due to splitting by the OH proton; it collapses to a triplet when a trace of dilute aqueous HCl is added. ^{13}C NMR ($CDCl_3$): δ 135.08, 118.27, 62.08, 35.64, 30.69, 15.19, 12.89. MS: m/z 114 (100, M^+), 115 (7.7, M + 1).

6-Bromo-3-methyl-2-hexene. The procedure of Johnson et al. was used.[16] A two-neck 100-mL flask was equipped with a $CaCl_2$ drying tube and an ice–water bath. A mixture of the hexenol (5 g, 0.043 mol), *p*-toluenesulfonyl chloride (10 g, 0.052 mol), and pyridine (17 g, 0.22 mol, previously distilled from P_2O_5) was stirred at 0 °C. A pink precipitate formed; after 2 h, 50 mL of ether was added, and this mixture was washed five times with cold water to remove the pyridine, dried over anhydrous $MgSO_4$, and flash evaporated to give a yellow liquid. This was added to a mixture of 100 mL of dry acetone and 7.6 g (0.0877 mol) of anhydrous LiBr. After refluxing for a half hour, the solvent was flash evaporated, 100 mL of ether was added, the mixture was washed several times with water, and the ether was flash evaporated to give a colorless liquid, which was distilled at 17 Torr and 69–70 °C; the yield was 86%. ^1H NMR ($CDCl_3$): δ 5.27 (q, 1 H, C=CH), 3.62 (t, 2 H, CH_2Br), 1.95 (m, 4 H, $CH_2CH_2CH_2Br$), 1.55 (m, 6 H, CH_3); MS: m/z 176 (100, M^+), 178 (93, M + 2).

5-Methyl-1-phenylhept-5-en-1-ol. The procedure of Pearce et al. was used.[17] A mixture of the bromide (1 g, 0.0056 mol) and dry benzaldehyde (0.71 g, 0.0067 mol) in 30 mL of dry THF was treated with small pieces of lithium metal (0.2 g, 0.029 mol) under nitrogen. This mixture was stirred at room temperature until most of lithium metal was consumed during the reaction. After filtration, 20 mL of cold saturated aqueous ammonium chloride was added to the yellow mixture; it was extracted with ether, the organic layer was washed three times with water and dried over anhydrous $MgSO_4$, the solvent was evaporated, and a pale yellow viscous liquid was isolated. Chromatography with silica gel and 1:50 ethyl acetate–petroleum ether gave excess benzaldehyde followed by the desired product (0.529 g, 46%). IR (neat): 3400 cm^{-1} (b, –OH), 2950 (m, –Ph) cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.35 (m, 5 H, Ph), 5.27 (q, 1 H, C=CH), 4.60 (t, 1 H, PhCHOH), 1.95 (m, 6 H, CH_2), 1.55 (m, 6 H, CH_3). ^{13}C NMR ($CDCl_3$): δ 144.00, 135.40, 128.31, 127.39, 125.83, 118.51 74.47, 39.22, 38.51, 23.93, 15.36, 13.21.

7-Chloro-3-methyl-7-phenyl-2-heptene (1). The procedure of Stork et al. was used.[18] Into a solution of the heptenol (100 mg, 9.49 mmol) in 5 mL of anhydrous ether and 1 mL of dry hexamethylphosphoramide, methyllithium (0.64 mmol) was slowly injected under nitrogen, followed by dry methanesulfonyl chloride (0.112 g, 0.98 mmol). A white precipitate formed; anhydrous lithium chloride (0.021 g, 0.98 mmol) was added immediately after. This reaction mixture was stirred at room temperature for about 20 min. After evaporation of the solvent, the residue was eluted through a silica gel column (previously saturated with triethylamine) with petroleum ether to give a mixture of the desired product (80–85%) and cyclized materials (15–20%). This mixture was used without further purification. ^1H NMR ($CDCl_3$): δ 7.35 (m, 5 H, Ph), 5.18 (m, 1 H, vinyl H), 4.85 (dd, 1 H, J_{H-H} = 8.1 Hz, ClCH). MS: m/z 222 (100, M^+), 224 (39, M + 2).

4-Methylhex-4-en-1-al. 3-Methylbut-3-en-2-ol (5 g, 0.0438 mol) in 100 mL of dry dichloromethane was treated with 13.8 g (0.064 mol) of pyridinium chlorochromate,[19] initially at 0 °C, but refluxing began soon and the solution became dark brown. After the action was over, the liquid was decanted, filtered through Florosil, and distilled at 70 °C and 25 Torr to furnish the aldehyde in 51% yield. ^1H NMR ($CDCl_3$): δ 9.75 (*t*, 1 H, CHO), 5.27 (m, 1 H, C=CH), 2.38 (m, 4 H, CH_2), 1.54 (m, 6 H, CH_3).

2,6-Dimethylocta-1,6-dien-3-ol. The procedure of Fieser and Fieser[20] was employed. Magnesium ribbon (0.034 g, 1.4 mmol) was covered with 40 mL of anhydrous tetrahydrofuran in a well-dried flask, and the mixture was treated dropwise with 3.85 g (0.032 mol) of 2-bromopropene at 0 °C. After reaction, 0.336 g (0.03 mol) of 4-methylhex-4-en-1-al in 10 mL of dry THF was added slowly; 50 mL of cold saturated aqueous ammonium chloride was added, the organic layer was washed three times with water, and the solvent was evaporated to give a yellow liquid. IR (neat): 3400 cm^{-1} (b, –OH).

Ethyl 4,8-Dimethyl-4,8-decadienoate. Johnson's procedure[15] was employed as above, with the crude dienol. ^1H NMR ($CDCl_3$): δ 5.15 (m, 2 H, C=CH), 4.10 (q, 2 H, OCH_2CH_3), 2.35 (m, 4 H, $CH_2CH_2COOC_2H_5$), 1.59 (m, 9 H, C=CHCH$_3$).

4,8-Dimethyl-4,8-decadien-1-ol. The ester was reduced in the same way as that described above. IR: 3400 cm^{-1} (b, –OH). ^1H NMR ($CDCl_3$): δ 5.27 (b m, 2 H, C=CH), 3.62 (t, 2 H, CH_2OH), 1.55 (m, 9 H, CH_3), 2.0 (m, 8 H, CH_2).

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10-Bromo-3,7-dimethyl-2,6-decadiene. The procedure was that described above; bp 130 °C at 0.5 Torr. ^{1}H NMR ($CDCl_3$): δ 5.15 (m, 2 H, C=C*H*), 3.36 (t, 2 H, BrCH_2), 2.05 (m, 8 H, CH_2CH_2), 1.59 (m, 9 H, C=CCH_3). ^{13}C NMR: δ 135.34, 132.74, 125.72, 118.41, 39.55, 37.76, 33.36, 30.80, 26.47, 15.73, 15.54, 13.33.

5,9-Dimethyl-1-phenylundeca-5,9-dien-1-ol. This phenyl derivative was prepared in the manner described above. IR (neat): 3400 cm^{-1} (b, -OH). ^{1}H NMR ($CDCl_3$): δ 7.25 (m, 5 H, Ph), 5.15 (m, 2 H, C=C*H*), 4.66 (dd, 1 H, Ph(OH)C*H*), 2.0 (m, 10 H, CH_2), 1.59 (m, 10 H, C=CHCH_3 and OH). ^{13}C NMR ($CDCl_3$): δ 144.83, 135.59, 134.52, 128.30, 127.34, 125.80, 124.54, 118.22, 74.48, 39.65, 39.33, 38.46, 26.53, 23.94, 15.27, 15.01, 13.30.

11-Chloro-3,7-dimethyl-11-phenyl-2,6-undecadiene (2). The procedure used was the same as that described above for **1**. GC analysis showed the product to contain 70% of the desired chloride and 30% of cyclization products. ^{1}H NMR ($CDCl_3$): δ 7.34 (m, 5 H, Ph), 5.15 (m, 2 H, C=CH), 4.83 (dd, 1 H, PhClCH), 1.98 (m, 10 H, CH_2), 1.58 (m, 9 H, C=CHCH_3). ^{13}C NMR ($CDCl_3$): δ 141.96, 135.51, 134.05, 128.26, 128.02, 126.63, 124.99, 118.34, 63.99, 39.62, 39.31, 38.80, 26.50, 25.10, 15.88, 15.68, 13.34.

Solvolysis. The rate constants were measured in 80% (v/v) aqueous ethanol by means of the Guggenheim method as previously described.[21] For the purpose of calibration, the rate constant for α-phenylethyl chloride was measured at 50.0 °C and compared with Winstein's;[22] our result (16.3×10^{-5}, s^{-1}) agreed to within 4%. The rates of **1** and **2** were measured at 45.0 °C. A single batch of solvent was used for all experiments. In each of these, 5 mg of substrate was dissolved in 25 mL, and the solution was transferred to the conductance cell, and this was suspended in a thermostatted high-pressure vessel.[14] The resistance was measured periodically to at least 99% reaction.

Product Analysis. Remaining samples of **1** and **2** were methanolyzed at atmospheric pressure and at 600 MPa. The product solutions in each case were treated with 2 mg of 5% palladium on carbon catalyst and hydrogenated with 2 atm of hydrogen pressure in a hydrogenation apparatus for about 2 h. After filtration of the catalyst, the solvent was evaporated to yield residues that were analyzed by means of GC–MS.

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Asymmetric Synthesis of the Methyl and Benzyl Ethers of *erythro*-α,β-Diphenyl-β-hydroxyethanol and *erythro*-α,β-Diphenyl-β-hydroxyethylamine from (+)-(*S*)-Benzoin

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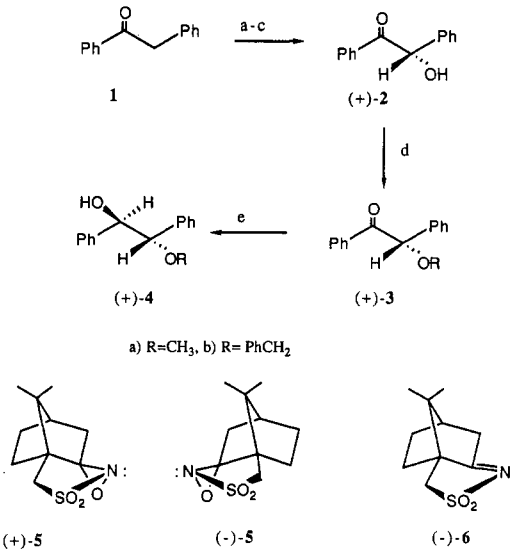
In connection with our interest in the synthesis and application of optically active α-hydroxy acids we needed to prepare the methyl and benzyl ethers of *erythro*-α,β-diphenyl-β-hydroxyethanol, **4a** and **4b**, respectively.[1-3] These compounds were required as chiral auxiliaries in studies of double asymmetric synthesis for the asymmetric oxidation of chiral enolates to α-hydroxy carbonyl compounds with (camphorylsulfonyl)oxaziridine (+)-**5** and (−)-**5**.[1] This protocol has recently been demonstrated in the enantioselective synthesis of atrolactic acid (88–91% ee).[1]

Scheme I[a]



[a] (a) NaHMDS, THF, −78 °C; (b) (+)-**5**, NH_4I; (c) $(CF_3CO)_2O$, 5% NaOH; (d) Ag_2O, MeI, $CHCl_3$ or benzyl trichloroacetimidate; (e) DIBAL-H, THF, −78 °C.

Our synthetic strategy is outlined in Scheme I and begins with the preparation of enantiomerically pure (+)-(*S*)-benzoin (**2**). This compound can be prepared in >96% optical purity and 84% isolated yield by oxidation of the sodium enolate of deoxybenzoin (**1**) with (+)-(2*R*,8a*S*)-(camphorylsulfonyl)oxaziridine (**5**).[2] On a small scale (0.5 mmol) (+)-**2** is separated from the sulfonimine **6** byproduct by preparative TLC or flash chromatography. To avoid the chromatographic separation on a larger scale synthesis of (+)-**2** (50 mmol) the hydroxyl group is transformed into the triflate ester by treatment of the crude reaction mixture with trifluoroacetic anhydride. The triflate ester was separated from the polar sulfonimine (−)-**6** by extraction into *n*-pentane. Hydrolysis of the triflate ester with 5% NaOH gives **2** in 67% overall yield from **1**. Attempts to remove the triflate ester with dilute HCl resulted in racemization. Recrystallization from ethanol increases the optical purity of (+)-**2** from 96% ee to 98% ee as determined by HPLC with a chiral column.

Routes to enantiomerically pure (+)-**2** and (−)-**2** include resolution,[4] enzymatic reduction of benzil,[5] and oxidation of optically active ethyl 2-amino-1,2-diphenylacetate.[6] This asymmetric enolate oxidation approach to (+)-benzoin (**2**) (+)-**2** is particularly efficient since (+)-**5** is readily available.[7] An additional advantage of this methodology is that both (+)-**2** and (−)-**2** can be easily prepared because the configuration of the oxaziridine three-membered ring in (+)-**5** and (−)-**5** controls the product stereochemistry.[7]

The alkylation of enolates derived from α-hydroxy ketones with carbon electrophiles is reported to occur at the carbon atom bearing the hydroxy group.[8] Indeed, at-

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