telluronium ylides as intermediates. It was not necessary to manipulate under nitrogen and at low temperature or to prepare the corresponding telluronium salt and ylide. Secondly, the total yields were also enhanced greatly. Since this reaction does not need to use a strong base, it was possible to synthesize the α,β-unsaturated compounds with base-sensitive functional groups.

Experimental Section

Synthesis of Telluronium Salts. 1. (Cyanomethyl)dibutyltelluronium Chloride. An equimolar mixture of dibutyl telluride and chloroacetonitrile was stirred under nitrogen at room temperature overnight to afford a colorless crystal: Yield 95%; mp 92–93 °C; IR (cm^{-1}) 2235 (C≡N); ^1H NMR (ppm) 1.0 (6 H, t), 1.45 (4 H, m), 2.0 (4 H, m), 3.14 (4 H, t), 3.09 (2 H, s). Anal. Found: C, 37.85; H, 6.35; N, 4.41 (theoretical values: C, 37.87; H, 6.42; N, 4.29.

2. Phenacyldibutyltelluronium Bromide. An equimolar mixture of dibutyl telluride and 2-bromoacetophenone was stirred at room temperature for 3 h to afford a colorless crystal: yield 93%; mp 104–106 °C; IR (cm^{-1}) 1665, 1610, 1590, 1455. Anal. Found: C, 43.66; H, 5.79 (theoretical values: C, 43.59; H, 5.72.

3. (Carbomethoxymethyl)dibutyltelluronium Bromide. An equimolar mixture of dibutyl telluride and methyl bromoacetate was stirred at room temperature for 3 h to afford a colorless crystal: yield 90%; mp 68–70 °C.

Synthesis of α,β-Unsaturated Esters, Ketones, and Nitriles: Typical Experimental Procedures. 1. Using Telluronium Ylides. Method A. Cyanomethyldibutyltelluronium chloride (0.34 g, 2.5 mmol) in dry THF (25 mL) was syringed into a solution of potassium *tert*-butoxide (0.43 g, 3.8 mmol) in THF at −20 °C under nitrogen. After a few minutes, the solution of *p*-chlorobenzaldehyde (0.35 g, 2.5 mmol) in THF (6 mL) was added. The mixture was stirred for 3 h at −20 °C, quenched with water, extracted with ethyl ether. The organic extract was dried and evaporated. The residue product was purified by column chromatography on silica gel to afford pure 4-chlorocinnamonitrile (83%, E/Z = 16/3).

2. Using Telluronium Salts. Method B. A mixture of carbethoxydibutyltelluronium bromide (0.99 g, 2.5 mmol) and 4-nitrobenzaldehyde (0.38 g, 2.5 mmol) was refluxed in THF (30 mL). After 6 h, it was quenched with water and extracted with ether. The organic extract was purified by recrystallization to afford pure methyl 3-(4′-nitrophenyl)propenoate (yield 95%, E configuration).

3. Using Dibutyl Telluride. Method C. A mixture of 3-nitrobenzaldehyde (0.38 g 2.5 mol), methyl bromoacetate (0.38 g, 2.5 mmol), and dibutyl telluride (0.61 g, 2.5 mmol) was refluxed in THF. After 6 h, it was worked up as method B to give pure methyl 3-(3′-nitrophenyl)propenoate (yield 89%, E configuration).

All products were confirmed by their melting points (boiling points) and IR and ^1H NMR spectra (Tables IV and V).

Acknowledgment. This research was supported by the Science Fund of the Chinese Academy of Science.

Registry No. **1a**, 111873-50-8; **1b**, 111873-49-5; **1c**, 111873-48-4; C_6H_5CH=CHCN, 4360-47-8; *p*-ClC_6H_4CH=CHCN, 28446-72-2; *p*-$CH_3OC_6H_4CH$=CHCN, 28446-68-6; *p*-$NO_2C_6H_4CH$=CHCN, 27892-88-2; *p*-BrC_6H_4CH=CHCN, 76386-57-7; *o*-ClC_6H_4CH=CHCN, 74738-21-9; *p*-$CH_3C_6H_4CH$=CHCN, 28446-70-0; $(CH_3)_2C$=CHCN, 4786-24-7; c-C_6H_{10}=CHCN, 4435-18-1; *p*-ClC_6H_4CH=CHCOPh, 956-04-7; *p*-BrC_6H_4CH=CHCOPh, 1774-66-9; C_6H_5CHO, 100-52-7; *p*-ClC_6H_4CHO, 104-88-1; *p*-$CH_3OC_6H_4CHO$, 123-11-5; *p*-$NO_2C_6H_4CHO$, 555-16-8; *p*-BrC_6H_4CHO, 1122-91-4; *o*-ClC_6H_4CHO, 89-98-5; *p*-$CH_3C_6H_4CHO$, 104-87-0; $CH_3C(O)CH_3$, 67-64-1; c-C_6H_{10}=O, 108-94-1; *p*-$NO_2C_6H_4CH$=$CHCOOCH_3$, 1608-36-2; *m*-$NO_2C_6H_4CH$=$CHCOOCH_3$, 1664-59-1; *m*-$NO_2C_6H_4CH$=CHCOPh, 614-48-2; *p*-$NO_2C_6H_4CH$=CHCOPh, 1222-98-6; *m*-$NO_2C_6H_4CHO$, 99-61-6; *n*-Bu_2Te, 38788-38-4; $ClCH_2CN$, 107-14-2; *p*-BrC_6H_4CH=$CHCOOCH_3$, 3650-78-0; *p*-$NO_2C_6H_4CH$=$CHCOOC_2H_5$, 953-26-4; $BrCH_2COOC_2H_5$, 105-36-2; ω-bromoacetophenone, 70-11-1; methyl bromoacetate, 96-32-2.

Asymmetric Synthesis of (2*R*)-2-Hydroxy-2-(2(*Z*)-octenyl)-1-cyclopentanone

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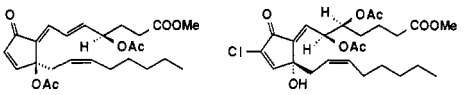
Received November 30, 1987

Marine eicosanoids such as clavulones and punaglandins are of interest because of their relationship to prostaglandins, their antitumor activity, and also the pathway of biosynthesis.[1] Recently we have achieved efficient total syntheses of (+)-clavulone II (1) and (+)-punaglandin 4 (2) utilizing (±)-2-hydroxy-2-(2(*Z*)-octenyl)-1-cyclopentanone as a key intermediate, readily obtainable from 1,2-bis[(trimethylsilyl)oxy]cyclopentene.[2c,g] In order to improve our synthetic routes to (+)-**1** and (+)-**2**, we have undertaken an efficient asymmetric synthesis of 2-hydroxy-2-(2(*Z*)-octenyl)-1-cyclopentanone, which is described in this paper.



1 2

In order to construct the quarternary carbon atom of **13** in optically pure form, it was expected that asymmetric hydride reduction of the dienone **8** would be a useful approach owing to the fact that stereocontrolled transformation of the resulting alcohol **10** into **13** would be possible. At the outset, the substrate (dienone) **8** for asymmetric reduction was synthesized by the route shown in Scheme I. Treatment of 1-[(trimethylsilyl)oxy]cyclopentene (**3**) with the α,β-unsaturated aldehyde **4** in the presence of a catalytic amount of titanium tetrachloride afforded the β-[(trimethylsilyl)oxy]cyclopentanone derivative **5**, which was deprotected to give the β-hydroxycyclopentanone **6** in 69% overall yield. Transformation of **6** to the acetate **7** followed by treatment with potassium *tert*-butoxide in THF provided the dienone **8** in 74% overall yield. The stereochemistry of **8** was supported by the following two facts. The C–H coupling constant between the carbonyl carbon and the β-hydrogen was 5 Hz, indicating that the stereochemistry of the exocyclic olefin is E.[3] Furthermore, comparison with the stereoisomer **9**, which had actually been synthesized, showed that the stereochemistry of the disubstituted olefin was Z[4] (Scheme I).

With an efficient synthesis of the dienone **8** in hand, the asymmetric hydride reduction of **8** was investigated. Reduction of **8** with the complex[5] formed from lithium aluminum hydride and "Darvon alcohol", (+)-(2*S*,3*R*)-4-(dimethylamino)-3-methyl-1,2-diphenyl-2-butanol, was carried out, affording the (*R*)-cyclopentanol derivative **10** in 78% yield with 78% ee. The enantiomeric excess of **10** thus obtained was determined by 400-MHz NMR analysis of its MTPA derivative, but the absolute configuration of **10** was not clear at this stage. Several asymmetric hydride reductions of **8** were further examined in order to improve the enantiomeric excess as well as the chemical yield. We were pleased to find that reduction of **8** with lithium aluminum hydride partially decomposed by (−)-*N*-methyl-

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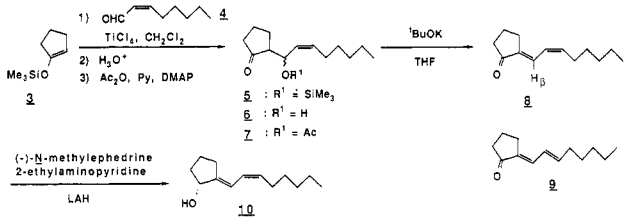
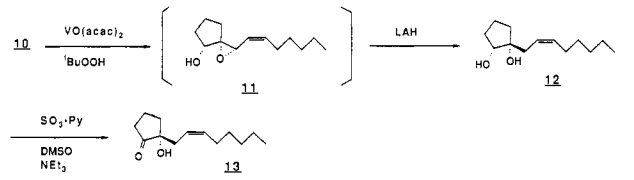
Scheme I



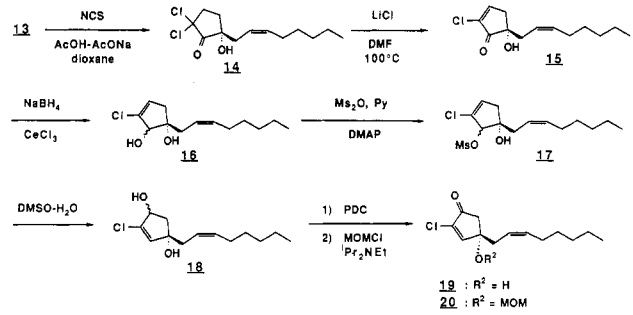
Scheme II



ephedrine and 2-(ethylamino)pyridine[6] provided the (*R*)-cyclopentanol derivative **10** in 91% yield with 96% ee.

Our next goal was to convert **10** to (2*R*)-2-hydroxy-2-(2(*Z*)-octenyl)-1-cyclopentanone (**13**) efficiently in a stereocontrolled manner. Toward this end, **10** was treated with *tert*-butyl hydroperoxide in the presence of vanadyl acetylacetonate[7] at room temperature, resulting in the formation of the rather unstable epoxide **11**, which was directly reduced with lithium aluminum hydride to give the diol **12** in 93% overall yield. Similarly, epoxidation reaction using *m*-CPBA in methylene chloride at −10 to −20 °C and subsequent reduction with lithium aluminum hydride afforded **12** in 76% overall yield. Oxidation of the diol **12** with sulfur trioxide–pyridine in DMSO containing triethylamine provided (2*R*)-2-hydroxy-2-(2(*Z*)-octenyl)-1-cyclopentanone (**13**) in 84% yield. The optical purity of **13** thus obtained was determined to be >95% by 400-MHz NMR analysis using the chiral shift reagent, tris-[3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorato]europium(III) derivative. Based on the optical purity of **13** together with a consideration of the mechanism of the epoxidation reaction, it was concluded that both the epoxidation reactions occurred in a highly stereocontrolled manner to give the α-epoxide **11** (Scheme II).

Scheme III



(2*R*)-2-Hydroxy-2-(2(*Z*)-octenyl)-1-cyclopentanone (**13**) was then transformed into another key intermediate (**20**) for punaglandin 4 (**2**) by the route shown in Scheme III.[2g] The absolute configuration of **20** thus obtained, $[\alpha]^{20}_D$ +50.2° (*c* 0.315, $CHCl_3$), was unequivocally determined to be *S* in comparison with the Yamada intermediate **20**, $[\alpha]_D$ +43.7° (*c* 1.82, $CHCl_3$)[2e] (Scheme III).

The present asymmetric synthesis of (2*R*)-2-hydroxy-2-(2(*Z*)-octenyl)-1-cyclopentanone (**13**) has made our (+)-punaglandin 4 (**2**) synthesis much more efficient. Furthermore, the use of (+)-*N*-methylephedrine in place of (−)-*N*-methylephedrine would provide (2*S*)-2-hydroxy-2-(2(*Z*)-octenyl)-1-cyclopentanone, a key intermediate for our (+)-clavulone II (**1**) synthesis.

Experimental Section

IR spectra were measured on a JASCO A-202 diffraction grating infrared spectrophotometer. ^1H NMR spectra were recorded with a Varian EM390 NMR spectrometer or a Hitachi R-90H Fourier transform NMR spectrometer or a Bruker AN-400 spectrometer with tetramethylsilane as an internal standard. ^{13}C NMR spectra were recorded with a Bruker AN-400 spectrometer with tetramethylsilane as an internal standard. Low-resolution mass spectra were obtained from a Hitachi RMU-6MG mass spectrometer and high-resolution mass spectra from a Hitachi M-80A mass spectrometer. Optical rotation was measured on a Horiba SEPA-200 high sensitive polarimeter.

In general, reactions were carried out in dry solvents under an argon atmosphere unless otherwise mentioned. Dry solvents were obtained as follows: tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone; methylene chloride (CH_2Cl_2), benzene, and *N*,*N*-dimethylformamide were distilled from calcium hydride.

2(*Z*)-Octenal (4). To a stirred solution of 1-heptyne (10.00 g, 104 mmol) in THF (50 mL) was added BuLi (64.6 mL, 1.61 M hexane solution) at −15 °C. After stirring for 20 min at the same temperature, formaldehyde gas generated from paraformaldehyde at 220 °C was bubbled at a stretch (−25 °C). After being stirred for 15 min, the reaction mixture was warmed to 23 °C, quenched with saturated aqueous NH_4Cl, filtered through Celite, and extracted with ether. The combined ether extracts were washed with brine, dried ($MgSO_4$), and concentrated. The product was purified by distillation, bp_{23} 115 °C, to give 2-octyn-1-ol (9.01 g, 69 %) as a colorless oil: ^1H NMR ($CDCl_3$) δ 0.93 (t, *J* = 6 Hz, 3 H), 1.10–1.77 (m, 6 H), 1.90 (br s, 1 H), 2.09–2.40 (m, 2 H), 4.30 (s, 2 H). A suspension of 2-octyn-1-ol (6.84 g, 54 mmol), quinoline (0.7 mL), and Lindlar catalyst (513 mg) in hexane (80 mL) was stirred under an H_2 atmosphere at 23 °C for 4.5 h, filtered through Celite, and concentrated. The product was purified by silica gel column chromatography (hexane–ethyl acetate, 15:1 → 8:1) to give 2(*Z*)-octen-1-ol (6.72 g, 97%) as a nearly colorless oil: ^1H NMR ($CDCl_3$) δ 0.89 (t, *J* = 7 Hz, 3 H), 1.10–1.60 (m, 7 H), 1.70–2.30 (m, 2 H), 4.22 (d, *J* = 6 Hz, 2 H), 5.40–5.80 (2 H, m); mass spectrum, *m*/*e* 128, 110; HR-MS (M^+) calcd for $C_8H_{16}O$ 128.1201, found 128.1210. To a stirred solution of 2(*Z*)-octen-1-ol (1.00 g, 7.8mmol) in CH_2Cl_2 (100 mL) was added activated

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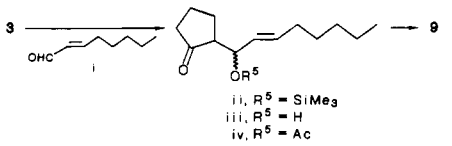
(3) In general, the C–H coupling constant between the carbonyl carbon and the trans β-hydrogen is 11–15 Hz, while that between the carbonyl carbon and the cis β-hydrogen is 4–8 Hz.

(4) The stereoisomer **9** was synthesized by the route shown below.



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manganese dioxide (23.76 g, 270 mmol) in an ice bath. After being stirred for 70 min at the same temperature, the reaction mixture was filtered through Celite. The filtrate was concentrated to give an oily residue, which was purified by silica gel column chromatography (hexane–ether, 5:1), to give 2(*Z*)-octenal (**4**) as a nearly colorless oil (906 mg, 92%): ^{1}H NMR ($CDCl_3$) δ 0.92 (t, J = 6 Hz, 3 H), 1.05–1.08 (m, 6 H), 2.40–2.80 (dt, J = 8.5, 8 Hz, 1 H), 5.97 (ddt, J = 11.5, 8, 1.5 Hz, 1 H), 6.65 (dt, J = 11.5, 8.5 Hz, 1 H), 9.55 (d, J = 8 Hz, 1 H); IR (neat) 1680 cm^{-1}.

2(*E*)-[2(*Z*)-Octenylidene]-1-cyclopentanone (8). To a stirred solution of **4** (1.74 g, 13.8 mmol) in CH_2Cl_2 (130 mL) was added **3** (3.23 g, 20.7 mmol) in 20 mL of CH_2Cl_2 at −90 to −100 °C. After addition of titanium tetrachloride (150 μL), the whole reaction mixture was stirred for 65 min at the same temperature. The reaction was quenched with saturated aqueous NH_4Cl, gradually warmed to 23 °C with vigorous stirring, extracted with ether, washed with brine, dried ($MgSO_4$), and concentrated. The crude oily residue was treated with MeOH–H_2O–AcOH (20:1:1). After evaporation of solvent, the product was purified by silica gel column chromatography (hexane–ether, 4:1) to give **6** as a nearly colorless oil (1.96 g, 69%): ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 6 Hz, 1 H), 1.09–1.50 (m, 6 H), 1.60–2.60 (m, 10 H), 4.90 (m, 1 H), 5.30–5.80 (m, 2 H); IR (neat) 3465, 1735, 1660, 1465, 1450, 1405, 1375, 1330, 1270, 1150 cm^{-1}; mass spectrum, m/e 210 (M^+), 192, 139, 127, 126, 121, 109, 84, 83, 70, 67, 57; HR-MS (M^+) calcd for $C_{13}H_{22}O_2$ 210.1620, found 210.1606. To a stirred solution of **6** (205 mg, 0.98 mmol) in pyridine (1 mL) was added acetic anhydride (0.5 mL) and a catalytic amount of 4-(dimethylamino)-pyridine (8 mg) in an ice bath. After being stirred for 110 min, the reaction was quenched with ether and saturated aqueous $NaHCO_3$, stirred further for an additional 0.5 h, and extracted with ether. The combined ether extracts were successively washed with saturated aqueous $NaHCO_3$, saturated aqueous $CuSO_4$, 5% aqueous HCl, saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated to give **7** (245 mg, 100%) as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6 Hz, 3 H), 1.07–1.50 (m, 6 H), 1.70–2.50 (m, 12 H), 5.09–5.80 (m, 2 H), 5.90 (dd, J = 9, 3 Hz, 1 H); mass spectrum, m/e 252 (M^+), 209, 193, 192, 150, 139, 127, 126, 125, 121, 109, 93, 84, 83, 80, 79, 67; HR-MS (M^+) calcd for $C_{15}H_{24}O_3$ 252.1726, found 252.1739. To a stirred solution of **7** (463 mg, 1.84 mmol) in THF (2 mL) was added potassium *tert*-butoxide (226 mg, 2.01 mmol) in THF (10 mL) at −78 °C, and the whole reaction mixture was stirred for 20 min at the same temperature. The reaction was quenched with saturated aqueous NH_4Cl, extracted with ether, washed with brine, dried ($MgSO_4$), and concentrated. The product was purified by silica gel column chromatography (hexane–ether–CH_2Cl_2, 15:1:1) to afford **8** (263 mg, 74%) as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 7 Hz, 3 H), 1.24–1.48 (m, 6 H), 1.97 (dt, J = 7.6, 7.5 Hz, 2 H), 2.28–2.40 (m, 4 H), 2.70 (dt, J = 7.2, 2.5 Hz, 2 H), 5.99 (m, 1 H), 6.12 (m, 1 H), 7.25 (m, 1 H); IR (neat) 1715, 1625, 1605, 1470, 1435, 1415, 1380, 1300, 1290, 1270, 1230, 1190 cm^{-1}; mass spectrum, m/e 192 (M^+), 149, 135, 123, 122, 121, 95, 94, 93, 91, 81, 80, 79, 78, 77, 76, 67, 66, 65, 55; HR-MS (M^+) calcd for $C_{13}H_{20}O_1$ 192.1514, found 192.1496.

Asymmetric Hydride Reduction of 8. To a stirred suspension of lithium aluminum hydride (130 mg, 3.10 mmol) in ether (5 mL) was gradually added (−)-*N*-methylephedrine (672 mg, 3.75 mmol) in ether (5–7 mL) at 0–5 °C, and then the whole reaction mixture was refluxed for 1 h and again cooled to 0–5 °C. To this mixture was gradually added 2-(ethylamino)pyridine (915 mg, 7.5 mmol) in ether (5 mL), and the resulting mixture was again refluxed for 1 h to give a pale yellow suspension. To a cooled (−78 °C) suspension was gradually added **8** (200 mg, 1.04 mmol) in ether (3 mL). After being stirred for 4 h at −78 °C, the reaction was quenched with MeOH (0.1 mL) and 0.5 M aqueous HCl, extracted with ether, washed with brine, dried ($MgSO_4$), and concentrated. The product was purified by silica gel column chromatography (hexane–ether–CH_2Cl_2, 8:1:1) to give **10** (185 mg, 92%) as a nearly colorless oil together with **8** (9 mg): $[\alpha]^{20}_D$ −164° (*c* 1.36, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 7 Hz, 3 H), 1.09–1.50 (m, 7 H), 1.53–2.00 (m, 4 H), 2.00–2.67 (m, 4 H), 4.52 (br s, 1 H), 5.50 (dt, J = 11, 7.5 Hz, 1 H), 6.06 (dd, J = 11, 11 Hz, 1 H), 6.45 (d, J = 11 Hz, 1 H); IR (neat) 3330, 1645, 1610, 1465, 1425, 1375, 1310, 1290, 1170, 1135, 1090, 1070, 1020 cm^{-1}; mass spectrum, m/e 194 (M^+) 176, 123, 119, 110, 97, 95, 91, 84, 79, 77, 69, 67; HR-MS (M^+) calcd for $C_{13}H_{22}O_1$ 194.1671, found 194.1685.

(1*R*,2*R*)-2-Hydroxy-2-[2(*Z*)-octenyl]-1-cyclopentanol (12). To a stirred suspension of a catalytic amount of $VO(acac)_2$ (0.3 mg) in benzene (1 mL) was added **10** (50 mg, 0.26 mmol) in benzene (1 mL). To this suspension was then gradually added *tert*-butyl hydroperoxide in a CH_2Cl_2 solution (5.8 M solution, 50 μL) at 23 °C. After being stirred for 3 h at the same temperature, the reaction was quenched by the addition of $Na_2S_2O_3 \cdot 7H_2O$, filtered through Celite, and concentrated. The oily residue in ether (3 mL) was treated with a THF solution of LAH (1.0 M, 0.5 mL) at −10 °C. After being stirred for 20 min at the same temperature, the reaction was quenched with $Na_2SO_4 \cdot 10H_2O$ (0–5 °C), diluted with ether, filtered through Celite, dried (Na_2SO_4), and concentrated. The oily residue was purified by silica gel column chromatography (hexane–AcOEt, 3:1) to give **12** (51 mg, 93%) as a nearly colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 6.9 Hz, 3 H), 1.24–1.40 (m, 6 H), 1.42–1.54 (m, 1 H), 1.61–1.72 (m, 2 H), 1.73–1.85 (m, 2 H), 1.92–2.02 (m, 1 H), 2.03–2.10 (m, 2 H), 2.20 (br s, 2 H), 2.25 (dd, J = 14.3, 7.2 Hz, 1 H), 2.35 (dd, J = 14.3, 7.9 Hz, 1 H), 3.78 (m, 1 H), 5.51 (m, 1 H), 5.61 (m, 1 H); IR (neat) 3425, 1475, 1455, 1410, 1380, 1300, 1100, 1040, 1010 cm^{-1}; mass spectrum, m/e 212, 194, 156, 142, 139, 137, 123, 112, 102, 101, 100, 98, 97, 96, 93, 84, 83, 82, 81, 79, 77, 72, 71, 69, 67, 55; HR-MS (M^+) calcd for $C_{13}H_{24}O_2$ 212.1776, found 212.1739.

(2*R*)-2-Hydroxy-2-[2(*Z*)-octenyl]-1-cyclopentanone (13). To a stirred solution of **12** (350 mg, 1.65 mmol) in DMSO (2 mL) containing triethylamine (1.38 mL, 9.9 mmol) was added SO_3·Py complex (1.58 g, 9.9 mmol) in DMSO (7.5 mL) at 23 °C. After being stirred for 50 min at the same temperature, the reaction was quenched with ice–water, extracted with AcOEt, washed with brine, dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography (hexane–ether, 1:1) to give **13** (291 mg, 84%) as a nearly colorless oil: $[\alpha]^{20}_D$ −57.8° (*c* 1.035, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 6.9 Hz, 3 H), 1.23–1.40 (m, 7 H), 1.77–1.95 (m, 2 H), 1.96–2.07 (m, 3 H), 2.08–2.15 (m, 1 H), 2.21–2.29 (m, 1 H), 2.30–2.40 (m, 3 H), 5.38 (m, 1 H), 5.64 (m, 1 H); IR (neat) 3465, 1745, 1650, 1465, 1450, 1430, 1405, 1375, 1315, 1300, 1265, 1160, 1090, 1030 cm^{-1}; mass spectrum, m/e 210 (M^+), 125, 111, 100, 99, 97, 96, 71; HR-MS (M^+) calcd for $C_{13}H_{22}O_2$ 210, 1620, found 210.1624.

(2*R*)-5,5-Dichloro-2-hydroxy-2-[2(*Z*)-octenyl]-1-cyclopentanone (14). To a stirred solution of **13** (1.98 g, 9.39 mmol) in dioxane (20 mL) was added *N*-chlorosuccinimide (3.76 g, 28.1 mmol), CH_3COONa (1.54 g, 18.8 mmol), and acetic acid (5 mL) at 23 °C. After being stirred for 4 days at the same temperature, the reaction was diluted with ether (200 mL), washed with brine (100 mL), saturated aueous $NaHCO_3$ (200 mL × 2) and brine (100 mL), dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography (hexane–ether, 10:1) to give **14** (1.87 g, 72%) as a nearly colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 5 Hz, 3 H), 1.10–1.50 (m, 6 H), 1.80–2.17 (m, 4 H), 2.40 (m, 3 H), 2.67 (m, 2 H), 5.20–5.83 (m, 2 H); IR (neat) 3400, 1780 cm^{-1}; mass spectrum, m/e 252 (M^+ − CO), 250 (M^+ − CO); HR-MS (M^+ − CO) calcd for $C_{12}H_{20}O_1Cl_2$ 250, 0891, found 250.0886.

(2*R*)-5-Chloro-2-hydroxy-2-[2(*Z*)-octenyl]-4-cyclopenten-1-ol (16). A suspension of **14** (858 mg, 3.07 mmol) and LiCl (260 mg, 6.13 mmol) in DMF (10 mL) was vigorously stirred at 100 °C for 2 h. The reaction was quenched by the addition of ether (100 mL) and H_2O (100 mL), extracted with ether, dried (Na_2SO_4), and concentrated. The oily residue was purified by silica gel column chromatography (hexane–ether, 10:1 → 5:1) to give **15** (696 mg, 93%) as a nearly colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 5 Hz, 3 H), 1.17–1.50 (m, 6 H), 2.93 (m, 2 H), 2.37 (d, J = 8 Hz, 2 H), 2.87 (br s, 1 H), 2.67 (d, J = 3 Hz, 2 H), 5.10–5.80 (m, 2 H), 7.53 (t, J = 3 Hz, 1 H); IR (neat) 3400, 1730, 1600 cm^{-1}. To a stirred solution of **15** (126 mg, 0.52 mmol) and $CeCl_3 \cdot 7H_2O$ (309 mg, 0.83 mmol) in MeOH (2 mL) was added $NaBH_4$ (31 mg, 0.83 mmol) in an ice bath. After being stirred for 10 min at the same temperature, the reaction was quenched with ether (30 mL) and filtered. The filtrate was washed with H_2O (10 mL), dried (Na_2SO_4), and concentrated. The oily residue was purified by silica gel column chromatography (toluene–ethyl acetate, 20:1) to give **16** (111 mg, 87%) as a diastereomeric mixture: ^{1}H NMR ($CDCl_3$) δ 0.90 (t, J = 5 Hz, 3 H), 1.17–1.60 (m, 6 H), 1.93–2.27 (m, 4 H), 2.30–2.63 (m, 4 H), 4.33 (br s, 1 H), 5.33–5.83 (m, 2 H), 5.88 (t, J = 3 Hz, 1 H); IR (neat) 3400 cm^{-1}; mass spectrum, m/e

246 (M^+), 244 (M^+), 228, 226, 209; HR-MS (M^+) calcd for $C_{13}H_{21}O_2Cl$ 244.1231, found 244.1228.

(4*S*)-2-Chloro-4-hydroxy-4-[2(*Z*)-octenyl]-2-cyclopenten-1-one (19). To a stirred solution of **16** (332 mg, 1.38 mmol) in CH_2Cl_2 (19 mL) were successively added pyridine (3.6 mL), methanesulfonic anhydride (307 mg, 1.76 mmol), and 4-(dimethylamino)pyridine (33 mg, 0.27 mmol) in an ice bath. After being stirred for an additional 40 min, the reaction was quenched with ether (20 mL) and filtered. To the filtrate was added toluene (50 mL), and the solvents were evaporated in vacuo to give **17** as a pale yellow oil, to which was added 85% aqueous DMSO (20 mL). The resulting solution was stirred at 23 °C for 24 h and then diluted with ethyl acetate. The organic layer was successively washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated to give an oily residue **18**, to which was added DMF (3 mL) and pyridinium dichromate (800 mg, 2.13 mmol) in an ice bath. Stirring was continued at the same temperature for 15 h, and the reaction mixture was poured into water. Extraction with ether and evaporation of the dried solvent ($MgSO_4$) in vacuo gave the oily residue, which was purified by silica gel column chromatography (toluene–ethyl acetate, 10:1) to give **19** (169 mg, 51%) as a nearly colorless oil: ^1H NMR ($CDCl_3$) δ 0.90 (t, J = 5 Hz, 3 H), 1.10–1.57 (m, 6 H), 1.87–2.33 (m, 3 H), 2.57 (d, J = 6 Hz, 2 H), 2.67 (d, J =3 Hz, 2 H), 5.23–5.97 (m, 2 H), 7.38 (s, 1 H); IR (neat) 3350, 1730, 1600 cm^{-1}; mass spectrum, m/e 244 (M^+), 242 (M^+), 226, 224; HR-MS (M^+) calcd for $C_{13}H_{19}O_2Cl$ 242.1073, found 242.1084.

(4*S*)-2-Chloro-4-(methoxymethoxy)-4-[2(*Z*)-octenyl]-2-cyclopenten-1-one (20). A solution of **19** (18 mg, 0.074 mmol), diisopropylethylamine (0.13 mL, 0.74 mmol), and chloromethyl methyl ether (28 μL 0.37 mmol) was stirred at 60 °C for 4 h in a sealed tube. The reaction mixture was diluted with ether, and the ether layer was washed with H_2O. Concentration of the dried solvent ($MgSO_4$) afforded the oily residue, which was purified by silica gel column chromatography (hexane–ether, 8:1) to give **20** (18.3 mg, 86%) as a nearly colorless oil: $[\alpha]^{20}_D$ +50.2° (*c* 0.315, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.89 (t, J = 6.74 Hz, 3 H), 1.20–1.40 (m, 6 H), 2.01 (m, 2 H), 2.48–2.63 (m, 2 H), 2.59 (d, J = 18.8 Hz, 1 H), 2.79 (d, J = 18.8 Hz, 1 H), 3.37 (s, 3 H), 4.63 (d, J = 7.6 Hz, 1 H), 4.71 (d, J = 7.6 Hz, 1 H), 5.34 (m, 1 H), 5.59 (m, 1 H), 7.40 (s, 1 H); IR (neat) 1735, 1600 cm^{-1}; mass spectrum, m/e 288 (M^+), 286 (M^+), 227, 225, 177, 176, 175, 151, 149, 141, 124; HR-MS (M^+) calcd for $C_{15}H_{23}O_3Cl$ 286.1336, found 286.1336.

Efficient Synthesis of Silyl Azides Using Sodium Azide Impregnated on Amberlite XAD Resin

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Received April 4, 1988

Silyl azides,[1] which are useful reagents in organic synthesis, have generally been prepared by the reaction of silyl chlorides with LiN_3[2] or NaN_3.[3] However, most of these methods require a long reaction time, and LiN_3 is not commonly available. Among these methods, although the reaction of silyl chloride with NaN_3 in hexamethylphosphoric triamide (HMPT) or *N*,*N*-dimethylformamide (DMF) is more general,[3c] HMPT has been reported to be a potent chemical carcinogen, and DMF can react with the product, silyl azide. Furthermore, this method cannot be applied to the preparation of silyl azides possessing an Si—H or Si—C=CH_2 bond from the corresponding silyl chlorides.[3c]

In previous papers, it has been shown that the impregnation of anionic species on Amberlite XAD resin (XAD resin) enhances the substitution reaction toward alkyl halides,[4] and the reaction of silyl chloride with KCN or NaCN impregnated on XAD resin (KCN or NaCN/XAD) gives the corresponding silyl cyanides in good yields under mild conditions.[5] This paper describes that a large number of silyl azides, including silyl azides having a Si—H or Si—CH=CH_2 bond, can be prepared by the reaction of the corresponding silyl chlorides with NaN_3 impregnated on XAD resin (NaN_3/XAD) in good yields under mild conditions with common solvents.

$$R_{4-n}SiCl_n \xrightarrow{NaN_3/XAD} R_{4-n}Si(N_3)_n$$

Results and Discussion

In order to elucidate the solvent effect, the reaction was performed with trimethylsilyl chloride (Me_3SiCl) and NaN_3/XAD-4 in various solvents. Table I shows the results. In acetonitrile, the reaction was very fast and gave trimethylsilyl azide (Me_3SiN_3) in greater than 96% yield (~100% conversion) within 1 h. Interestingly, even in low-polar solvents, which were not suitable for the reaction of Me_3SiCl with KCN or NaCN/XAD,[5] the complete conversion of Me_3SiCl was observed after relatively short reaction times, and even the reaction without any solvent gave 67% yield of Me_3SiN_3 at 40 °C after 6 h. These results suggest that various solvents can be utilized for the reaction.

On the basis of the results, other silyl azides were prepared (Table II). In general, silyl azides were obtained in high yields under mild conditions. It is worth noting that silyl azides having a Si—H or Si—CH=CH_2 bond were obtained in high yields directly from the corresponding silyl chlorides. Previously reported methods could not produce these compounds directly from the corresponding silyl chlorides.[3c] R_2HSiN_3 was previously prepared by an exchange reaction between Me_3SiN_3 and R_2HSiCl.[6]

$$R_2HSiCl + Me_3SiN_3 \rightarrow R_2HSiN_3 + Me_3SiCl$$

Table I. Reaction of Me_3SiCl with NaN_3/XAD-4 in Various Solvents[a]

solvent	temp, °C	time, h	yield,[b] %
CH_3CN	40	<1	>96[c]
DME[d]	40	4	>96[c]
CH_2Cl_2	40	6	>98[c]
benzene	60	2	85
	60	6	>98[c]
hexane	60	2	85
	60	6	>98[c]
decalin	60	6	>98[c]
none	40	6	67

[a] All reactions were carried out with Me_3SiCl (7.5 mmol) and NaN_3 (15 mmol)/XAD-4 (3.75 g). [b] Determined by GLC with toluene as an internal standard. [c] Almost complete conversion was observed. [d] 1,2-Dimethoxyethane.

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0022-3263/88/1953-4867$01.50/0 © 1988 American Chemical Society