give the bicyclo[3.3.0] skeleton in 67% yield (Scheme III). This cyclization process may constitute an alternative entry to the key process developed by Noyori, Kurozumi, et al. in their synthesis of isocarbacyclin, an important chemotherapeutic agent, and realized by using lithium naphthalenide or Sm(II) reagent in 60–70% yields.[1b]

In conclusion, the V(III) aldehyde ketyls derived from alkanals bearing an internal activated *E* olefin or an acetylenic group lead to the cyclization products with a high trans selectivity. This intramolecular ketyl–alkene coupling process can compete with an intermolecular pinacol coupling depending on the kinds of an unsaturated bonds and their geometry.

Experimental Section

Starting aldehydes **1a**,[5] **1b**,[10] **1c**,[5] **1d**,[5] **1e**[10] and **1f**[6] were prepared in a similar manner as reported in the literature. Melting points and boiling points indicated by an air-bath temperature are uncorrected. IR spectra were recorded on a JASCO FT-5000 spectrometer. ^{1}H NMR spectra were taken in $CDCl_3$ (Me_4Si as an internal standard). Column chromatography was carried out with a Merck Kieselgel 60, Art. 7734 (silica gel) with hexane–AcOEt as an eluent.

Cyclization of Methyl (*E*)-7-Oxo-2-heptenoate (1a) with Vanadium(II) Reagent, a Typical Procedure. Freshly prepared pink powder of $VCl_3(THF)_3$ (560 mg, 1.5 mmol) was dried in a Schlenk tube under high vacuum for 10 min and then back-flushed with Ar. Dry CH_2Cl_2 (6 mL) and zinc dust (98 mg, 1.5 mmol) were added at room temperature under a pressure of Ar. The color of the solution changed from brown to green after being stirred for ca. 30 min, which secured the formation of divalent vanadium reagent. To the stirred suspension of this V(II) reagent in dry CH_2Cl_2 was added dropwise methyl (*E*)-7-oxo-2-heptenoate (**1a**, 76 mg, 0.5 mmol) at room temperature under Ar. After being stirred for 20 h, the mixture was poured into aqueous cold 5% tartaric acid (20 mL) and extracted with CH_2Cl_2 (20 mL × 3). The combined organic layers were washed with aqueous saturated $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated under vacuum. The crude products were purified by column chromatography (SiO_2, hexane/AcOEt = 5/1) to give methyl *trans*-(2-hydroxycyclopentyl)acetate[5] (**2a**, 51.3 mg, 68%) as a colorless oil: bp 38–40 °C (0.2 Torr); IR (neat) 3360 (OH), 2958, 2876, 1740 (CO), 1439, 1346, 1265, 1197, 1178, 1139, 1096 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.16–1.26 (m, 1 H), 1.54–1.64 (m, 2 H), 1.67–1.77 (m, 1 H), 1.91–1.99 (m, 2 H), 2.03–2.13 (m, 1 H), 2.39 (dd, *J* = 16.3, 8 Hz, 1 H, CH_2CO), 2.45 (ddd, *J* = 16.3, 6.1, 1.0 Hz, 1 H, CH_2CO), 2.51 (br s, 1 H, OH), 3.68 (s, 3 H, OMe), 3.85 (m, 1 H, CHO); ^{13}C NMR (126 MHz) δ 21.83, 30.70, 34.26, 38.17, 44.35, 51.77, 78.85, 174.64.

Physical properties along with spectral data of selected compounds listed in Table I are as follows.

Ethyl *trans*-2-(2-hydroxycyclopentyl)propionate (2c; a mixture of diastereoisomers (73:27) at the C-2 position of the ester group): bp 40–43 °C (0.2 Torr); IR (neat) 3386 (OH), 2962, 2878, 1734 (CO), 1456, 1379, 1342, 1259, 1183, 1158, 1100, 1044, 986, 861, 733 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.15, 1.20 (d, *J* = 7.1 Hz, 3 H, CH_3), 1.24, 1.25 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.22–1.32 (m, 1 H), 1.50–1.73 (m, 3 H), 1.79–2.01 (m, 3 H), 2.31, 2.50 (m, 1 H, $CHCO_2$), 2.37 (br s, 1 H, OH), 3.85–3.89, 4.00–4.04 (m, 1 H, CHO), 4.12, 4.14 (q, *J* = 7.1, 2 H, CH_2); ^{13}C NMR (126 MHz) δ 14.16 + 14.19, 14.46 + 16.18, 22.05 + 22.42, 28.53 + 29.28, 34.73 + 35.06, 41.74 + 43.58, 50.22 + 51.49, 60.42 + 60.56, 75.25 + 77.55, 176.91 + 177.36. Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.39; H, 10.00.

Methyl *trans*-(2-hydroxy-4,4-dimethylcyclopentyl)-propionate (2d): bp 42–45 °C (0.2 Torr); IR (neat) 3376 (OH), 2956, 2868, 1725, 1439, 1367, 1267, 1209, 1154, 1079, 1013, 913, 735 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.00, 1.09 (s, 6 H, CH_3), 1.12 (m, 1 H, CH_2), 1.50 (m, 1 H, CH_2), 1.72 (m, 1 H, CH_2), 1.87 (m, 1 H, CH_2), 2.22–2.31 (m, 1 H, CH), 2.39–2.50 (m, 2 H, CH_2CO), 3.04 (br s, 1 H, OH), 3.69 (s, 3 H, OMe), 3.92 (m, 1 H, CHO); ^{13}C NMR (126 MHz) δ 30.61, 31.02, 36.04, 38.47, 43.88, 46.03, 49.21, 51.81, 78.66, 174.88. Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.55; H, 9.65.

Methyl *anti*-(2-hydroxycyclopentylidene)acetate (2e): bp 43–45 °C (0.2 Torr); IR (neat) 3400 (OH), 2958, 2880, 1715 (CO), 1663, 1437, 1361, 1305, 1209, 1143, 1100, 1025, 965, 866 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.48–1.65 (m, 2 H), 1.65 (br s, 1 H, OH), 1.84–1.92 (m, 1 H), 2.02–2.08 (m, 1 H), 2.74–2:90 (m, 2 H), 3.69 (s, 3 H, OMe), 4.48 (m, 1 H, CHO), 5.96 (m, 1 H, CH=); ^{13}C NMR (126 MHz) δ 21.07, 30.22, 34.60, 51.07, 76.36, 112.73, 167.35, 168.14. Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.75. Found: C, 61.30; H, 7.77.

Dimethyl 7,8-dihydroxy-2(*Z*),12(*Z*)-tetradecadienedioate (4b; a mixture of *dl* and meso isomers): IR (neat) 3370 (OH), 2950, 2866, 1723, 1647, 1439, 1408, 1180, 1116, 1075, 1019, 820, 731 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.42–1.58, 1.59–1.71 (m, 8 H), 1.98, 2.51 (br s, 1 H, OH), 2.55–2.64, 2.66–2.75 (m, 4 H, CH_2), 3.42, 3.67 (m, 1 H, CHO), 3.69 (s, 6 H, OMe), 5.78 (dt, *J* = 11.5, 1.6 Hz, 2 H, CH=), 6.22–6.27 (m, 2 H, CH=); ^{13}C NMR (126 MHz) δ 24.93, 25.27, 28.60, 30.56, 32.78, 51.07, 73.99, 74.09, 119.51, 150.43, 166.89.

Dimethyl 7-hydroxy-8-(2-hydroxycyclopentylidene)-2-nonanedioate (4e, less polar component): IR (neat) 3344 (OH), 2958, 2238, 1715 (CO), 1437, 1263, 1197, 1079, 754 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.62–1.70, 1.73–1.93 (m, 8 H), 2.33–2.45 (m, 2 H), 2.50–2.58 (m, 1 H), 2.81–2.88 (m, 1 H), 2.71 (br s, 2 H, OH), 3.74 (s, 3 H, OMe), 3.76 (s, 3 H, OMe), 4.75 (m, 1 H, CHO), 4.89 (m, 1 H, CHO); ^{13}C NMR (126 MHz) δ 18.23, 22.70, 24.09, 33.18 (2 C), 35.55, 51.50, 52.59, 70.69, 72.97, 73.03, 89.80, 129.63, 154.37, 159.46, 168.79. Polar component: IR (neat) 3290 (OH), 2958, 2238, 1700 (CO), 1437, 1261, 1197, 1079, 978, 754 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.57–1.65, 1.68–1.92 (m, 8 H), 2.38 (br s, 2 H, OH), 2.32–2.45 (m, 2 H), 2.51–2.58 (m, 1 H), 2.68–2.75 (m, 1 H), 3.75 (s, 3 H, OMe), 3.79 (s, 3 H, OMe), 4.68 (m, 1 H, CHO), 4.84 (m, 1 H, CHO); ^{13}C NMR (126 MHz) δ 18.42, 22.85, 24.11, 32.84, 34.79, 35.23, 51.51, 52.60, 70.69, 72.87, 73.19, 89.24, 129.42, 154.19, 159.05, 168.61.

Dimethyl 8,9-dihydroxy-2(*E*),14(*E*)-hexadecadienedioate (4f): IR (KBr) 3212, 2940, 1727, 1659, 1439, 1290, 1176, 980, 837, 663 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.30–1.57 (m, 12 H), 2.12–2.24 (m, 6 H, CH_2, OH), 3.37, 3.56 (m, 2 H, CHO), 3.70 (s, 3 H, OMe), 5.80 (dt, *J* = 15.6, 1.5 Hz, 2 H, CH=), 6.95 (dt, *J* = 15.6, 7.1 Hz, 2 H, CH=); ^{13}C NMR (126 MHz) δ 25.19, 25.53, 27.99, 30.95, 32.08, 33.34, 51.40, 74.22, 74.48, 120.98, 149.37, 167.15.

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Supplementary Material Available: Spectral data of *cis*-**2f**, *trans*-**2f**, **7a**, and **7b** and ^{1}H NMR spectra of the compounds **4b**, **4e**, and **4f** (6 pages). Ordering information is given on any current masthead page.

A Simple Chromatographic Technique for the Purification of Organic Stannanes

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Organic stannanes have recently gained wide acceptance as useful synthons,[1] and in particular their use in palladium-catalyzed cross-coupling reactions has received widespread attention.[2] One particular problem associated

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with their use is, in our experience, their difficult purification. The tributyltin derivatives, which are commonly employed in the cross-coupling reaction, are typically viscous oils or liquids with very high boiling points. When working on a small scale, fractional distillations are extremely impractical. A chromatographic purification would be ideal for small-scale work. Unfortunately, organic stannanes often elute with the solvent front on silica gel even with hexane as eluant, unless polar functionalities are present in the molecule. Furthermore, unsaturated stannanes are rather sensitive to silica gel, and partial destannylation is often observed during chromatography.[3]

We have developed a convenient chromatographic technique that allows the purification of stannanes on a 0.01–10-g scale. The method is essentially a reversed-phase flash chromatography on C-18 (a silica support rendered hydrophobic by capping the silanol residues with octadecyldimethylsilyl groups). The technique is also very useful for the characterization of novel stannanes, since these compounds are often recovered in an analytically pure form after the reversed-phase purification.

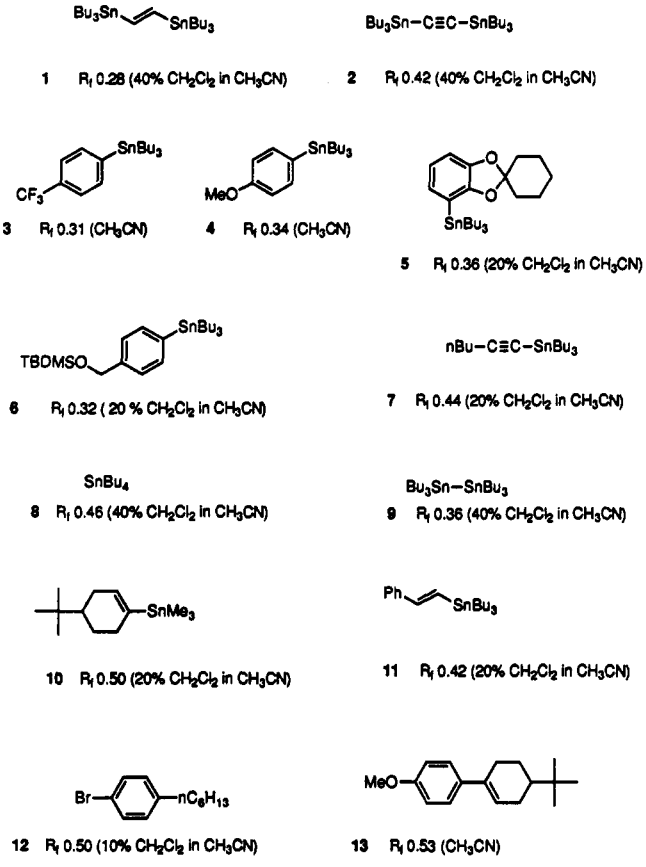
Reversed-phase chromatography is usually considered an analytical technique.[4] Its application in preparative work is hampered by the very high cost of the equipment involved, and its "low-tech" versions[5,6] have not received widespread acceptance, probably because for most organic compounds elution requires mixtures of organic solvents and aqueous buffers. The recovery of the desired material is therefore extremely inconvenient, especially if compared with the simplicity of Still's flash chromatography,[7] probably the most used purification procedure in the modern organic laboratory.

Most organic compounds of low polarity are characterized by a very high affinity for the C-18 support, so that pure organic solvents have to be used to elute them. This suggests that organic stannanes could be purified on C-18 without the use of water or buffers.

We have indeed found that purification of organic stannanes can be carried out with high efficiency on C-18 in complete analogy with Still's technique. Mixtures of CH_2Cl_2 and CH_3CN are used as eluting medium. The faster eluting solvent here is CH_2Cl_2, which corresponds to ethyl acetate in Still's method, while CH_3CN is the slower eluting solvent, corresponding to hexane in the silica gel version.

Scheme I contains some of the stannanes we have purified by this method. The equipment used is the same as required for silica gel flash chromatography (we employ the set marketed by Aldrich), and the bulk C-18 (55–105 μm) was obtained from Waters and packed dry. Although expensive (ca. $1000/kg), we have used our columns dozens of times without apparent loss of resolution. A wash with CH_2Cl_2 removes even the most hydrophobic impurities. As shown in Scheme I, for example, even very nonpolar stannanes like tetrabutyltin can be conveniently eluted (and purified, if necessary) with our technique. For workers who cannot afford the commercial C-18 even with the possibility of reuse, preparation by silylation of commercially available silica gel is a very easy procedure.[8]

Scheme I. Structures and Chromatographic Behavior on C-18 of Organic Stannanes and Other Nonpolar Compounds



As in Still's technique, the R_f of the compound of interest is set at ca. 0.35. Fractions can be monitored by C-18 TLC plates (available from Whatman). For stannanes without UV chromophores, staining with iodine invariably produces extremely bright orange spots. Although the success of the procedure does not crucially depend on flow rates, we have settled for a flow of ca. 2 cm/min. Faster flow rates speed up the procedure but negatively affect the resolution. Compounds with a δR_f of 0.10 (TLC) can be separated without problems, and successful separations with δR_f's as low as 0.05 can sometimes be achieved by reducing the column load.

The utility of the method is illustrated by a number of examples. For example bisstannane 1[9] was usually obtained in 80–85% purity (GC data) after distillation. Several tin-containing impurities were detected, and use of such batches in Stille couplings led to inferior results. A major impurity is acetylenic bisstannane 2. We found that the two compounds are readily separable by C-18 TLC (δR_f 0.14). Preparative-scale separation afforded batches of 1 that were usually >98% GC pure.

Arylstannane 5 decomposed when chromatography over silica was attempted. Use of the C-18 technique allowed instead >95% recovery of analytically pure stannane. This illustrates the mildness of the C-18 in comparison with the rather harsh nature of the untreated silica gel. Alkynyltins (e.g., 7) and vinyltins (e.g., 10, 11) can also be purified by this technique without destannylation.

Finally, the technique is not limited to stannanes. Organic compounds that are too nonpolar to be resolved on silica gel (i.e., when $R_f > 0.6$ with hexane as eluant) can be usually purified on C-18. Compounds 12 and 13 are

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only two of the many hydrocarbons that we have purified in this way.

We feel that this simple procedure, which has been a standard in our laboratory for years, can be of utility to other chemists who make use of organic stannanes in their synthetic work.

Experimental Part

Bulk C-18 (55-105 μm) was obtained from Waters, and C-18 TLC plates are available from Whatman ($MKC_{18}F$ reversed-phase TLC plates, 1 × 3 in., 200-μm thickness). The stannanes were obtained as follows: 1,[9] 2,[9] 3,[10] 4,[11] 7,[12] 10,[13] and 11,[14] were prepared as in the literature, and aryltins 5 and 6 were prepared from the corresponding organolithium reagents and tributyltin chloride (see supplementary material). Compound 12 is a known compound,[15] while 13 was prepared by the palladium-catalyzed coupling of (4-methoxyphenyl)tributyltin with 4-*tert*-butylcyclohexen-1-yl triflate.[16]

Model Separation: Reversed-Phase Flash Chromatography of 1 and 2. A flash chromatography column (from Aldrich, 1-in. diameter), fitted with a glass wool plug, was dry packed with C-18 up to a height of 10 in., and the column bed was equilibrated with the eluant (40% CH_2Cl_2, 60% CH_3CN) under pressure. When all the air had been removed (as shown by a change in color from white to a translucent grayish), a mixture of 1 and 2 (100 mg each) in 1 mL 1:1 CH_2Cl_2/CH_3CN was applied to the top of the C-18 bed, allowed to settle by opening the stopcock, and the walls of the column were rinsed with two 1-mL batches of the eluant. The column was then filled with the rest of the eluant, and the needle valve was adjusted so that the flow was ca. 2 cm/min. Twenty-five 12-mL fractions were collected and analyzed by C-18 TLC, staining after elution in an iodine chamber. Both compounds gave rise to bright orange spots that slowly faded when removed from the chamber. Charring with a variety of staining solutions was less satisfactory. The whole plate typically assumed an intense color that made spot detection difficult or impossible.

Fractions 9–14 contained compound 2, and fractions 16–24 contained 1. Evaporation of the solvent at the rotary evaporator and then under high vacuum gave TLC-pure 1 (89 mg) and 2 (93 mg). The column was then washed with fresh eluant (200 mL). The separation was repeated with essentially identical results.

Supplementary Material Available: Experimental procedures and spectral data for stannanes 5 and 6 (2 pages). Ordering information is given on any current masthead page.

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Ozonolyses of Cytosines and Guanine

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Damage to biological systems by a photochemical oxidant, whose major component consists of ozone, has been reported.[1] The study of the ozonization reaction of cellular substances is one of the most important subjects in ozone chemistry. On the basis of biological evidence, the relationships between mutagenesis or carcinogenesis and ozone have been reported.[2] Christensen and Giese have reported that the nucleic acid base moiety is preferentially decomposed in the reaction of ozone with DNA and RNA.[3] Fetner has reported ozone-induced chromosome breakage in human cell cultures.[4] Ishizaki et al. have reported that a direct ozone attack process on nucleic acid bases is predominant in the cases of nucleotides derived from cytidine, uridine, thymidine, and guanosine, while the reaction of a hydroxyl radical, a decomposition product of ozone in water, is important in the case of the nucleotide derived from adenosine.[5] Therefore, it is of interest to examine the reaction of nucleic acid bases with ozone. We have reported the reactions of uracils,[6] thio- and azauracils,[7] and pyrimidine nucleosides[8] with ozone. In our continuing series of studies on the reaction of nucleic acid bases with ozone, the ozonolyses of cytosines and guanine are examined in this report.

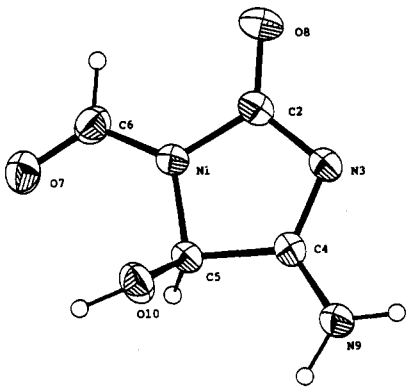

Figure 1. ORTEP view of **2a**.

Table I. Ozonolysis of Cytosines 1

run	compd	substituent R^1	R^2	R^3	yield, of 2, %[a]
1	**a**	NH_2	H	H	66
2	**b**	NHMe	H	H	45
3	**c**	NHC_5H_9	H	H	52
4	**d**	NHC_6H_{11}	H	H	36
5	**e**	NHC_7H_{13}	H	H	54
6	**f**	$NHCH(Me)C_6H_5$	H	H	30
7	**g**	NMe_2	H	H	56
8	**h**	$N(CH_2)_4$	H	H	18
9	**i**	$N(CH_2)_5$	H	H	23
10	**j**	$N(CH_2CH_2OCH_2CH_2)$	H	H	7
11	**k**	NH_2	Me	H	20
12	**l**	NH_2	H	Me	46

[a] Isolated yield.

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