conformational flexibility to the active site allowing different substrates to enter the catalytic center of the enzyme as shown for the L-enantiomers in Table I.

The higher initial rates obtained with *N*-acetyl-L-amino acids present during the bio-imprinting procedure than those obtained without ligand are noteworthy.

After an initial lag phase (24–36 h for D-ester synthesis and 1–3 h for L-ester synthesis) the enzyme lost some of its induced substrate specificity and was able to also synthesize the esters of the two N-acetylated amino acids not present during the bio-imprinting. However, this took place at a lower rate, 2–30% of the rate obtained when the substrate was used during the bio-imprinting. The lost specificity might be due to conformational changes which may occur due to water molecules produced during the enzymatic reaction. For the L-ester synthesis it was shown in preliminary experiments that small additions of water at the outset reduced the lag phase considerably (data not shown). This is in accordance with the discussion above concerning water addition.

Two-thirds (68%) of the active sites were accessible to the substrates as determined with active site titration with *trans*-cinnamoylimidazole.[2d,9] Furthermore, α-chymotrypsin irreversibly inhibited with phenylmethylsulfonyl fluoride[10] prior to bio-imprinting was completely inactive in the synthesis of ester indicating that the active site serine is involved in catalysis. The effects of bio-imprinting are thus active-site related and not a general protein-related property.

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Supplementary Material Available: Bio-imprinting procedure, product determination, and identification (2 pages). Ordering information is given on any current masthead page.

(8) Bio-imprinted (8 mg) α-chymotrypsin was suspended in 2 mL of cyclohexane and sonicated (1 min). Ethanol (0.5 ml) with 0.1 M N-acetylated amino acid was added. Product formation was followed with HPLC. Optical purity of the product was determined to be at least 98% as judged by measuring the specific rotation polarimetrically.

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1,4-Silylstannation of 1,3-Dienes Catalyzed by Platinum Complex

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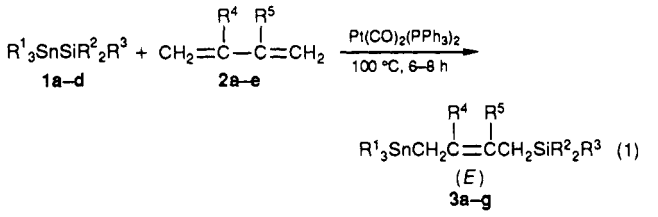
Transformations of typical metal reagents by transition-metal catalysis provide new methodology for selective organic synthesis.[1] Recently, considerable attention has been paid to organosilylstannanes, R_3SnSiR_3' (**1**).[2-5] Silylstannanes (**1**) add to 1-alkynes in the presence of $Pd(PPh_3)_4$ to give alkenes having vicinal silyl and stannyl substituents.[4] The same catalyst induces the insertion of isonitriles into the Sn–Si bond of **1**.[5] The stannyl and silyl moieties in those products[4,5] can be utilized in further functionalizations.[4b,6] However, to our knowledge, there have been no reports on the addition of **1** to dienes and unactivated olefins.

We disclose here the first example of 1,4-silylstannation of 1,3-dienes (eq 1). The reaction is highly regio- and stereoselective.



1a–d **2a–e** **3a–g**

All the products in this study are new compounds, which possess allylic silane and allylic stannane functionalities in the same molecule sharing the same carbon–carbon double bond. The allylic silanes[7] and allylic stannanes[8] are extremely important in selective organic synthesis. Therefore, the present 1,4-silylstannation will offer a new class of versatile building block.

When (trimethylsilyl)tributylstannane (**1a**) was allowed to react with 3 equiv of 1,3-butadiene (**2a**) in the presence of a catalytic amount (5 mol %) of $Pt(CO)_2(PPh_3)_2$ in toluene at 100 °C for 6 h, the 1,4-silylstannation product (**3a**) was obtained as a single isomer in excellent yield (Table I, entry 1).[9] All the spectral data[10] show that the adduct has exclusively (*E*)-1,4 structure. The nature of the catalyst precursor has a critical effect on the reaction. The palladium(0) complexes, which were the most effective catalyst precursors in the precedent studies using **1**,[2a,3-5] are almost inactive with the substrates reported here (yield of **3a**: $Pd(PPh_3)_4$ trace (entry 3), $Pd(CO)(PPh_3)_3$ 2%). Among the platinum complexes examined, $Pt(CO)_2(PPh_3)_2$ gave the best result. Other platinum complexes give less favorable results (yield of **3a**: $Pt(PPh_3)_4$ 29%, $Pt(C_2H_4)(PPh_3)_2$ 13%, $PtCl_2(PPh_3)_2$ trace, $Pt(DBA)_2$ 0%, $Pt(DBA)_2 + 2PPh_3$ 12%).[12]

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(9) A typical procedure is as follows: 1,3-Butadiene (1.5 mmol, 0.94 mL of 1.6 M stock solution in toluene), $Pt(CO)_2(PPh_3)_2$ (19 mg, 0.025 mmol), **1a** (181 mg, 0.5 mmol), toluene (2.0 mL), and a magnetic stirring bar were placed under argon flow in a 30 mL stainless steel autoclave containing an inserted glass tube. An air purge was confirmed by three pressurization (20 atm)–depressurization sequences with argon. After the reaction, the mixture was passed through a short Florisil column (8 mm i.d. × 50 mm) and the product (**3a**) was isolated by Kugelrohr distillation (pot temperature 115 °C (0.5 mmHg); 175 mg, 84%).

(10) **3a**: ^1H NMR ($CDCl_3$) δ −0.02 (s, 9 H), 0.82–0.94 (m, 15 H), 1.24–1.55 (m, 12 H), 1.48 (d, 2 H), 1.70 (d, 2 H, $^2J_{Sn-H}$ = 58 Hz), 5.19 (dt, 1 H, *J* = 15 Hz, 7 Hz), 5.38 (dt, 1 H, *J* = 15 Hz, 7 Hz); ^{13}C NMR ($CDCl_3$) δ −1.87 (q), 9.15 (t, $^1J_{Sn-C}$ = 296 Hz, 310 Hz), 13.74 (q), 14.26 (t), 22.61 (t, $^1J_{Sn-C}$ = 261, 270 Hz), 27.42 (t, $^2J_{Sn-C}$ = 65 Hz), 29.26 (t, $^3J_{Sn-C}$ = 24 Hz), 121.5 (d, J_{Sn-C} = 48 Hz), 127.6 (d, J_{Sn-C} = 44 Hz); ^{119}Sn NMR (C_6D_6) −17.74 ppm; MS (EI) *m/e* 418 (M^+). Anal. Found: C, 54.40; H, 10.08. Calcd for $C_{19}H_{42}SnSi$: C, 54.68; H, 10.14. **3b**: ^1H NMR ($CDCl_3$) δ −0.01 (s, 9 H), 0.83–0.96 (m, 15 H), 1.24–1.56 (m, 12 H), 1.50 (d, 2 H), 1.55 (s, 3 H), 1.77 (s, 2 H, $^2J_{Sn-H}$ = 59 Hz[11]), 5.03 (t, 1 H); ^{13}C NMR ($CDCl_3$) δ −1.57 (q), 9.54 (t, $^1J_{Sn-C}$ = 292, 306 Hz), 13.77 (q), 18.46 (q), 18.73 (t), 22.25 (t, $^1J_{Sn-C}$ = 261, 271 Hz), 27.55 (t, $^2J_{Sn-C}$ = 54 Hz), 29.32 (t, $^3J_{Sn-C}$ = 24 Hz), 115.9 (d, $^3J_{Sn-C}$ = 44 Hz), 132.3 (s, $^2J_{Sn-C}$ = 44 Hz); ^{119}Sn NMR −16.04 ppm; MS (EI) *m/e* 432 (M^+). Anal. Found: C, 55.40; H, 10.52. Calcd for $C_{20}H_{44}SnSi$: C, 55.69; H, 10.28.

(11) Only one side (lower field) of the satellite peaks was observed. The pair (higher field) to the observed side could not be distinguished because of overlap with other proton resonances.

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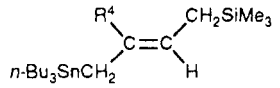
Table I. 1,4-Silylstannation of 1,3-Dienes[a]

entry	silylstannane 1				diene 2			product 3	
		R^1	R^2	R^3		R^4	R^5		yield,[b] %
1	**a**	*n*-Bu	Me	Me	**a**	H	H	**a**	84, 93[c] (98)
2[d]	**a**	*n*-Bu	Me	Me	**a**	H	H	**a**	52 (62)
3[e]	**a**	*n*-Bu	Me	Me	**a**	H	H	**a**	*trace*
4	**a**	*n*-Bu	Me	Me	**b**	Me	H	**b**	84
5[f]	**a**	*n*-Bu	Me	Me	**c**	C_6H_5	H	**c**	85
6	**b**	*n*-Bu	Me	*t*-Bu	**a**	H	H		0
7	**c**	Me	Me	C_6H_5	**a**	H	H	**d**	35
8	**c**	Me	Me	C_6H_5	**b**	Me	H	**e**	30
9	**d**	Me	Me	*t*-Bu	**a**	H	H	**f**	26
10	**a**	*n*-Bu	Me	Me	**d**	Me	Me	**g**[g]	70

[a] **1** (0.5 mmol), **2** (1.5 mmol), $Pt(CO)_2(PPh_3)_2$ (0.025 mmol), toluene (2.0 mL), at 100 °C for 6-8 h. [b] Isolated yield. Numbers in parentheses show GLC yields determined by the internal standard method. [c] Isolated yield from larger scale reaction (**1a**; 1.0 mmol). [d] At 80 °C. [e] Catalyst; $Pd(PPh_3)_4$ (0.025 mmol). [f] **2c** (0.5 mmol). [g] The stereochemistry is not determined.

Isoprene (**2b**) and 2-phenyl-1,3-butadiene (**2c**) also react with **1a** to afford the corresponding single 1,4-silylstannation products in high isolated yield (Table I, entries 4 and 5). The most important feature of the reaction is its high regio- and stereoselectivities. The regiochemistry of the products was determined by C-H COSY spectra. For the isoprene adduct (**3b**), the methylene carbon resonance (δ 22.25: with ^{117,119}Sn-satellites; $^1J_{Sn-C}$ = 261, 271 Hz) of the Sn—CH_2—C= linkage has a cross peak coupled with the proton resonance (δ 1.77) which appears as a *singlet*. The same type of C-H correlation was obtained for 2-phenyl-1,3-butadiene adduct (**3c**). These observations definitely indicate



3b: $R^4 = CH_3$
3c: $R^4 = C_6H_5$

that the regiochemistry of the products is what is shown by the structures of **3b** and **3c**. As for the stereochemistry, the (*E*)-1,4 configurations are unambiguously confirmed by NOE difference spectra with irradiation at the olefin protons. Thus, the 1,4-silylstannation of **2a**, **2b**, and **2c** is found to be highly regio- and stereoselective, affording the corresponding single (*E*)-1,4 isomer exclusively.[13]

Other organosilylstannanes with more bulky substituents are less reactive. (*tert*-Butyldimethylsilyl)tributylstannane (**1b**) did not give the 1,4-silylstannation product (entry 6). However, (dimethylphenylsilyl)trimethylstannane (**1c**) and (*tert*-butyldimethylsilyl)trimethylstannane (**1d**) afforded the corresponding single 1,4-silylstannation products (**3d-f**) regio- and stereoselectively (entries 7-9), although the yields decreased considerably as compared with **1a**. With 2,3-dimethyl-1,3-butadiene (**2d**), the reaction proceeded regioselectively (1,4-addition) in high yield (entry 10). The reaction of 1,3-pentadiene (**2e**) with **1a** was sluggish, giving (*E*)-1,4 adduct in a low yield (25%) and with low regioselectivity. Further studies on the scope and limitation of the 1,4-silylstannation and on reactivity and synthetic utility of the 1,4-silylstannation products are currently under investigation.

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Supplementary Material Available: ^{1}H, ^{13}C NMR, and MS spectral and elemental analysis data for **3c**, NOE difference spectral data for **3b**, **3c**, and **3e**, and ^{1}H and ^{13}C NMR and some MS spectral data for **3d-g** (4 pages). Ordering information is given on any current masthead page.

(12) Other selected transition-metal catalyst precursors (5 mol %) such as $RhCl(PPh_3)_3$, $IrCl(CO)(PPh_3)_2$, Ru(COD)(COT), and $Mn_2(CO)_{10}$ did not give any 1,4-silylstannation products at all.

(13) The reaction of **1**[4] or disilanes[14] with alkynes affords only (*Z*)-alkenes stereoselectively. 1,4-Disilylation of 1,3-dienes with disilanes[15] also gave (*Z*)-1,4-disilyl products. In the present 1,4-silylstannation reaction, there might be some possibility that (*Z*)-1,4 adducts are kinetic products and the (*E*)-1,4 products are formed via (*Z*)-(*E*) isomerization. However, any (*Z*)-1,4 adducts were not detected in the reaction mixtures even at lower conversions of **1**, indicating that such (*Z*)-(*E*) isomerization during the course of the reaction is unlikely.

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Synthesis of (+)-(15,16,19,20,23,24)-*hexepi*-Uvaricin: A Bis(tetrahydrofuranyl) Annonaceous Acetogenin Analogue

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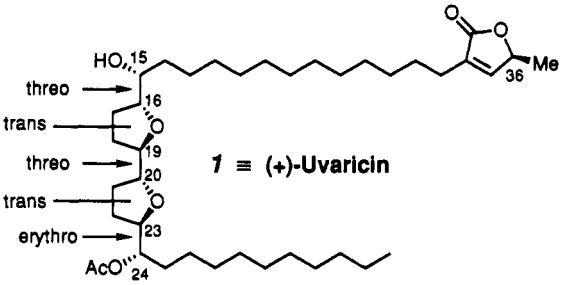
Uvaricin (**1**) was the first reported member of the family of Annonaceous acetogenins.[2] Over thirty relatives are now known; their structural and considerable biological features have been recently reviewed.[3] Our interest in this area was provoked by the opportunity to develop polyepoxide cascade reactions[4a,b] for the purpose of determining important stereochemical issues[4c,d] related to the relative configurations of the central tetrahydrofuran rings present in these natural products. It continues with synthesis issues. Described here is the first preparation of a member of this series—albeit a diastereomeric, non-natural one (vide infra).



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