1 F); MS m/z (relative intensity) 314 (M^+, 0.1), 276 (1), 190 (16), 107 (100), 105 (29), 79 (49). 1,2-Threo-2,3-threo isomer: 87% yield (99% isomerically pure); IR (Nujol) 3480, 2924, 1229, 1179, 1122, 1047 cm^{-1}; ^1H NMR δ 7.5–7.1 (m, 10 H), 4.97 (d, J = 13.4 Hz, 2 H), 2.9–2.6 (m, 2 H); ^{19}F NMR δ –68.85 (d, J = 7.3 Hz, 3 F), –182.95 (ddq, J = 13.4, 13.4, 7.3 Hz, 1 F). Anal. Calcd for $C_{16}H_{14}F_4O_2$: C, 61.15; H, 4.49; F, 24.18. Found: C, 61.23; H, 4.60; F, 24.09.

Conversion of 8f and 8g into Acetonides 9f and 9g. A mixture of 1,2-threo-2,3-erythro isomer of **8f** (0.280 g, 1.0 mmol), 2,2-dimethoxypropane (1.04 g, 10.0 mmol), and *p*-toluenesulfonic acid monohydrate (0.021 g, 0.11 mmol) in THF (5 mL) was refluxed for 24 h with stirring. After cooling to room temperature, the reaction mixture was poured into a saturated $NaHCO_3$ solution (10 mL), followed by extraction with diethyl ether (20 mL × 3), drying (Na_2SO_4), filtration, and concentration. The residue was purified by silica gel column chromatography (hexane–AcOEt) to give the 4,5-threo-5,6-erythro isomer of 5-fluoro-2,2-dimethyl-4-phenyl-6-propyl-5-(trifluoromethyl)-1,3-dioxane (**9f**) (0.316 g): IR (neat) 3066, 2960, 1263, 1200, 1182, 1115, 1083 cm^{-1}; ^1H NMR δ 7.6–7.4 (m, 5 H), 5.03 (dq, J = 15.8, 1.5 Hz, 1 H), 4.09 (ddd, J = 24.6, 8.8, 2.9 Hz, 1 H), 1.9–1.4 (m, 10 H), 1.1–1.0 (m, 3 H); ^{19}F NMR δ –75.55 (d, J = 7.9 Hz, 3 F), –181.41 (ddq, J = 24.6, 15.8, 7.9 Hz, 1 F); MS m/z (relative intensity) 320 (M^+, 0.1), 305 (1), 263 (12), 262 (3), 108 (46), 106 (13), 60 (100). The 4,5-threo-5,6-threo isomer of **9f** was prepared similarly: IR (neat) 3066, 2960, 1263, 1193, 1151, 1089 cm^{-1}; ^1H NMR δ 7.6–7.3 (m, 5 H), 5.09 (dq, J = 8.0, 1.8 Hz, 1 H), 4.11 (dddq, J = 10.0, 5.6, 2.3, 2.2 Hz, 1 H), 2.0–1.2 (m, 10 H), 1.1–0.9 (m, 3 H); ^{19}F NMR δ –67.67 (d, J = 8.9 Hz, 3 F), –182.24 (ddq, J = 10.0, 8.0, 8.9 Hz, 1 F).

5-Fluoro-2,2-dimethyl-4,6-diphenyl-5-(trifluoromethyl)-1,3-dioxane (9g). 4,5-Threo-5,6-erythro isomer: IR (Nujol) 2920, 2852, 1266, 1198, 1171, 1087 cm^{-1}; ^1H NMR δ 7.6–7.5 (m, 4 H), 7.5–7.3 (m, 6 H), 5.30 (dq, J = 15.7, 1.8 Hz, 1 H), 5.26 (d, J = 23.6 Hz, 1 H), 1.60 (s, 3 H), 1.55 (s, 3 H); ^{19}F NMR δ –74.41 (d, J = 7.9 Hz, 3 F), –172.98 (ddq, J = 23.6, 15.7, 7.9 Hz, 1 F); MS m/z (relative intensity) 354 (M^+, 0.1), 339 (0.1), 297 (2), 249 (2), 191 (100). 4,5-Threo-5,6-threo isomer: IR (Nujol) 2920, 2852, 1253, 1186, 1177, 1074 cm^{-1}; ^1H NMR δ 7.6–7.5 (m, 4 H), 7.5–7.3 (m, 6 H), 5.35 (dq, J = 7.9, 1.8 Hz, 2 H), 1.50 (s, 3 H), 1.46 (s, 3 H); ^{19}F NMR δ –66.96 (d, J = 7.9 Hz, 3 F), –179.10 (ddq, J = 7.9, 7.9, 7.9 Hz, 1 F).

Palladium-Catalyzed Coupling Reactions of (α-Ethoxyvinyl)trimethylstannane with Vinyl and Aryl Triflates†,‡

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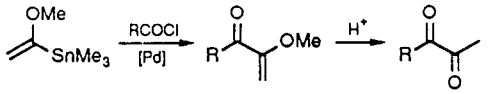
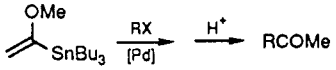
The palladium-catalyzed cross-coupling reaction of vinyl triflates and halides with (α-ethoxyvinyl)trimethylstannane gives high yields of 2-ethoxy 1,3-dienes, which can be hydrolyzed to the corresponding α,β-unsaturated ketones. Aryl triflates undergo an analogous coupling reaction, providing a facile method for replacing the hydroxyl group of a phenol by an acyl group. The use of (α-ethoxyvinyl)trimethylstannane in palladium-catalyzed carbonylative coupling gives rise to vinyl and aryl α-ethoxyvinyl ketones and indirectly to the corresponding α-diketones (which result from their hydrolysis) and glyoxylates (which result from their ozonolysis).

The palladium-catalyzed reaction of organostannanes with organic electrophiles can provide high yields of coupled products under mild reaction conditions.[1] A variety of functional groups can be brought into the coupling reaction as substituents on either or both of the coupling partners. When an (α-alkoxyvinyl)tin reagent is used in the coupling reaction, the product is an α-substituted vinyl ether; its hydrolysis yields the corresponding ketone. Thus the tin reagent serves as an acyl anion equivalent.[2] Such coupling reactions have been carried out primarily with acid chlorides[3a] (which yield α-diketones) and with arylbromides[3b] (eqs 1 and 2).



(1)



(2)

Vinyl and aryl triflates[4] can serve as electrophilic partners with a variety of tin reagents in palladium-catalyzed reactions, provided that an excess (≥3 equiv/equiv of substrate) of chloride, bromide, or iodide ion (usually introduced as the lithium salt) is present.[1] Apparently coordination of the halide ion permits the organopalladium species to undergo the transmetalation reaction with the organotin reagent. In this paper the direct[5] and carbonylative[6] coupling of (α-ethoxyvinyl)trimethylstannane with vinyl and aryl triflates is reported.

Direct Coupling. The palladium-catalyzed direct coupling reaction of (α-ethoxyvinyl)trimethylstannane with vinyl triflates gives high yields of 2-ethoxy 1,3-dienes. The latter can be hydrolyzed to the corresponding α,β-unsaturated ketones (Table I). For comparison, the tin reagent couples with vinyl bromide (entry 5) to produce 2-eth-

† This paper is dedicated to the memory of our friend and mentor, the late Professor J. K. Stille.

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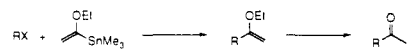
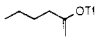
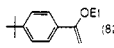
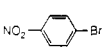
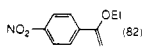
(1) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.
(2) Hase, T. A.; Koskimies, J. K. *Aldrichchimica Acta* **1982**, *15*, 35.
(3) (a) Soderquist, J. A.; Leong, W. W.-H. *Tetrahedron Lett.* **1983**, *24*, 2361. (b) Kosugi, M.; Sumiya, T.; Obara, Y.; Suzuki, M.; Sano, H.; Migita, T. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 767.
(4) Scott, W. J.; McMurry, J. E. *Acc. Chem. Res.* **1988**, *21*, 47.
(5) For examples of direct coupling reactions of triflates, see: (a) Scott, W. J.; Crisp, G. T.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4630. (b) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 3033. Aryl triflate: (c) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478.
(6) For examples of carbonylative coupling reactions of triflates, see: Enol triflates (a) Crisp, G. T.; Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 7500. Aryl triflates: (b) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 1557.

0022-3263/90/1955-3114$02.50/0

Table I[a]



	electrophile	solvent	T, °C	t, h	vinyl ether (%)	ketone (%)[b]
1		THF	60	16	 (82)	 (91)
2		THF	60	18	 (93)	 (82)
3		THF	60	48	 (94)	 (78)
4		THF	60	48	 (94)	 (84)
5		neat	80	12	 (80)	—
6	PhOTf		95	18	—	 (100)
7			95	18	—	 (44)
8	PhBr	$PhCH_3$	105	48	 (71)	 (83)
9	PhI		95	96	(92)	(85)
10		$PhCH_3$	105	48	 (82)	 (95)
11		$PhCH_3$	105	18	 (82)	 (96)

[a] Coupling reactions were run on a 1–5-mmol scale with 2 mol % of tetrakis(triphenylphosphine)palladium(0). In reactions of triflate electrophiles, 3 equiv of lithium chloride was used. [b] The yield is the overall yield of both steps when the enol ether was hydrolyzed directly to the ketone.

oxy-1,3-butadiene in 80% yield.

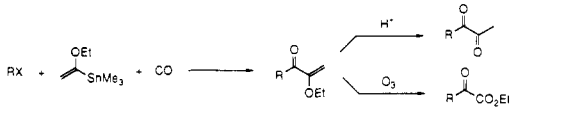
Alkoxy 1,3-dienes are versatile intermediates in organic synthesis. Andersson and Hallberg have already reported[7] the preparation of such dienes by another palladium-catalyzed route, the Heck[8] vinylation of an enol ether by a vinyl triflate. However, the Andersson and Hallberg route requires the presence of at least a stoichiometric amount of base; furthermore, Andersson and Hallberg always use an excess of the enol ether and obtain another diene (the regioisomer resulting from vinylation at the β-position of the enol ether) as well as the desired product. The present route requires no base, needs only a stoichiometric amount of the α-stannyl enol ether and gives no regioisomeric byproducts.

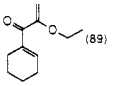
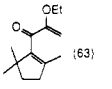
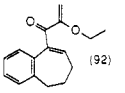
Phenyl triflate also undergoes coupling with (α-ethoxyvinyl)trimethylstannane (entry 6) to give, after hydrolysis, acetophenone in higher yield than do the corresponding phenyl halides (entries 8 and 9). The results of similar coupling reactions with another aryl triflate and other aryl halides are also given in Table I. (With aryl halides as electrophiles the addition of lithium chloride is not necessary.)

Aryl ketones have also been prepared by Andersson and Hallberg by the palladium-catalyzed arylation of an enol

(7) Andersson, C.-M.; Hallberg, A. *J. Org. Chem.* **1989**, *54*, 1502.
(8) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic: New York, 1985. Heck, R. F. *Org. React. (N.Y.)* **1982**, *27*, 345.

Table II[a]



	electrophile	solvent	T, °C	t, h	divinyl ketone (%)	α-diketone or ethyl glyoxylate (%)[b]
1		THF	55	18	 (89)	 (63)
2		THF	55	16	 (63)	 (68)
3		THF	55	21	 (92)	 (60)
4	PhI		95	19.5	(67)	(68)
						(24)[c]
5				24		(78)
6				25.5		(23)
7				21.5		(62)
8				24		

[a] Reactions were carried out on a 1–3 mmol scale using 15 mL of solvent (3 mmol) and 2 mol % tetrakis(triphenylphosphine)palladium(0), under 1 atm on CO. LiCl (3 equiv) was added to coupling reactions of triflates. [b] The yield is the overall yield of both steps. [c] Yield of Schiff base, 2-methyl-3-phenylquinoxaline.

ether with an aryl halide,[9a] an aroyl chloride,[9b] or an aryl triflate.[9c] As with the Andersson/Hallberg route to dienes, these reactions require the presence of at least a stoichiometric amount of base; an excess of the enol ether is always used, and regiochemistry is a problem: substantial β-arylation always occurs. The palladium-catalyzed reaction of aryl halides or triflates with (α-ethoxyvinyl)trimethylstannanes requires no base, needs only a stoichiometric amount of the α-stannyl enol ether, and gives no regioisomeric byproducts.

In each of the reactions described above, an oxygen atom is replaced by a carbon atom. For example, the oxygen of a carbonyl group can be replaced with an acyl substituent after the carbonyl has been transformed into a vinyl triflate; the oxygen of a phenol can also be replaced by an acyl substituent. The latter transformation has two significant advantages: (1) there are a wide variety of readily available phenols (many more than aryl halides), and (2) the hydroxyl group of a phenol can be used to direct electrophilic substitution on the aromatic ring in an ortho/para sense and can then be converted to the meta-

(9) (a) Andersson, C.-M.; Hallberg, A.; Daves, G. D., Jr. *J. Org. Chem.* **1987**, *52*, 3529. (b) Andersson, C.-M.; Hallberg, A. *J. Org. Chem.* **1988**, *53*, 235 and references therein. (c) Andersson, C.-M.; Hallberg, A. *J. Org. Chem.* **1988**, *53*, 2122. (d) Andersson, C.-M.; Hallberg, A. *J. Org. Chem.* **1988**, *53*, 4257.

directing acyl group. Thus the hydroxyl group of a phenol can be used either for its directing/activating ability or for effecting reactions unique to phenols (e.g. Claisen, Kolbe/Schmitt, Reimer-Tiemann), and can then be transformed into an acyl group by the present methodology.

Carbonylative Coupling. The reaction of vinyl triflates with (α-ethoxyvinyl)trimethylstannane in the presence of carbon monoxide gives vinyl α-ethoxyvinyl ketones (Table II, entries 1–3). Similar coupling reactions with aryl iodides give aryl α-ethoxyvinyl ketones; although the latter can be observed by ^{1}H NMR spectroscopy, they are difficult to isolate and were therefore converted to the corresponding glyoxylates by ozonolysis (entries 4–8). In one case (entry 4) the intermediate aryl α-ethoxyvinyl ketone was hydrolyzed, the resulting α-diketone was condensed with *o*-phenylenediamine, and the resulting Schiff base was isolated.

Aryl α-ethoxyvinyl ketones cannot be obtained by the method of Andersson and Hallberg. The palladium-catalyzed aroylation of an enol ether gives β-aroylated enol ethers (as well as considerable decarbonylation).[9b]

Hydrolysis of the ethoxyvinyl ketones formed from the carbonylative coupling of (α-ethoxyvinyl)trimethylstannane with triflates leads to α-diketones. The same α-diketones could in principle be obtained from the double carbonylation of an electrophile with tetramethylstannane. Although the double carbonylation of a variety of electrophiles has been observed in the presence of alcohols or secondary amines,[8,10] such double carbonylation has not been observed in the coupling reactions of electrophiles with main group organometallics.

In summary, the use of (α-ethoxyvinyl)trimethylstannane in palladium-catalyzed direct coupling reactions permits the synthesis of 2-ethoxy 1,3-dienes, α-ethoxystyrenes, and the vinyl and aryl methyl ketones resulting from their hydrolysis. The use of (α-ethoxyvinyl)trimethylstannane in palladium-catalyzed carbonylative coupling yields vinyl and aryl α-ethoxyvinyl ketones and the α-diketones resulting from the hydrolysis of these ketones; glyoxylates can be formed by the ozonolysis of the aryl α-ethoxyvinyl ketones.

Experimental Section

^{1}H NMR spectra were recorded at 270 MHz on an IBM WP 270 or at 300 MHz on a Bruker AC300P spectrometer. ^{13}C NMR spectra were obtained at 75.0 MHz on a Bruker AC300P spectrometer. Infrared spectra were measured on a Beckman 4250 or a Perkin-Elmer 1600 FT-IR spectrometer. Elemental analyses were performed by Atlantic Microlab, Atlanta, GA. Melting points were determined with a Mel-Temp capillary melting point apparatus and are uncorrected.

1,4-Dioxane and toluene were distilled from calcium hydride. Tetrahydrofuran (THF) was distilled from sodium/benzophenone. Triethylamine was distilled from potassium hydroxide.

Cyclohex-1-en-1-yl triflate,[11] 4-*tert*-butylcyclohex-1-en-1-yl triflate,[12] phenyl triflate,[13] 2,5,5-trimethylcyclopent-1-en-1-yl triflate,[6a] hex-1-en-2-yl triflate,[14] 4-((trifluoromethyl)-sulfonato)-*N*-tosylindole,[15] (α-ethoxyvinyl)trimethyltin,[16] and tetrakis(triphenylphosphine)palladium ($Pd(PPh_3)_4$)[17] were prepared according to the literature.

All reactions were run under an argon atmosphere unless otherwise stated.

Procedure A: Palladium-Catalyzed Direct Coupling of Vinyl Triflates with (α-Ethoxyvinyl)trimethylstannane (Table I, entries 1–4). **1-(1-Ethoxyvinyl)cyclohexene** (entry 1).[7] To a solution of cyclohex-1-en-1-yl triflate (460 mg, 2 mmol) in 15 mL of THF were added (1-ethoxyvinyl)trimethyltin (470 mg, 2 mmol), LiCl (254 mg, 6 mmol), and $Pd(PPh_3)_4$ (46 mg, 0.04 mmol). The resulting orange suspension was stirred at reflux for 16 h. The black suspension was diluted with diethyl ether and washed with a 5% aqueous ammonium hydroxide solution, water, and brine. The organic layer was dried ($MgSO_4$) and concentrated to a yellow oil. Bulb-to-bulb distillation (75–80 °C, 20 mmHg) gave 1-(1-ethoxyvinyl)cyclohexene[7] as a colorless liquid (250 mg, 82%). **Procedure B: Hydrolysis of Crude Product to 1-Acetylcyclohexene.**[18] The crude 1-(1-ethoxyvinyl)cyclohexene thus obtained was dissolved in 10 mL of THF and 2 mL of 2 N HCl and stirred at room temperature for 3 h. The reaction mixture was partitioned between water and diethyl ether. The organic layer was dried ($MgSO_4$) and concentrated to give a light yellow liquid. Bulb-to-bulb distillation (85–90 °C, 0.1 mmHg) gave 1-acetylcyclohexene as a white solid (219 mg, 91% from triflate): mp 71–72 °C.[18]

1-(1-Ethoxyvinyl)-4-*tert*-butylcyclohex-1-ene (Table I, entry 2). According to procedure A, 4-*tert*-butylcyclohex-1-enyl triflate (575 mg, 2 mmol) was treated with (1-ethoxyvinyl)trimethyltin (470 mg, 2 mmol) in the presence of LiCl (254 mg, 6 mmol) and $Pd(PPh_3)_4$ (46 mg, 0.04 mmol) to give 1-(1-ethoxyvinyl)-4-*tert*-butylcyclohex-1-ene (371 mg, 89%) as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 6.32 (m, 1 H), 4.15 (d, J = 2.1 Hz, 1 H), 3.99 (d, J = 2.1 Hz, 1 H), 3.79 (q, J = 7.0 Hz, 2 H), 2.30–2.10 (m, 3 H), 2.0–1.85 (m, 2 H), 1.34 (t, J = 7.0 Hz, 3 H), 1.15–1.30 (m, 2 H), 0.88 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 160.38, 132.03, 125.06, 80.78, 62.65, 43.88, 32.13, 27.16, 26.36, 26.71, 24.10, 14.53; IR (neat) 2961, 1713, 1655, 1577, 1478, 1382, 1365, 1313, 1277, 1173, 1121, 1096, 1064, 977, 917, 791 cm^{-1}. **1-Acetyl-4-*tert*-butylcyclohex-1-ene.**[19] According to procedure B, crude 1-(1-ethoxyvinyl)-4-*tert*-butylcyclohex-1-ene was hydrolyzed to give 1-acetyl-4-*tert*-butylcyclohex-1-ene (296 mg, 82% from triflate) as a colorless liquid, bp 135–138 °C (14 mmHg).[19]

1-(1-Ethoxyvinyl)-2,2,5-trimethylcyclopent-1-ene (Table I, entry 3) was prepared by procedure A: ^{1}H NMR ($CDCl_3$) δ 4.16 (d, J = 1.4 Hz, 1 H), 3.86 (d, J = 1.4 Hz, 1 H), 3.74 (q, J = 7.0 Hz, 2 H), 2.27 (t, J = 7.8 Hz, 2 H), 1.74 (s, 3 H), 1.64 (t, J = 7.8 Hz, 2 H), 1.32 (t, J = 7.0 Hz, 3 H), 1.08 (s, 6 H). **1-Acetyl-2,2,5-trimethylcyclopent-1-ene** was prepared by procedure B: ^{1}H NMR ($CDCl_3$) δ 2.37 (tq, J = 7.2, 2.1 Hz, 2 H), 2.29 (s, 3 H), 1.85 (t, J = 2.1 Hz, 3 H), 1.63 (t, J = 7.2 Hz, 2 H), 1.18 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 200.7, 148.8, 145.6, 47.9, 39.8, 37.4, 31.8, 26.9, 17.3; IR (neat) 2348, 2863, 2837, 1659, 1618, 1455, 1432, 1376, 1356, 1332, 1308, 1277 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O$: 78.89; H, 10.60. Found: C, 78.79; H, 10.58.

2-(1-Ethoxyvinyl)hex-1-ene (Table I, entry 4) was prepared by procedure A: ^{1}H NMR ($CDCl_3$) δ 5.49 (d, J = 2.2 Hz, 1 H), 4.95 (m, 1 H), 4.29 (d, J = 2.2 Hz, 1 H), 4.09 (m, 1 H), 3.78 (q, J = 6.7 Hz, 2 H), 2.21 (q, J = 7.8 Hz, 2 H), 1.10–1.60 (m, 7 H), 0.90 (t, J = 5.3 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.8, 143.8, 111.0, 82.9, 62.8, 30.9, 22.5, 15.2, 14.4; IR (neat) 3169, 2958, 2946, 2930, 1644, 1584, 1215, 1067 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.99; H, 11.73. **2-Acetylhex-1-ene** was prepared by procedure B.[20]

Palladium-Catalyzed Direct Coupling of Vinyl Bromide with (α-Ethoxyvinyl)trimethylstannane: 2-Ethoxy-1,3-butadiene (Table I, entry 5).[21] (1-Ethoxyvinyl)trimethylstannane

(10) For recent reports, see: (a) Ozawa, F.; Kawasaki, N.; Okamote, H.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1987**, *6*, 1640. (b) Sakurada, T.; Yamashita, H.; Kobayashi, T.; Hayashi, T.; Tanaka, M. *J. Org. Chem.* **1987**, *52*, 5773. (c) Sen, A.; Chen, J.-T.; Vetter, W. M.; Whittle, R. R. *J. Am. Chem. Soc.* **1987**, *109*, 148 and references therein.

(11) Stang, P. *Synthesis* **1980**, 283.

(12) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1983**, *24*, 979.

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(3.0 g, 12.8 mmol), vinyl bromide (1.64 g, 15.3 mmol), and Pd(PPh_3)$_4$ (288 mg, 0.25 mmol) were combined in a Pyrex tube with a screw cap. The tube was heated to 80 °C and stirred for 12 h. The reaction mixture was cooled, and the volatiles were transferred under vacuum. Distillation of the volatiles yielded 2-ethoxy-1,3-butadiene[21] as a colorless oil (1.0 g, 80%).

Procedure C: Palladium-Catalyzed Direct Coupling of Aryl Triflates and (α-Ethoxyvinyl)trimethylstannane Followed by Hydrolysis (Table I, entries 6 and 7). **Acetophenone** (entry 6). To a solution of phenyl triflate (1.13 g, 5 mmol) and (1-ethoxyvinyl)trimethylstannane (1.175 g, 5 mmol) in dioxane (20 mL) were added Pd(PPh_3)$_4$ (11.6 mg, 0.1 mmol) and LiCl (636 mg, 15 mmol). The mixture was heated to reflux and stirred for 18 h. The reaction mixture was cooled, diluted with 50 mL of ether, and washed with water, 5% aqueous ammonia, and brine. The organic layer was concentrated, and the crude product dissolved in THF (10 mL) and 4 N HCl (3 mL). The mixture was stirred (3 h, 25 °C) and extracted with ether (30 mL × 3). The combined ether layer was dried ($MgSO_4$) and concentrated to give acetophenone as a yellow oil (600 mg, 100%).

4-Acetyl-*N*-tosylindole (Table I, entry 7).[15] According to procedure C, 4-((trifluoromethyl)sulfonato)-*N*-tosylindole (293 mg, 0.69 mmol) was treated with (1-ethoxyvinyl)trimethylstannane (165 mg, 0.7 mmol) to give crude 4-acetyl-*N*-tosylindole. Flash column chromatography on silica gel (hexane/ethyl acetate, 3:1) gave pure 4-acetyl-*N*-tosylindole (97 mg, 44%): mp 141–143 °C.[15]

Procedure D: Palladium-Catalyzed Direct Coupling of Aryl Halides with (1-Ethoxyvinyl)trimethyltin (Table I, entries 8–11). **α-Ethoxystyrene** (entry 8). To a solution of bromobenzene (314 mg, 2 mmol) and (1-ethoxyvinyl)trimethylstannane (470 mg, 2 mmol) in toluene (10 mL) was added Pd(PPh_3)$_4$ (46 mg, 0.04 mmol). The mixture was warmed to 100 °C and stirred for 105 h. The reaction mixture was diluted with ether (50 mL) and washed with water, 5% aqueous ammonia, and brine. The organic layer was dried ($MgSO_4$) and concentrated. The crude product was purified by bulb-to-bulb distillation (80–85 °C, 20 mmHg) to give (1-ethoxyvinyl)benzene (210 mg, 71%) as a clear liquid. **Acetophenone** was obtained by procedure B. Crude (1-ethoxyvinyl)benzene thus obtained was dissolved in THF (10 mL) and 2 N HCl (3 mL). After the mixture was stirred for 3 h at room temperature, the mixture was extracted with ether (20 mL × 3). The combined organic layers were dried (Na_2SO_4) and concentrated. The crude product was purified by bulb-to-bulb distillation at 80–85 °C (10 mmHg) to give acetophenone (199.5 mg, 83%).

4-*tert*-Butyl-1-(1-ethoxyvinyl)benzene (Table I, entry 10). According to procedure D, the reaction of 1-bromo-4-*tert*-butylbenzene (426 mg, 2 mmol) and (1-ethoxyvinyl)trimethyltin (470 mg, 2 mmol) gave 4-*tert*-butyl-1-(1-ethoxyvinyl)benzene (335 mg, 82%): ^{1}H NMR ($CDCl_3$) δ 7.55 (m, 2 H), 7.35 (m, 2 H), 4.59 (d, J = 2.4 Hz, 1 H), 4.14 (d, J = 2.4 Hz, 1 H), 3.91 (q, J = 7.0 Hz, 2 H), 1.41 (t, J = 7.0 Hz, 3 H), 1.31 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 197.8, 156.8, 134.6, 133.1, 128.5, 128.3, 125.5, 35.1, 31.1, 26.5; IR (neat) 3058, 2965, 2906, 2870, 1682, 1606 cm^{-1}. **4-*tert*-Butylphenyl methyl ketone** was obtained by procedure B. The crude 4-*tert*-butyl-1-(1-ethoxyvinyl)benzene was hydrolyzed to give 4-*tert*-butylphenyl methyl ketone 345.5 mg, 98% from bromide); ^{1}H NMR ($CDCl_3$) δ 7.90 (m, 2 H), 7.48 (m, 2 H), 2.59 (s, 3 H), 1.34 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 197.8, 156.8, 134.6, 128.3, 125.5, 35.1, 31.1, 26.5; IR (neat) 3040, 2965, 2901, 2870, 1683, 1607, 1564 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.79; H, 9.16.

4-Nitro-1-(1-ethoxyvinyl)benzene (Table I, entry 11) was obtained by procedure D. The reaction of 4-nitro-1-bromobenzene (404 mg, 2 mmol) and (1-ethoxyvinyl)trimethylstannane (470 mg, 2 mmol) gave 4-nitro-1-(1-ethoxyvinyl)benzene as a yellow powder: mp 47–48 °C (317 mg, 82%); ^{1}H NMR ($CDCl_3$) δ 8.15–8.20 (m, 2 H), 7.60–7.75 (m, 2 H), 4.81 (d, J = 3.1 Hz, 1 H), 4.40 (d, J = 3.1 Hz, 1 H), 3.95 (q, J = 6.9 Hz, 2 H), 1.45 (t, J = 6.9 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 157.8, 147.6, 142.7, 126.0, 123.4, 85.7, 63.7, 14.4; IR (KBr disk) 3088, 2976, 2926, 1688, 1683, 1636, 1593, 1516, 1343, 1305, 1289, 1129 cm^{-1}. Anal. Calcd for $C_{10}H_{11}NO_3$: C, 62.16; H, 5.74. Found: C, 62.15; H, 5.75. **4-Nitrophenyl methyl ketone** was obtained by procedure B. 4-Nitro-1-(1-ethoxyvinyl)benzene (crude product) was hydrolyzed to give 4-nitrophenyl methyl ketone (300 mg, 96%) as a yellow powder, mp 77–79 °C.[18]

Procedure E: Palladium-Catalyzed Carbonylative Coupling of Vinyl Triflate and (1-Ethoxyvinyl)trimethyltin (Table II, entries 1–3). **2-Ethoxy-1-cyclohex-1-enylprop-2-en-1-one** (entry 1). To a solution of cyclohex-1-enyltriflate (230 mg, 1 mmol) and (1-ethoxyvinyl)trimethylstannane (234 mg, 1 mmol) in THF (10 mL) were added LiCl (127 mg, 3 mmol) and Pd(PPh_3)$_4$ (23 mg, 0.02 mmol). Carbon monoxide was bubbled through the solution for 15 min, and a static pressure of 15 psi of carbon monoxide was maintained over the reaction mixture by means of a Fisher rubber gas bag. The mixture was heated at 55 °C for 18 h, cooled to room temperature, and diluted with pentane (50 mL). This solution was washed with water (2 × 20 mL) and brine (2 × 20 mL), dried (Na_2SO_4), and concentrated. The resulting oil was purified on a basic alumina column (hexane/ethyl acetate, 3:1, with 2% Et_3N) to yield 2-ethoxy-1-cyclohex-1-enylprop-2-en-1-one (160 mg, 83%) as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 6.91 (m, 1 H), 4.70 (d, J = 2 Hz, 1 H), 4.50 (d, J = 2 Hz, 1 H), 3.85 (q, J = 7 Hz, 2 H), 2.30 (m, 4 H), 1.60 (m, 4 H), 1.40 (t, J = 7 Hz, 3 H); IR (neat) 1680, 1620, 1600 cm^{-1}. **Procedure F: Hydrolysis of Crude Product to α-Diketone. 1-Cyclohex-1-enylpropane-1,2-dione.** The crude 2-ethoxy-1-cyclohex-1-enylprop-2-en-1-one was dissolved in THF (10 mL) and 2 N HCl (2 mL) and stirred at 25 °C for 60 h. The reaction mixture was partitioned between water and diethyl ether. The organic layer was dried ($MgSO_4$), concentrated, and then chromatographed on silica gel (hexane/EtOAc, 4:1) to give 1-cyclohex-1-enylpropane-1,2-dione[26] (96 mg, 63%).

2-Ethoxy-1-(2,2,5-trimethylcyclopent-1-enyl)prop-2-en-1-one (Table II, entry 2). According to procedure E, the reaction of 2,2,5-trimethylcyclopentenyl triflate (258 mg, 1 mmol) and (1-ethoxyvinyl)trimethyltin (235 mg, 1 mmol) gave 2-ethoxy-1-(2,2,5-trimethylcyclopentenyl)prop-2-en-1-one (132 mg, 63%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 4.7 (d, J = 2.0 Hz, 1 H), 4.0 (d, J = 2.0 Hz, 1 H), 3.6 (q, J = 6.0 Hz, 2 H), 2.2 (m, 2 H), 1.8 (m, 5 H), 1.3 (m, 9 H); IR (neat) 1680, 1600 cm^{-1}. **1-(2,2,5-Trimethylcyclopent-1-enyl)propane-1,2-dione.** Hydrolysis according to procedure F gave clear liquid 1-(2,2,5-trimethylcyclopent-1-enyl)propane-1,2-dione (123 mg, 68%): ^{1}H NMR ($CDCl_3$) δ 2.47 (dt, J = 7.3, 1.1 Hz, 2 H), 2.40 (s, 3 H), 1.83 (t, J = 1.1 Hz, 3 H), 1.71 (t, J = 7.3 Hz, 2 H), 1.21 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 201.34, 193.90, 157.58, 140.15, 48.20, 39.42, 38.15, 26.54, 25.39, 17.66; IR (neat) 2953, 2866, 1713, 1643 cm^{-1}. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.06; H, 8.92.

2-Ethoxy-1-(2,3-benzocyclohept-1-enyl)prop-2-en-1-one (Table II, entry 3). According to procedure E, the reaction of 2,3-benzocyclohept-1-en-1-yltriflate (292 mg, 1 mmol) and (1-ethoxyvinyl)trimethylstannane (235 mg, 1 mmol) gave 2-ethoxy-1-(2,3-benzocyclohept-1-en-1-yl)prop-2-en-1-one (223 mg, 92%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.0–7.5 (m, 4 H), 6.9 (br s, 1 H), 4.5 (d, J = 2.0 Hz, 1 H), 4.3 (d, J = 2.0 Hz, 1 H), 3.61 (q, J = 6.0 Hz, 2 H), 2.7 (m, 2 H), 1.2 (m, 7 H); IR (neat) 1710, 1690, 1600 cm^{-1}. Hydrolysis according to procedure F gave clear liquid **1-(2,3-benzocyclohept-1-enyl)propane-1,2-dione** (129 mg, 60%): ^{1}H NMR ($CDCl_3$) δ 7.35 (t, J = 7.2 Hz, 1 H), 7.31–7.22 (m, 4 H), 2.58 (t, J = 6.8 Hz, 2 H), 2.47 (s, 3 H), 2.28–2.20 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 201.7, 192.9, 150.9, 141.1, 137.8, 133.3, 129.3, 128.9, 128.3, 126.0, 33.8, 31.8, 26.8, 26.2; IR (neat) 3059, 3022, 2934, 2860, 1712, 1662 cm^{-1}. Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.38; H, 6.60.

Procedure G: Palladium-Catalyzed Carbonylative Coupling of Aryl Iodides and (1-Ethoxyvinyl)trimethylstannane Followed by Ozonolysis (Table II, entries 4–8). **Ethyl Phenylglyoxylate**[23] (entry 4). To a solution of iodobenzene (204 mg, 1 mmol) and (1-ethoxyvinyl)trimethylstannane (235 mg, 1 mmol) in dioxane (10 mL) was added Pd(PPh_3)$_4$ (23 mg, 0.02 mmol). Carbon monoxide was bubbled through the solution for 45 min, and a static pressure of 15 psi of carbon monoxide was maintained over the reaction mixture by means of a Fisher rubber gas bag. The mixture was heated at 95 °C for 20 h, cooled to room tem-

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perature, and diluted with pentane (50 mL). This pentane solution was washed with water and brine, dried ($MgSO_4$), and concentrated. The crude product was dissolved in MeOH (20 mL), and the solution was cooled to −78 °C. Ozone was bubbled through this solution at −78 °C for 40 min, and then oxygen gas was passed through the solution for 30 min at the same temperature. The reaction was quenched by the addition of dimethyl sulfide (2 mL), and warmed to room temperature, then concentrated. The resulting mixture was dissolved in ethyl acetate (50 mL), washed with water (2 × 20 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated. The resulting oil was purified on a silica gel column (hexane/ethyl acetate, 3:1) to yield the known ethyl phenylglyoxylate[23] (120 mg, 67%) as a colorless oil.

Ethyl (4-Chlorophenyl)glyoxylate (Table II, entry 5).[24] The reaction of 1-chloro-4-iodobenzene (238 mg, 1 mmol) and (1-ethoxyvinyl)trimethylstannane (235 mg, 1 mmol) according to procedure G, gave the known ethyl (4-chlorophenyl)glyoxylate[24] (166 mg, 78%).

Ethyl (4-Nitrophenyl)glyoxylate (Table II, entry 6).[24] By use of procedure G, 1-iodo-4-nitrobenzene (239 mg, 1 mmol) gave the known ethyl (4-nitrophenyl)glyoxylate (51 mg, 23%).[24]

Ethyl (4-Methoxyphenyl)glyoxylate (Table II, entry 7).[24] By use of procedure G, 4-iodoanisole (234 mg, 1 mmol) gave the known ethyl (4-methoxyphenyl)glyoxylate (129 mg, 62%).[24]

Ethyl (4-Phenylphenyl)glyoxylate (Table II, entry 8). By use of procedure G, the reaction of 4-iodobiphenyl (280 mg, 1 mmol) gave ethyl (*p*-phenylphenyl)glyoxylate (183 mg, 72%) as a colorless liquid: ^1H NMR ($CDCl_3$) δ 7.7–8.1 (m, 4 H), 7.4–7.6 (m, 5 H), 4.45 (q, J = 7.2 Hz, 2 H), 1.43 (t, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 185.9, 163.8, 147.6, 139.5, 131.2, 130.6, 129.0, 128.6, 127.5, 127.3, 62.3, 14.1; IR (neat) 1735, 1683 cm^{-1}. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.48; H, 5.57.

2-Ethoxy-1-phenyl-2-propen-1-one (Table II, entry 4)[22] was isolated from the reaction mixture of the carbonylative coupling of iodobenzene (204 mg, 1 mmol) and (α-ethoxyvinyl)trimethylstannane (235 mg, 1 mmol) as a clear liquid (118 mg, 67%) by chromatographic separation on a basic alumina column with (hexane/ethyl acetate, 3:1, with 2% Et_3N). The compound was identified by comparison of its ^1H NMR and IR spectra with those reported.[22]

2-Methyl-3-phenylquinoxaline (Table II, entry 4).[25] Crude 2-ethoxy-1-phenyl-2-propen-1-one (obtained from 204 mg of iodobenzene, 1 mmol) was dissolved in THF (10 mL) and 2 N HCl (2 mL) and stirred for 16 h at room temperature. The reaction mixture was diluted with hexane (50 mL), washed with water (2 × 10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The crude product of hydrolysis was treated with *o*-diaminobenzene (108 mg, 1 mmol) in benzene (10 mL) with 100 mg of activated 4-Å molecular sieves for 5 h at room temperature. Solids were removed from the reaction mixture by filtration; the filtrate was concentrated and 2-methyl-3-phenylquinoxaline[25] was purified by recrystallization from ethanol (52 mg, 24%): mp 53–55 °C.

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Registry No. $H_3C(CH_2)_3C(=CH_2)OSO_2CF_3$, 37555-23-0; $H_2C=CHBr$, 593-60-2; PhOTf, 17763-67-6; PhBr, 108-86-1; PhI, 591-50-4; $PhCoC(=CH_2)OEt$, 85616-23-5; cyclohex-1-en-1-yl triflate, 28075-50-5; 1-(1-ethoxyvinyl)cyclohexene, 118716-32-8; 1-acetylcyclohexene, 932-66-1; 4-*tert*-butylcyclohex-1-enyl triflate, 77412-96-5; 1-(1-ethoxyvinyl)-4-*tert*-butylcyclohex-1-ene, 125950-34-7; 1-acetyl-4-*tert*-butylcyclohex-1-ene, 37881-09-7; 2,2,5-trimethylcyclopent-1-enyl triflate, 91158-82-6; 1-(1-ethoxyvinyl)-2,2,5-trimethylcyclopent-1-ene, 125952-09-2; 1-acetyl-2,2,5-trimethylcyclopent-1-ene, 125952-10-5; 2-(1-ethoxyvinyl)-hex-1-ene, 125952-11-6; 2-acetylhex-1-ene, 65818-30-6; 2-ethoxy-1,3-butene, 4747-05-1; acetophenone, 98-86-2; 4-((trifluoromethyl)sulfonato)-*N*-tosylindole, 112970-71-5; 4-acetyl-*N*-tosylindole, 112970-73-7; α-ethoxystyrene, 6230-62-2; 1-bromo-4-*tert*-butylbenzene, 3972-65-4; 4-*tert*-butyl-1-(1-ethoxyvinyl)-benzene, 125952-12-7; 4-*tert*-butylphenyl methyl ketone, 943-27-1; 4-nitro-1-bromobenzene, 586-78-7; 4-nitro-1-(1-ethoxyvinyl)-benzene, 59938-04-4; 4-nitrophenyl methyl ketone, 100-19-6; 2-ethoxy-1-cyclohex-1-enylprop-2-en-1-one, 125952-13-8; 1-cyclohex-1-enylpropane-1,2-dione, 28123-53-7; 2-ethoxy-1-(2,2,5-trimethylcyclopent-1-enyl)prop-2-en-1-one, 125952-14-9; 1-(2,2,5-trimethylcyclopent-1-enyl)propane-1,2-dione, 125952-15-0; 2,3-benzocyclohept-1-en-1-yl triflate, 125952-16-1; 2-ethoxy-1-(2,3-benzocyclohept-1-enyl)prop-2-en-1-one, 125952-17-2; 1-(2,3-benzocyclohept-1-enyl)propane-1,2-dione, 125952-18-3; ethyl phenylglyoxylate, 1603-79-8; 2-methyl-3-phenylquinoxaline, 125952-19-4; 1-chloro-4-iodobenzene, 637-87-6; ethyl (4-chlorophenyl)glyoxylate, 34966-48-8; 1-iodo-4-nitrobenzene, 636-98-6; ethyl (4-nitrophenyl)glycoxylate, 70091-75-7; 4-iodoanisole, 696-62-8; ethyl (4-methoxyphenyl)glyoxylate, 40140-16-7; 4-iodobiphenyl, 1591-31-7; ethyl (4-phenylphenyl)glyoxylate, 6244-53-7; (1-ethoxyvinyl)trimethylstannane, 112713-84-5.

Stabilization and Activation of Dienolates with Germanium and Tin. Stereo- and Regioselective Aldol Reactions, Regioselective Coupling Reactions, and Regioselective Synthesis of Amino Acid Derivatives

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The reaction of lithium dienolates with tin chlorides Bu_xSnCl_{4-x} (x = 0, 1, 2, 3) produces the γ-stannylated α,β-unsaturated esters, whereas in general the same reaction with trimethylsilyl chloride gives the O-silylated dienol ethers. Quite interestingly, the reaction of certain lithium dienolates with trimethylgermanium halides produces the α-trimethylgermylated β,γ-unsaturated esters. Further synthetic applications via the γ-stannyl (Sn-masked dienolates) and α-germyl (Ge-masked dienolates) derivatives have been studied. Regio- and stereoselective aldol condensations with aldehydes are accomplished with either Lewis acid mediated or tetrabutylammonium fluoride induced reactions of Sn-masked dienolates. Arylation, acylation, and vinylation of dienolates at the γ-position are realized by the palladium-catalyzed reactions of Sn-masked dienolates. The C–C bond formation at the γ-position is achieved by the reactions of Ge-masked dienolates with variety of electrophiles. Either the α- or γ-amino acid derivatives can be prepared with very high regioselectivity by treating diethyl azodicarboxylate with (i) lithium dienolates themselves in certain cases, (ii) Sn-masked dienolates, or (iii) Ge-masked dienolates.

In order to enhance regio-, chemo-, and stereoselectivities, the stabilization–activation procedure of anionic species has frequently been used in recent synthetic organic chemistry. Some nucleophiles can be converted to derivatives of lowered reactivity which can react with weaker electrophiles, if the latter's reactivity is enhanced

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