Pergamon

Tetrahedron, Vol. 52, No. 21, pp. 7265-7276, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00250-5

Allylated Aromatics *via* Ni-Catalyzed Couplings of Benzylic Chlorides and Vinylic Organometallics#

Bruce H. Lipshutz,* Gerd Bülow, Richard F. Lowe, and Kirk L. Stevens

Department of Chemistry

University of California, Santa Barbara, CA 93106-9510

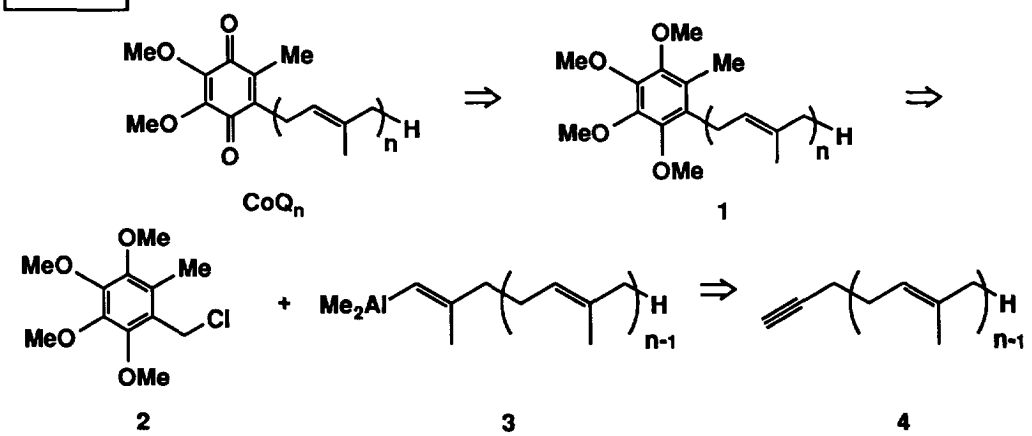
Fax: 805-893-8265; E-mail: lipshutz@sbmm1.ucsb.edu

#Dedicated with respect and admiration to Professor Ei-ichi Negishi on the occasion of his 60th birthday.

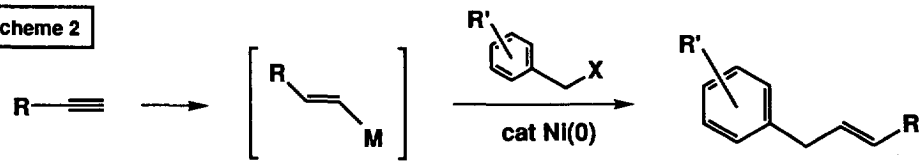
Abstract. *Hydroalumination and hydrozirconation of alkynes lead to vinylic organometallics which react with benzylic chlorides at room temperature under the influence of in situ-generated, catalytic quantities of (presumably) Ni(0), to afford allylated aromatics in good yields.* Copyright © 1996 Elsevier Science Ltd

In a recent report from these laboratories, we disclosed a novel approach to precursors **1** of the ubiquinones (CoQ_n) involving carboalumination of 1-alkynes, *e.g.*, **4** to **3**, followed by a Ni(0)-catalyzed cross-coupling with benzylic halides, *e.g.*, **2** (Scheme 1).[1] While the structural requirements of the ubiquinones necessitated an initial *carbo*alumination,[2] the corresponding disubstituted *E*-vinylalanes are likely to be of more general utility in syntheses of allylated aromatic rings. We now report that catalytic amounts of nickel can be effectively used, following either *hydro*alumination[3] to **5** or *hydro*zirconation[4] to **6** of a terminal acetylene, to generate aromatics **7** bearing a disubstituted allylic moiety of *E*-olefin geometry (Scheme 2).

Scheme 1



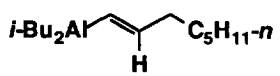
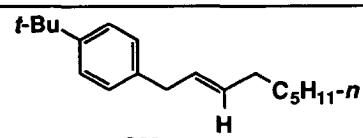
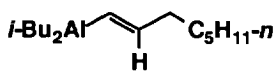
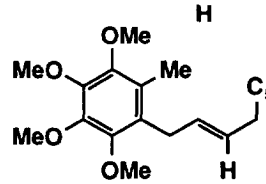
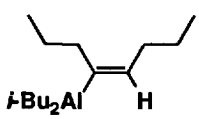
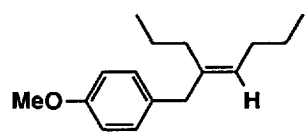
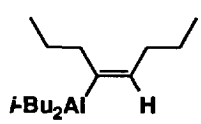
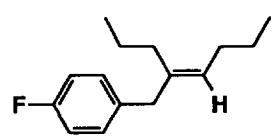
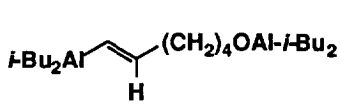
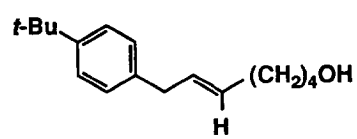
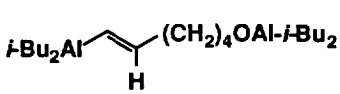
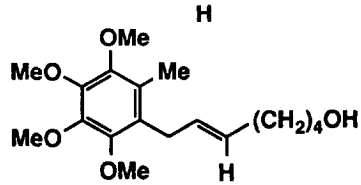
Scheme 2



5, M = Al-*i*-Bu$_2$
6, M = ZrCp$_2$Cl

7

Table 1. *Cross-couplings of vinylalanes with benzylic chlorides mediated by 5 mol % Ni(0)*

Entry	Vinylalane[a]	Benzylic chloride[b]	Product[c]	%[d]
1		*p*-*t*-Bu-BnCl		92[e]
2		2		77
3		*p*-MeO-BnCl		76
4		*p*-F-BnCl		70
5		*p*-*t*-Bu-BnCl		71
6		2		77

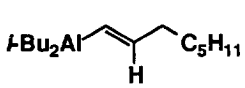
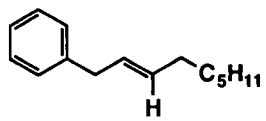
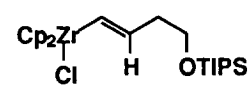
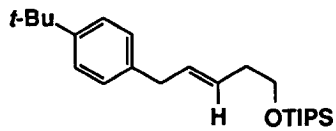
[a] Prepared according to standard procedures; see experimental section. [b] Commercially available except for **2**; see experimental section. [c] Fully characterized; see experimental section. [d] Yield of isolated, chromatographically purified material. [e] *E*:*Z* ratio 96:4 by ^{1}H NMR.

Treatment of a 1-alkyne in dry hexanes with neat DIBAL-H at room temperature and then 40-50 °C for 6-12 hours afforded vinylalanes **5**.[3] The benzylic chloride was then added neat by syringe to preformed, deep red $Ni(PPh_3)_4$ (5 mol %), prepared from commercially available $Ni(PPh_3)_2Cl_2$ with 2 PPh_3 and 2 *n*-BuLi in THF.[5] Upon transfer of the catalyst-containing solution to the colorless vinylalane, a deep brown-black mixture results which retains this coloration throughout the time required for the coupling to occur (usually 2-6 hours). Representative examples are illustrated in Table 1.[6]

Importantly, both electron-rich and -poor educts participate with equal facility. Free hydroxyl-containing substrates could be used by simply employing an extra equivalent of DIBAL-H, or better yet, 2 eq of triisobutylaluminum (entries 5,6).[7] Stereodefined trisubstituted allylated aromatics could also be obtained, demonstrated in the case of 4-octyne as precursor, although the symmetry requirements of the educt in the hydroalumination step places limitations on the scope of this particular coupling.[3b] Interestingly, relative to related reactions of vinylzirconocenes with highly electron rich benzylic chlorides, *e.g.*, **2** (*vide infra*), vinylalanes appear to couple rather straightforwardly (entries 2, 6).

Of the cases examined for comparison purposes in which an equal percentage of Pd(0) was used as catalyst under identical conditions at ambient temperatures (Table 2, entries 1-3),[8] yields in all cases were inferior relative to those realized with Ni(0). Extended reaction times did not improve the net results. On the other hand, heating a reaction solution containing vinylalane, a benzylic chloride, and $Pd(PPh_3)_4$ for comparable periods of time led to yields that approximate those realized with catalytic Ni(0) [*cf.* entry 1 *vs* 3].

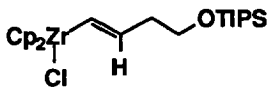
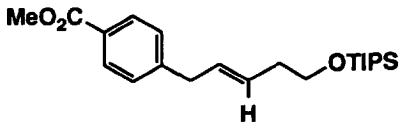
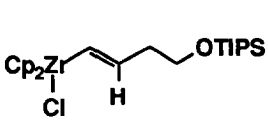
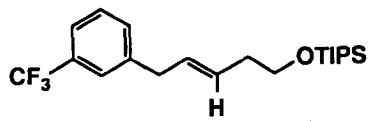
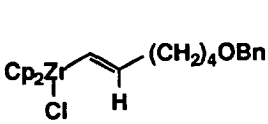
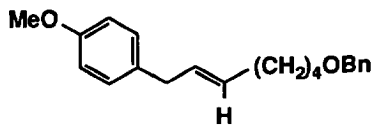
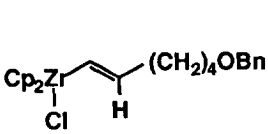
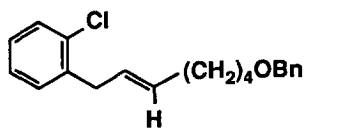
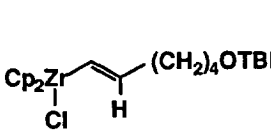
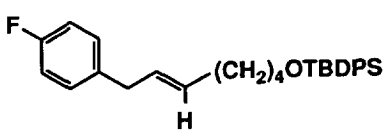
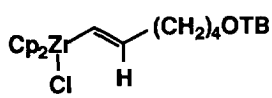
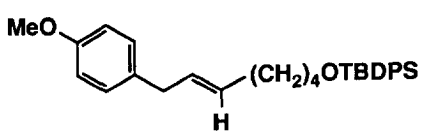
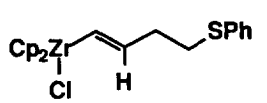
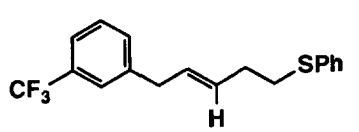
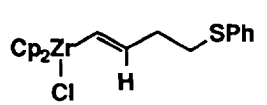
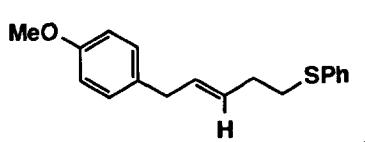
Table 2. *Comparison of Ni(0) and Pd(0) catalysts in cross-couplings of vinylorganometallics*

Entry	Catalyst	%	Conditions	Vinylmetal	Product	%
1	Ni(0)	5	rt, 2 h			87[a]
2	Pd(0)	5	rt, 120 h			32
3	Pd(0)	5	50 °C, 2 h			80
4	Ni(0)	10	rt, 2 h			86
5	Pd(0)	10	rt, 96 h			54
6	Pd(0)	10	50 °C, 2 h			98

[a] *E:Z* ratio 96:4 by GC.

An alternative to hydroalumination for achieving disubstituted, *E*-olefinic products **7** was studied based on an initial hydrozirconation to **6**.[4] By contrast, the latter process proceeds in THF at ambient temperatures far more rapidly, and in general, allows for incorporation of a greater variety of functionality in the parent alkyne. Cross-couplings of the intermediate vinylzirconocenes **6** with the same benzylic chlorides could also be effected under the influence of 5-10 mol % of a Ni(0) catalyst (Table 3).

Table 3. *Cross-couplings of vinylzirconocenes with benzylic chlorides mediated by 5 mol % Ni(0)*

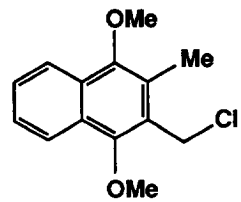
Entry	Vinylzirconocene[a]	Benzylic chloride[b]	Product[c]	%[d]
1		*p*-MeO_2C-BnCl		86
2		*m*-CF_3-BnCl		83[e]
3		*p*-MeO-BnCl		81
4		*o*-Cl-BnCl		67[e]
5		*p*-F-BnCl		93
6		*p*-MeO-BnCl		89
7		*m*-CF_3-BnCl		79
8		*p*-MeO-BnCl		72[e]

[a] Prepared according to standard procedures; see experimental section. [b] Commercially available. [c] Fully characterized; see experimental section. [d] Yield of isolated, chromatographically purified material. [e] Using 10 mol % Ni(0).

Particularly noteworthy are the observations that (1) the presence of an ester moiety in the electrophile (entry 1) does not detract from the overall efficiency, and (2) the integrity of the vinylic zirconocene is maintained throughout the coupling, notwithstanding precedent for modest erosion of *E* / *Z* selectivity in the

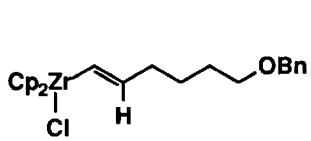
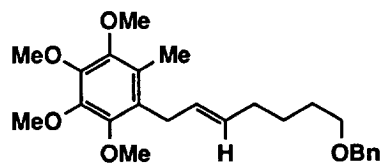
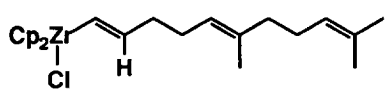
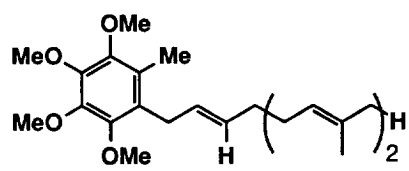
presence of Ni(0).[9] Again, at room temperature, Pd(0) was not nearly as successful in mediating this type of coupling [*cf.* Table 2, entry 5]. However, upon warming the reaction mixture to 50 °C, an excellent yield of allylated aromatic could be obtained in the same 2 hour time frame routinely employed with catalytic Ni(0).

As seen with vinylalanes, the electronic nature of the benzylic coupling partner appears to be of little consequence, except in the case of especially electron-rich systems, as found with ubiquinone and vitamin K components **2** and **8**,[10] respectively. With the former, significant amounts (*e.g.*, averaging *ca.* 30%) of homocoupling products involving the aromatic nucleus were observed under our standard Ni(0)-catalyzed coupling conditions, with a corresponding drop in the yield of the desired product (Table 4).



8

Table 4. *Cross-couplings involving electron-rich benzylic chloride* **2**

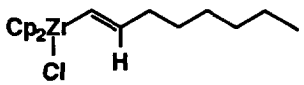
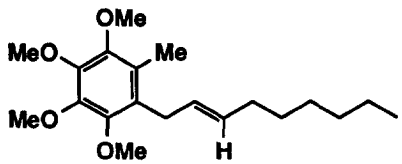
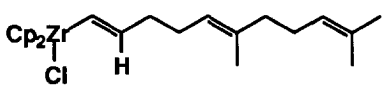
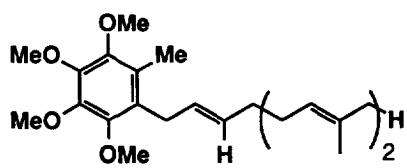
Entry	Vinylzirconocene	Equiv	Product	%[a]
1		1.65		66[b]
2		2.0		31[c]

9

[a] Yield of isolated, chromatographically purified material. [b] Using 10 mol % $Ni(PPh_3)_4$. [c] Using 5 mol % $Ni(PPh_3)_4$.

In time, it was found that a Ni(0) catalyst consisting of $Ni(cod)_2$ and 2 PPh_3 (5-10 mol %) afforded the cross-coupled products in good yields with only 5-10% of aromatic homo-coupled material (Table 5). Although a similar observation was made by replacing Ni(0) with Pd(0), <50% of the desired product had formed after 36 hours in THF at 50 °C. The choice of this alternative Ni(0) reagent was predicated on the contributions of Bartsch, *et al*,[11a] and Carmona and co-workers,[11b] whose extensive and insightful studies on the preparation and reactions of benzyl nickel complexes suggested that lesser amounts of phosphine should encourage the formation of a greater percentage of cross-, as opposed to homo-, coupling products. Indeed, extension of this modified procedure to the polyprenoidal series led to the preparation of desmethylated CoQ_3 precursor **9** in good yield.

Table 5. *Couplings using Ni(0) prepared from $Ni(cod)_2$ + 2 PPh_3*

Entry	Vinylzirconocene	Equiv	Product	%[a]
1		2.0		82[b]
2		1.5		66[c]

9

[a] Yield of isolated, chromatographically purified material. [b] Using 10 mol % Ni(0). [c] Using 5 mol % Ni(0).

In summary, novel methodology for the preparation of di- or tri-substituted, *E*-allylated phenyl rings has been developed. Vinylalanes or vinylzirconocenes can be employed, together with a wide range of benzylic chlorides, in cross-coupling reactions catalyzed by 5-10 mol % Ni(0). These procedures potentially allow for rapid construction of desmethylated analogs of CoQ_n and vitamins K_1 and K_2,[12] further work on which is ongoing.

General.

Diisobutylaluminum hydride (DIBAL-H), triisobutylaluminum, lithium aluminum hydride, $Ni(PPh_3)_2Cl_2$ and $Pd(PPh_3)_4$ were purchased from Aldrich. $Ni(cod)_2$ was purchased from Strem Chemicals Inc. All benzyl chlorides were purchased from Aldrich with the exception of **2** (*vide infra*). Schwartz's reagent was prepared according to the procedure of Buchwald *et. al.*[13] THF and hexane were distilled from Na / benzophenone ketyl prior to use. Petrol refers to the fraction of hydrocarbons boiling at 38-56 °C. Column chromatography was performed on ICN BioMedical's ICN Silica, 32-63, 60 Å. TLC was carried out on pre-coated silica gel 60 F_{254} plates (EMx Science), 0.25 mm layer thickness. ^1H NMR spectra were run at 500 MHz, and ^{13}C spectra were run at 125 MHz on a General Electric GN-500 spectrometer. IR spectra were run on a 2020 Galaxy FTIR spectrometer. Mass spectra were obtained from either a VG-Autospec or an analytical VG 70-250 HF instrument. All reactions were carried out under an inert atmosphere of Ar using oven-dried glassware and standard syringe/septa techniques.

Preparation of Ni(0) catalysts.

Method 1. *n*-BuLi in hexanes (2 equiv) was added dropwise at rt to a suspension of $Ni(PPh_3)_2Cl_2$ (1 equiv) and PPh_3 (2 equiv) in THF (1 mL). After stirring for 5 min, the mixture was used as required.

Method 2. THF (1 mL) was added at rt to a mixture of $Ni(cod)_2$ (1 equiv) and PPh_3 (2 equiv) and the deep red solution was cooled to -30 °C. After stirring for 5 min, the mixture was used as required.

Preparation of benzyl chloride 2. To a solution of 2,3-dimethoxy-5-methyl-1,4-benzoquinone (4.0 g, 21.7 mmol) in THF (150 mL) at 0 °C was added dropwise, a solution of $LiAlH_4$ (0.62 g, 16.3 mmol) in dry diethyl ether (17 mL). After 40 min, the reaction was quenched by the addition of EtOAc followed by 5% aqueous HCl. The mixture was extracted with EtOAc (3x) and the organic layer washed successively with water and brine, dried ($MgSO_4$) and evaporated *in vacuo*. The crude hydroquinone (4.2 g) was dissolved in EtOH (20 mL) and to this solution at rt was added in six portions simultaneously, a solution of NaOH (2.2 g in 6 mL H_2O) and dimethyl sulfate (5.30 mL, 56 mmol) with cooling in a water bath. After 45 min, 5% aqueous HCl was added and the mixture was extracted with EtOAc (3x). The organic layer was washed successively with water and brine, dried ($MgSO_4$) and evaporated. The crude 2,3,4,5-tetramethoxytoluene (4.02 g) was dissolved in conc HCl (25 mL) and warmed to 40 °C. Paraformaldehyde (1.4 g) was added and HCl gas was bubbled through the mixture for 15 min. After stirring for an additional 20 min, ether was added and the organic layer was separated, washed successively with water (4x), brine, dried ($MgSO_4$) and evaporated *in vacuo*. Silica gel chromatography of the residue (10% EtOAc-petrol, 1% Et_3N) afforded benzyl chloride **2** (3.58 g, 63% from the parent quinone) as a clear oil. R_f = 0.53 (25% EtOAc-hexanes); IR (neat) cm^{-1} 2962, 2935, 2862, 2829, 1406, 1352, 1279, 1196, 1109, 1072, 1039; ^1H NMR ($CDCl_3$) δ 4.67 (s, 2 H, $ArCH_2$), 3.91, 3.90, 3.88, 3.77 (each s, each 3 H, 4 x OCH_3), 2.27 (s, 3 H, $ArCH_3$); ^{13}C NMR ($CDCl_3$) δ 148.45, 148.00, 147.65, 144.68, 126.59, 124.72, 61.66, 60.99, 60.65, 38.54, 11.09; LREIMS 260 (M^+, 94), 225 (96), 210 (27), 149 (100); HREIMS calcd for $C_{12}H_{17}O_4Cl$ $(M)^+$ 260.0815, found 260.0817.

General procedure for preparation and Ni(0)-catalyzed couplings of vinylalanes derived from hydrocarbons. To a solution of the alkyne (1.50 mmol) in dry hexane (2 mL) under argon at room temperature was added dropwise, neat diisobutylaluminum hydride (1.80 mmol). The mixture was stirred and heated at 50 °C. On completion of the hydroalumination (monitored by GC, typically 6–8 h), the reaction mixture was cooled to room temperature and the solvent was reduced to half-volume *in vacuo*. In a separate flask, the benzylic chloride (1.80 mmol) was slowly added to a solution of $Ni(PPh_3)_4$ (0.075 mmol) in dry THF, prepared as described in Method 1. After stirring for 5-10 min, this mixture was added to the vinylalane *via* cannula, with cooling in ice. The mixture was allowed to warm to room temperature and stirred. After completion of the reaction (followed by GC; *ca.* 2-6 h), the reaction mixture was poured into ice cold 5% aqueous HCl and extracted with ether (4x). The organic phase was washed successively with 5% aqueous HCl, water and brine, dried ($MgSO_4$) and evaporated *in vacuo*. Purification of the residue by silica gel chromatography afforded the desired *E*–allylated aromatic.

General procedure for preparation and Ni(0)-catalyzed couplings of vinylalanes derived from alkynols. To a solution of the alkynol (1.50 mmol) in dry hexane at 0 °C was added dropwise over 10 min, a solution of triisobutylaluminum (3.0 mmol, 1.0 M solution in toluene). After 15 min, neat diisobutylaluminum hydride (1.80 mmol) was added and the mixture was heated at 50 °C. On completion of

the hydroalumination (monitored by GC, typically 12–16 h), THF (1 mL) was added to the gel-like mixture and the solvent was reduced to half-volume *in vacuo*. The cross-coupling reaction and work-up procedures were carried out as described above with the exception of the use of EtOAc for the extraction. Purification of the residue by silica gel chromatography afforded the desired *E*–allylated aromatic.

General procedure for the preparation and Ni(0)-catalyzed couplings of vinylzirconocenes. A suspension of the alkyne (0.75 mmol) and zirconocene chloride hydride (0.75 mmol) in THF (2 mL) was stirred under argon in the dark until a clear solution was obtained (*ca.* 30 min). In a separate flask, the benzylic chloride (0.60 mmol) was slowly added to a solution of $Ni(PPh_3)_4$ (0.030 mmol) in dry THF, prepared as described in Method 1 (In the case of Method 2, the benzyl chloride as a solution in THF was added to the catalyst at -30°C, warmed to rt and this mixture added to the vinylzirconocene). After stirring for 5-10 min, this mixture was added to the vinylzirconocene *via* cannula. The mixture was allowed to stir at room temperature for 1.5 hours, after which time GC analysis showed complete disappearance of the benzylic chloride. Hydrogen peroxide (0.09 mL of a 30% solution in water) was added, the mixture stirred for 10 min and then filtered (hydrogen peroxide was not added in reactions using benzyl chloride **2**). The filtrate was quenched with 5% aqueous HCl and extracted with EtOAc (4x). The organic layer was washed successively with water and brine, dried ($MgSO_4$) and evaporated *in vacuo*. Silica gel column chromatography of the residue afforded the desired *E*-allylated aromatic.

Table 1, entry 1. R_f = 0.52 (hexanes); chromatography solvent: hexanes; IR (neat) cm^{-1} 2957, 2928, 2855, 1514, 1465, 1361, 1268, 965, 824; ^1H NMR ($CDCl_3$) δ 7.30, 7.11 (each d, *J* = 8 Hz, each 2 H, C_6H_4), 5.58-5.47 (m, 2 H, HC=CH), 3.29 (d, *J* = 6 Hz, 2 H, $ArCH_2$), 2.00 (dt, *J* = 7 Hz, 2 H, CH_2), 1.37-1.24 (m, 8 H, 4 x CH_2), 0.87 (t, *J* = 7 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 148.59, 138.08, 131.94, 128.85, 128.10, 125.20, 38.59, 32.58, 31.80, 31.43, 29.53, 28.93, 22.68, 14.11; LREIMS 258 (M^+, 47), 243 (100), 189 (82), 117 (34); HREIMS calcd for $C_{19}H_{30}$ $(M)^+$ 258.2348, found 258.2349.

Table 1, entry 2. R_f = 0.45 (10% acetone-petrol); chromatography solvents: 10% PhMe-petrol then 2:8:90 EtOAc-PhMe-petrol; IR (neat) cm^{-1} 2926, 2850, 1464, 1406, 1350, 1196, 1105, 1076, 1041, 1012, 976; ^1H NMR ($CDCl_3$) δ 5.46-5.31 (m, 2 H, HC=CH), 3.89, 3.88, 3.78, 3.76 (each s, each 3 H, 4 x OCH_3), 3.29 (d, *J* = 5.5 Hz, 2 H, $ArCH_2$), 2.13 (s, 3 H, $ArCH_3$), 1.94 (dt, *J* = 7 Hz, 2 H, CH_2), 1.31-1.21 (m, 8 H, 4 x CH_2), 0.84 (t, *J* = 7 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 147.79, 147.70, 145.02, 144.62, 131.02, 121.87, 127.71, 125.47, 61.13, 60.99, 60.92, 60.53, 32.49, 31.67, 29.76, 29.44, 28.80, 22.56, 13.98, 11.52; LREIMS 336 (M^+, 100), 321 (13), 43 (21); HREIMS calcd for $C_{20}H_{32}O_4$ $(M)^+$ 336.2301, found 336.2299.

Table 1, entry 3. R_f = 0.28 (hexanes); chromatography solvent: hexanes; IR (neat) cm^{-1} 2956, 2930, 2869, 2836, 1609, 1512, 1466, 1248, 1173, 1037, 845, 824; ^1H NMR ($CDCl_3$) δ 7.06, 6.80 (each d, *J* = 8.5 Hz, each 2 H, C_6H_4), 5.17 (t, *J* = 7 Hz, 1 H, =CH), 3.77 (s, 2 H, $ArCH_2$), 1.98 (dt, *J* = 7.5 Hz, 2 H, CH_2), 1.88 (t, *J* = 7.5 Hz, 2 H, CH_2), 1.38-1.32 (m, 4 H, 2 x CH_2), 0.89, 0.84 (each t, *J* = 7 Hz, each 3 H, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ 157.78, 138.90, 132.80, 129.77, 127.09, 113.54, 55.20, 42.69, 31.58, 29.92,

23.19, 21.42, 14.11, 13.89; LREIMS 232 (M^+, 100), 189 (85), 147 (41), 122 (61); HREIMS calcd for $C_{16}H_{24}O$ $(M)^+$ 232.1827, found 232.1818.

Table 1, entry 4. R_f = 0.65 (hexanes); chromatography solvent: hexanes; IR (neat) cm^{-1} 2957, 2929, 2869, 1605, 1467, 1510, 1221, 1168, 822; ^1H NMR ($CDCl_3$) δ 7.11-7.08, 6.95-6.91 (each m, each 2 H, C_6H_4), 5.17 (t, J = 7 Hz, 1 H, =CH), 3.24 (s, 2 H, $ArCH_2$), 1.99 (dt, J = 7.5 Hz, 2 H, CH_2), 1.90-1.87 (m, 2 H, CH_2), 1.37-1.29 (m, 4 H, 2 x CH_2), 0.88, 0.84 (each t, J = 7.5 Hz, each 3 H, 2 x CH_3); ^{13}C NMR ($CDCl_3$) δ 162.28, 138.46, 136.28, 130.30, 130.12, 127.60, 114.90, 114.73, 42.74, 31.57, 29.89, 23.13, 21.39, 12.06, 13.85; LREIMS 220 (M^+, 36), 135 (75), 111 (24), 109 (95), 69 (100), 55 (36); HREIMS calcd for $C_{15}H_{21}F$ $(M)^+$ 220.1627, found 220.1638.

Table 1, entry 5. R_f = 0.69 (50% EtOAc-hexanes); chromatography solvents: 25% EtOAc-petrol; IR (neat) cm^{-1} 3325, 2962, 2868, 1507, 1475, 1373, 1270, 1056, 1020, 967, 814; ^1H NMR ($CDCl_3$) 7.30, 7.10 (each d, J = 8 Hz, each 2 H, C_6H_4), 5.60-5.46 (m, 2 H, HC=CH), 3.63 (t, J = 6.5 Hz, 2 H, OCH_2), 3.28 (d, J = 6.5 Hz, 2 H, $ArCH_2$), 2.04 (dt, J = 7 Hz, 2 H, CH_2), 1.60-1.54, 1.47-1.39 (each m, each 2 H, 2 x CH_2), 1.29 (s, 9 H, ^{t}Bu); LREIMS 246 (M^+, 39), 231 (82), 147 (35), 131 (100), 129 (37), 91 (37), 57 (94); HREIMS calcd for $C_{17}H_{26}O$ $(M)^+$ 246.1984, found 246.1990.

Table 1, entry 6. R_f = 0.33 (25% acetone-hexanes); chromatography solvents: 15% acetone-petrol; IR (neat) cm^{-1} 3391, 2932, 2862, 1471, 1422, 1416, 1351, 1196, 1105, 1042, 1078, 976; ^1H NMR ($CDCl_3$) δ 5.49-5.30 (m, 2 H, HC=CH), 3.89, 3.88, 3.78, 3.76 (each s, each 3 H, 4 x OCH_3), 3.60 (t, J = 6.5 Hz, 2 H, OCH_2), 3.29 (d, J = 5.5 Hz, 2 H, $ArCH_2$), 2.12 (s, 3 H, $ArCH_3$), 1.99 (dt, J = 7 Hz, 2 H, CH_2), 1.55-1.50, 1.41-1.35 (each m, each 2 H, 2 x CH_2); ^{13}C NMR ($CDCl_3$) δ 147.72, 147.60, 144.99, 144.56, 130.46, 128.11, 127.72, 125.44, 62.63, 61.14, 61.09, 60.94, 60.60, 32.16, 29.70, 25.52, 11.52; LREIMS 324 (M^+, 100), 225 (16), 211 (15); HREIMS calcd for $C_{18}H_{28}O_5$ $(M)^+$ 324.1937, found 324.1929.

Table 2, entries 1-3. R_f = 0.55 (hexanes); chromatography solvent: hexanes; IR (neat) cm^{-1} 3026, 2954, 2926, 2855, 1506, 1460, 965, 743; ^1H NMR ($CDCl_3$) δ 7.29-7.24, 7.17-7.16 (each m, 2 H, 3 H, C_6H_5), 5.57-5.46 (m, 2 H, HC=CH), 3.31 (d, J = 6 Hz, 2 H, $ArCH_2$), 2.00 (dt, J = 7 Hz, 2 H, CH_2), 1.36-1.19 (m, 8 H, 4 x CH_2), 0.86 (t, J = 7 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 141.12, 132.12, 128.70, 128.45, 128.29, 125.82, 39.09, 32.54, 31.75, 29.47, 28.88, 22.65, 14.07; LREIMS 202 (M^+, 53), 131 (20), 118 (21), 117 (88), 104 (100); HREIMS calcd for $C_{15}H_{22}$ $(M)^+$ 202.1722, found 202.1725.

Table 3, entry 1. R_f = 0.49 (5% acetone-petrol); chromatography solvents: 3% acetone-petrol; IR (neat) cm^{-1} 2945, 2868, 1722, 1608, 1459, 1437, 1276, 1180, 1108; ^1H NMR ($CDCl_3$) δ 7.93, 7.22 (each d, J = 8.5 Hz, 4 H, C_6H_4), 5.64-5.51 (m, 2 H, HC=CH), 3.88 (s, 3 H, OCH_3), 3.69 (t, J = 6.5 Hz, 2 H, OCH_2), 3.36 (d, J = 6.5 Hz, 2 H, $ArCH_2$), 2.26 (dt, J = 6.5 Hz, 2 H, CH_2), 1.03-1.02 (m, 21 H, $Si(i\text{-}C_3H_7)_3$); ^{13}C NMR ($CDCl_3$) δ 167.00, 146.23, 129.63, 129.30, 128.46, 127.89, 63.20, 51.82, 39.03, 36.28, 17.95, 11.96; LREIMS 333 [$(M\text{-}C_3H_7)^+$, 100], 171 (27), 115 (10), 75 (17); HREIMS calcd for $C_{19}H_{29}O_3Si$ $(M\text{-}C_3H_7)^+$ 333.1886, found 333.1887.

Table 3, entry 2. R_f = 0.39 (hexanes); chromatography solvent: hexanes; IR (neat) cm^{-1} 2958, 2942, 2863, 1463, 1363, 1109, 1069, 967, 882; ^1H NMR ($CDCl_3$) δ 7.43-7.33 (m, 4 H, C_6H_4), 6.54-5.52 (m, 2 H, HC=CH), 3.70, (t, *J* = 6.5 Hz, 2 H, OCH_2), 3.37, (d, *J* = 6 Hz, 2 H, $ArCH_2$), 2.27 (dt, *J* = 6.5 Hz, 2 H, CH_2), 1.05-1.02 (m, 21 H, $Si(i\text{-}C_3H_7)_3$); ^{13}C NMR ($CDCl_3$) δ 141.74, 131.95, 129.68, 129.55, 125.24, 125.20, 122.78, 63.27, 38.88, 36.32, 18.00, 12.04; LREIMS 343 [$(M\text{-}C_3H_7)^+$, 30], 301 (53), 175 (27), 157 (20), 129 (22), 123 (100); HREIMS calcd for $C_{18}H_{26}OF_3Si$ $(M\text{-}C_3H_7)^+$ 343.1705, found 343.1704.

Table 3, entry 3. R_f = 0.80 (25% EtOAc-hexanes); chromatography solvents: hexanes to 2% acetone-hexanes, gradient elution; IR (neat) cm^{-1} 3031, 2932, 2856, 1612, 1510, 1464, 1247, 1103, 1036, 968, 819; ^1H NMR ($CDCl_3$) δ 7.25-7.24 (m, 5 H, C_6H_5), 7.00-6.98, 6.74-6.72 (each m, each 2 H, C_6H_4), 5.48-5.35 (m, 2 H, HC=CH), 4.40 (s, 2 H, OCH_2Ph), 3.69 (s, 3 H, OCH_3), 3.38 (t, *J* = 6.5 Hz, 2 H, OCH_2), 3.17 (d, *J* = 6.5 Hz, 2 H, CH_2Ar), 1.95 (dt, *J* = 7 Hz, 2 H, CH_2), 1.57-1.51, 1.40-1.34 (each m, each 2 H, 2 x CH_2); ^{13}C NMR ($CDCl_3$) δ 157.78, 138.61, 132.96, 131.20, 129.47, 129.26, 128.23, 127.49, 127.36, 113.69, 72.75, 70.20, 55.12, 38.05, 32.19, 29.19, 25.99; LREIMS 310 (M^+, 6), 219 (15), 201 (15), 159 (23), 147 (16), 121 (100), 91 (87); HREIMS calcd for $C_{21}H_{26}O_2$ $(M)^+$ 310.1933, found 310.1933.

Table 3, entry 4. R_f = 0.54 (5% acetone-hexanes); chromatography solvents: 5% acetone-petrol; IR (neat) cm^{-1} 3062, 3026, 2935, 2854, 1493, 1472, 1454, 1443, 1363, 1101, 1052, 970, 749, 734; ^1H NMR ($CDCl_3$) δ 7.31-7.11 (m, 9 H, C_6H_5, C_6H_4), 5.57-5.45 (m, 2 H, HC=CH), 4.48 (s, 2 H, OCH_2Ph), 3.45 (t, *J* = 6.5 Hz, 2 H, OCH_2), 3.41 (t, *J* = 6 Hz, 2 H, CH_2Ar), 2.03 (dt *J* = 7 Hz, 2 H, CH_2), 1.63-1.58, 1.48-1.41 (each m, each 2 H, 2 x CH_2); LRCIMS (NH_3), 332 [$(M+NH_4)^+$, 25], 315 (12), 237 (12), 223 (21),207 (17), 108 (19), 91 (100); HRCIMS (NH_3) calcd for $C_{20}H_{24}OCl$ $(M+H)^+$ 315.1516, found 315.1502.

Table 3, entry 5. R_f = 0.43 (10% CH_2Cl_2-hexanes); chromatography solvents: petrol then 1% CH_2Cl_2-petrol; IR (neat) cm^{-1} 3071, 3047, 2932, 2856, 1599, 1510, 1474, 1429, 1333, 1159, 1113, 973, 821; ^1H NMR ($CDCl_3$) δ 7.65-7.64, 7.39-7.33 (each m, 4 and 6 H, 2 x C_6H_5), 7.09 (dd, *J* 8.5, 5.5 Hz, 2 H, C_6H_2), 6.94 (dd, *J* 8.5 Hz, 2 H, C_6H_2), 5.52-5.42 (m, 2 H, HC=CH), 3.64 (t, *J* = 6.5 Hz, 2 H, OCH_2), 3.26 (d, *J* = 6 Hz, 2 H, CH_2Ar), 1.99 (dt, *J* = 6.5, 6.5 Hz, 2 H, CH_2), 1.58-1.52, 1.46-1.40 (each m, each 2 H, 2 x CH_2), 1.03 (s, 9 H $SiC(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 135.55, 134.10, 129.80, 129.72, 129.49, 128.79, 127.56, 115.09, 114.91, 63.79, 38.17, 32.15, 32.06, 26.88, 25.62; LREIMS 389 [$(M\text{-}C_4H_9)^+$, 100], 200 (12), 199 (66), 183 (24), 167 (66), 135 (20), 109 (33); HREIMS calcd for $C_{25}H_{26}OFSi$ $(M\text{-}C_4H_9)^+$ 389.1737, found 389.1750.

Table 3, entry 6. R_f = 0.14 (10% CH_2Cl_2-hexanes); chromatography solvents: 10% acetone-petrol; IR (neat) cm^{-1} 3068, 3010, 2929, 2855, 1612, 1510, 1473, 1465, 1429, 1243, 1113, 825; ^1H NMR ($CDCl_3$) δ 7.65-7.64, 7.39-7.34 (each m, 4, 6 H, 2 x C_6H_5), 7.07, 6.80 (each d, *J* = 8.5 Hz, each 2 H, C_6H_4), 5.53-5.41, m, 2 H, HC=CH), 3.77 (s, 3 H, OCH_3), 3.64 (t, *J* = 6.5 Hz, 2 H, OCH_2), 3.24 (d, *J* = 6 Hz, 2 H, CH_2Ar), 1.99 (dt, *J* = 7 Hz, CH_2), 1.58-1.52, 1.45-1.39 (each m, each 2 H, 2 x CH_2), 1.03 (s, 9 H, $SiC(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.53, 134.10, 133.07, 13.45, 129.46, 129.35, 129.31, 127.55, 113.74, 63.80, 55.18, 38.12, 32.16, 32.05, 26.87, 25.65; LREIMS 401 (M^+, 100), 199 (74), 183

(21), 149 (10), 121 (97), 91 (12), 77 (14); HREIMS calcd for $C_{26}H_{29}O_2Si$ $(M-C_4H_9)^+$ 401.1937, found 401.1945.

Table 3, entry 7. R_f = 0.65 (5% acetone-petrol); chromatography solvents: 5% acetone-petrol; IR (neat) cm^{-1} 3060, 3031, 2919, 2846, 1587, 1477, 1436, 1328, 1161, 1122, 1070, 968, 906, 734, 704; ^1H NMR ($CDCl_3$) δ 7.45-7.26, 7.17-7.14 (each m, 8 H, 1 H, C_6H_5, C_6H_4), 6.64-5.52 (m, 2 H, HC=CH), 3.38 (d, *J* = 6 Hz, 2 H, $ArCH_2$), 2.96 (t, *J* = 7 Hz, 2 H, SCH_2), 2.37 (dt , *J* = 7 Hz, 2 H, CH_2); ^{13}C NMR ($CDCl_3$) δ 141.44, 136.47, 131.91, 130.31, 129.86, 129.26, 128.83, 128.71, 125.90, 125.2, 122.88, 38.65, 33.48, 32.13; LREIMS 322 (M^+, 35), 212 (19), 159 (27), 143 (14), 123 (100), 109 (20); HREIMS calcd for $C_{18}H_{17}F_3S$ $(M)^+$ 322.1003, found 322.1011.

Table 3, entry 8. R_f = 0.25 (hexanes); chromatography solvents: 25% PhMe-petrol; IR (neat) cm^{-1} 3059, 3025, 2991, 2948, 2923, 2910, 2835, 1612, 1581, 1508, 1475, 1441, 1301, 1242, 1178, 1033, 972, 817, 736; ^1H NMR ($CDCl_3$) δ 7.32-7.14 (m, 5 H, C_6H_5), 7.07, 6.82 (each d, *J* = 8.5 Hz, each 2 H, C_6H_4), 6.64--5.47 (m, 2 H, HC=CH), 3.77 (s, 3 H, OCH_3), 3.26 (d, *J* = 6.5 Hz, 2 H, $ArCH_2$), 2.94 (t, *J* = 7 Hz, 2 H, SCH_2), 2.34 (dt, *J* = 7 Hz, 2 H, CH_2); ^{13}C NMR ($CDCl_3$) δ 157.90, 132.55, 131.33, 129.38, 129.18, 128.90, 128.79, 125.80, 113.78, 55.22, 38.03, 33.57, 32.19; LREIMS 284 (M^+, 51), 175 (75), 174 (100), 159 (36), 147 (24), 123 (93), 121 (83), 91 (26), 77 (25); HREIMS calcd for $C_{18}H_{20}OS$ $(M)^+$ 284.1235, found 284.1246.

Table 2, entries 4-6. R_f = 0.20 (hexanes); chromatography solvent: hexanes; IR (neat) cm^{-1} 3028, 2961, 2936, 2856, 1509, 1493, 1452, 1361, 1267, 1108, 967; ^1H NMR ($CDCl_3$) δ 7.29 and 7.10 (each d, *J* = 8.5 Hz, 4 H, C_6H_4), 5.65-5.49 (m, 2 H, HC=CH), 3.69 (t, *J* = 7 Hz, 2 H, OCH_2), 3.29, (d, *J* = 7 Hz, 2 H, $ArCH_2$), 2.26 (dt, *J* = 7 Hz, 2H, CH_2), 1.29 (s, 9 H, $C(CH_3)_3$), 1.05-1.02 (m, 21 H, $Si(^iC_3H_7)_3$); ^{13}C NMR ($CDCl_3$) δ 148.63, 137.74, 130.93, 128.70, 125.19, 63.45, 38.64, 36.41, 31.43, 18.05, 12.06; LREIMS 331 [$(M-C_3H_7)^{+\cdot}$ 64], 289 (11), 275 (13), 233 (21), 157 (33), 147 (30), 103 (26), 75 (26), 57 (100); HREIMS calcd for $C_{21}H_{35}OSi$ $(M-C_3H_7)^+$ 331.2457, found 331.2453.

Table 4, entry 1. R_f = 0.63 (25% EtOAc-hexanes); chromatography solvents: 10% EtOAc-petrol; IR (neat) cm^{-1} 2981, 2931, 2860, 1463, 1404, 1350, 1199, 1103, 1074, 1039, 972, 734, 696; ^1H NMR ($CDCl_3$) δ 7.31-7.30 (m, 5 H, C_6H_5), 5.47-5.30 (m, 2 H, HC=CH), 4.46 (s, 2 H, OCH_2Ph), 3.89, 3.88, 3.77, 3.76 (each s, each 3 H, 4 x OCH_3), 3.42 (t, *J* = 6.5 Hz, 2 H, OCH_2), 3.29 (dd, *J* = 6, 1 Hz, 2 H, $ArCH_2$), 2.12 (s, 3 H, CH_3),1.97 (dt, *J* = 7 Hz, 2 H, CH_2), 1.60-1.53, 1.42-1.36 (each m, each 2 H, 2 x CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.79, 147.68, 145.04, 144.63, 138.63, 130.59, 128.28, 128.10, 127.81, 127.55, 127.41, 125.49, 72.78, 70.22, 61.20, 61.05, 60.98, 60.63, 32.28, 29.77, 29.25, 26.04, 11.58; LREIMS 414 (M^+, 100), 225 (59), 195 (10), 111 (10), 105 (10), 91 (95); HREIMS calcd for $C_{25}H_{34}O_5$ $(M)^+$ 414.2406, found 414.2395.

Table 4, entry 2. R_f = 0.69 (10% acetone-petrol); chromatography solvents: petrol to 2% EtOAc-petrol, gradient elution; IR (neat) cm^{-1} 2960, 2933, 2854, 1410, 1350, 1199, 1103, 1080, 1043, 973, 737; ^1H NMR ($CDCl_3$) δ 5.49-5.33 (m, 2 H, HC=CH), 5.08-5.05 (m, 2 H, 2 x HC=C), 3.89, 3.88, 3.78, 3.76 (each s,

each 3 H, 4 x OCH_3), 3.30 (d, J = 6 Hz, 2 H, $ArCH_2$), 2.12 (br s, 2 H, $ArCH_2$), 2.04-1.92 (m, 8 H, 4 x CH_2), 1.66, 1.58, 1.55 (each s, each 3 H, 3 x CH_3); ^{13}C NMR ($CDCl_3$) δ 147.81, 147.71, 145.06, 144.64, 135.13, 131.21, 130.63, 128.00, 127.86, 125.54, 124.31, 123.95, 61.19, 61.05, 60.98, 60.62, 39.70, 32.73, 29.81, 27.97, 26.71, 25.65, 17.64, 16.01, 11.56; LREIMS 402 (M^+, 100), 225 (55), 191 (44), 81 (21), 69 (71); HREIMS calcd for $C_{25}H_{38}O_4$ $(M)^+$ 402.2770, found 402.2762.

Acknowledgements. Financial support provided by the National Institutes of Health (GM 40287) is greatly appreciated. We warmly express our thanks to NATO (postdoctoral fellowship to G.B.) and to the UCLA center for mass spectrometry for some of the MS data reported herein.

References.

1. Lipshutz, B. H.; Bülow, G.; Lowe, R. F.; Stevens, K. L., *J. Am. Chem. Soc.* in press.
2. Van Horn, D. E.; Negishi, E. *J. Am. Chem. Soc.* **1978**, *100*, 2252; Negishi, E.; Van Horn, D. E.; Yoshida, T. *J. Am. Chem. Soc.* **1985**, *107*, 6639; Matsushita, H.; Negishi, E. *Org. Synth.* **1984**, *63*, 31; Negishi, E. *Pure Appl. Chem.* **1981**, *53*, 2333.
3. (a) Eisch, J. J. in *Comprehensive Organic Chemistry*; Vol. 8, Trost, B. M., Fleming, I., Eds., Pergammon Press, 1991; (b) Zweifel, G.; Miller, J. A. *Org. React.* **1984**, *32*, 375 and references therein.
4. Schwartz, J.; Labinger, J. A. *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 333; Schwartz, J. *J. Organomet. Chem. Library* **1976**, 461.
5. Negishi has reported the preparation of $Pd(PPh_3)_4$ *via* reduction of $Pd(PPh_3)_2Cl_2$ with *n*-BuLi in the presence of 2 equiv PPh_3: Negishi, E.; Takahashi, T.; Akiyoshi, K. *J. Chem. Soc., Chem. Commun.* **1986**, 1338.
6. Some scrambling of *E* / *Z* geometry was observed for cases involving the hydrocarbon-based vinylalanes (Table 1, entry 1 and Table 2, entry 1). See also ref. 9.
7. Sih, C. J.; Salomon, R. G.; Price, P.; Sood, R.; Peruzzotti, G. *J. Am. Chem. Soc.* **1975**, *97*, 857.
8. Negishi, E.; Matsushita, H.; Okukada, N. *Tetrahedron Lett.* **1981**, *22*, 2715.
9. Negishi, E.; Takahashi, T.; Baba, S.; Van Horn, D. E.; Okukada, N. *J. Am. Chem. Soc.* **1987**, *109*, 2393, and references therein.
10. Smith, L. I.; Wawzonek, S.; Miller, H. C. *J. Org. Chem.* **1941**, *6*, 229.
11. (a) Bartsch, V. E.; Dinjus, E.; Fischer, R.; Uhlig, E. *Z. Anorg. Allg. Chem.* **1977**, *433*, 5; (b) Carmona, E.; Marin, J. M.; Paneque, M.; Poveda, M. L. *Organometallics* **1987**, *6*, 1757.
12. For recent syntheses of vitamins K_1 and K_2 see Tso, H-H.; Chen, Y-J. *J. Chem. Research* **1995**, 104; Kozhevnikov, I. V.; Kilikov, S. M.; Chukaeva, N. G.; Kirsanov, A. T.; Letunova, A. B.; Blinova, V. I. *React. Kinet. Catal. Lett.*, **1992**, *47*, 59; Schmid, R.; Antoulas, S.; Rüttimann, A.; Schmid, M.; Vecchi, M.; Weiser, H. *Helv. Chem. Acta.*, **1990**, *73*, 1276; for a review see Rüttimann, A. *Chimia*, **1986**, *40*, 290 and references therein; Masaki, Y.; Hashimoto, K.; Kaji, K. *Chem. Pharm. Bull.* **1984**, *32*, 3959.
13. Buchwald, S. L.; LaMaire, S. J.; Nielsen, R. B.; Watson, B. T.; King, S. M. *Tetrahedron Lett.* **1987**, *28*, 3395.

(*Received* 4 *October* 1995; *accepted* 20 *February* 1996)