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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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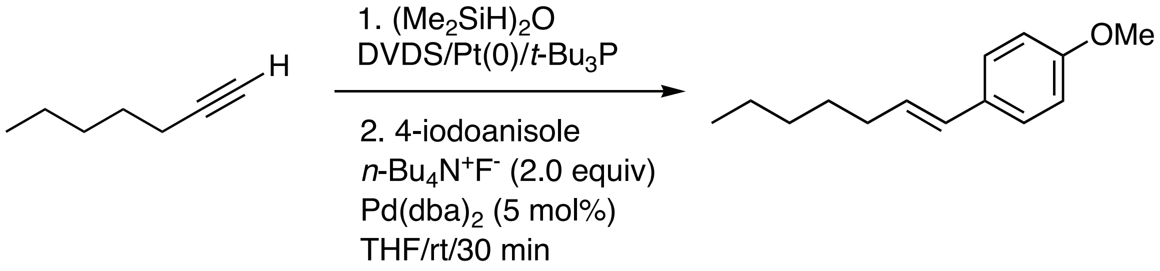
PLATINUM CATALYZED HYDROSILYLATION AND PALLADIUM CATALYZED CROSS-COUPLING: ONE-POT HYDROARYLATION OF 1-HEPTYNE TO (E)-1-(1-HEPTENYL)-4-METHOXYBENZENE

[Benzene, 1-(1E)-1-heptenyl-4-methoxy-]



Submitted by Scott E. Denmark and Zhigang Wang.[1]
Checked by Adam I. Keller and Dennis P. Curran.

1. Procedure

(E)-1-(1-Heptenyl)-4-methoxybenzene. A solution of 2.79 mL (2.12 g, 15.6 mmol) of 1,1,3,3-tetramethyldisiloxane in 3.0 mL of tetrahydrofuran (THF) is added to a flame-dried, three-necked, 250-mL, round-bottomed flask equipped with a temperature probe, addition funnel, argon inlet, and stirbar (Note 1). *t*-Bu$_3$P-Pt(0) complex (200 μL) (Notes 2 and 3) is added by syringe. 1-Heptyne (3.43 mL, 2.51 g, 26.0 mmol) (Note 4) is then slowly added by syringe with external cooling in a water bath so that the temperature of the reaction solution is not allowed to exceed 30 °C (Note 5). The mixture is stirred at room temperature for 60 min after complete addition of 1-heptyne. A solution of tetrabutylammonium fluoride in THF (40 mL, 1.0M, 40 mmol) is then added over 10 min (Notes 6 and 7). After complete addition of TBAF, the solution is stirred for 10 min and then 0.575 g (1.0 mmol) of Pd(dba)$_2$ is added in one portion (Note 8). A solution of 4-iodoanisole (Note 9) in THF (20 mL, 1.0M, 20 mmol) is then slowly added via the addition funnel such that the temperature of the reaction solution is kept between 30-33 °C

(addition time 45 min). The mixture is stirred at room temperature for 30 min after the complete addition of 4-iodoanisole. Diethyl ether (50 mL) is added and the mixture is stirred for an additional 5 min. The mixture is filtered through a short column of silica gel (Note 10), eluting with 200 mL of diethyl ether. The filtrate is concentrated by rotary evaporation and vacuum drying to give a residue that is purified by Kugelrohr distillation, chromatography, and Kugelrohr distillation to afford 3.38-3.42 g (83-84%) of (*E*)-1-(1-heptenyl)-4-methoxybenzene as a colorless oil, bp 90-95 °C/0.1 mm (lit.[4] 85-90 °C/ 1.2 mm) (Notes 11, 12, and 13).

2. Notes

1. 1,1,3,3-Tetramethydisiloxane was purchased from Lancaster Synthesis Inc. and used as received. THF was obtained from Mallinckrodt Inc. and freshly distilled from sodium/benzophenone ketyl.

2. *t*-Bu_3P-Pt(0) complex was prepared by the literature procedure:[2] *t*-Bu_3P (32 mg, 0.158 mmol) (Strem Chemicals) was dissolved in platinum(0)-1,3-divinyl-1,1,3,3-tetramethyldisiloxane complex (1.5 mL of xylene solution obtained from Aldrich Chemical Company, Inc., catalog number 47-951-9). The mixture was stirred at 65 °C (oil bath) for 5 min and then was slowly cooled to room temperature. This solution could be stored under N_2 in the freezer indefinitely.

3. *t*-Bu_3P is pyrophoric and should be handled and stored under an inert atmosphere of nitrogen or argon.

4. 1-Heptyne was purchased from GFS Chemicals Inc. and was used without further purification.

5. The hydrosilylation of 1-heptyne with 1,1,3,3-tetramethyldisiloxane is exothermic. If the temperature of the reaction exceeds 30 °C, the amount of the undesired α-isomer will increase. However, the solution should not be cooled to below 10 °C as the reaction becomes very sluggish.

6. A solution of tetrabutylammonium fluoride (TBAF) in THF (1.0M) was prepared from colorless, crystalline tetrabutylammonium fluoride trihydrate purchased from Fluka Chemical Corp.

7. Caution: TBAF reacts exothermally with the disiloxane mixture and the first few drops must be added very slowly and carefully.

8. $Pd(dba)_2$ was prepared by the literature procedure:[3] palladium chloride (1.05 g, 5.92 mmol) was added to hot (ca. 50 °C) methanol (150 mL) containing dibenzylideneacetone (DBA) (4.60 g, 19.6 mmol) and sodium acetate (3.90 g, 47.5 mmol). The mixture was stirred for 4 h at 40 °C to give a reddish-purple precipitate and allowed to cool to complete the precipitation. The precipitate was isolated by filtration, washed successively with water and acetone, and dried in vacuo.

9. 4-Iodoanisole was purchased from Aldrich Chemical Company, Inc., and was purified by chromatography on silica gel (elution with hexane/EtOAc, 50/1) prior to use.

10. Silica gel was purchased from VWR Scientific (230-400 mesh). A 45-mm diameter column was employed and 60 g of silica gel was loaded as a pentane slurry.

11. The boiling point (bp) corresponds to uncorrected air-bath temperature of a Büchi GKR-50 Kugelrohr.

12. The crude product was purified by Kugelrohr distillation (98-103°/0.2 mm) followed by column chromatography (55-mm diameter column, 200 g of silica gel, elution with pentane/EtOAc, 50/1), and another Kugelrohr distillation.

13. The analytical data are as follows: ^1H NMR (500 MHz, $CDCl_3$) δ: 0.91 (t, J = 7.1, 3 H), 1.33 (m, 4 H), 1.46 (m, 2 H), 2.18 (qd, J = 7.1, 1.5, 2 H), 3.80 (s, 3 H), 6.09 (dt, J = 15.9, 6.9, 1 H), 6.33 (d, J = 15.9, 1 H), 6.84 (d, J = 8.8, 2 H), 7.28 (d, J = 8.8, 2 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 14.1, 22.6, 29.2, 31.4, 33.0, 55.2, 113.8, 126.9, 128.9, 129.1, 130.8, 158.5; IR (NaCl) cm^{-1}: 2956, 2927, 2855, 1608, 1511, 1464, 1291, 1248, 1175, 1037, 964, 833; Anal. calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87; Found: C, 82.10; H, 10.07; GC analysis: $t_R(Z)$ = 6.07 min (1.6%), $t_R(E)$ = 6.56 min (95.3%), tR(α) = 5.91 min (3.1%) (HP-5, 250 °C, 15 psi).

Waste Disposal Information

All toxic materials were disposed of in accordance with “Prudent Practices in the Laboratory”, National Academy Press: Washington, DC, 1995.

3. Discussion

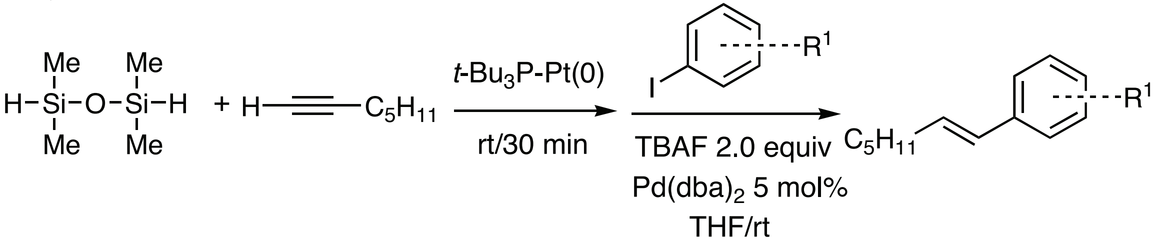
One-pot coupling reactions of organoboron- and organotin reagents with aryl or alkenyl halides and their applications in organic synthesis have been well documented.[5,6] There were only a few examples of hydrosilylation/cross-coupling applied to specific synthetic target molecules.[7,8] The procedures presented here provide a general route to (*E*)-olefins by palladium-catalyzed cross-coupling of alkenyl disiloxanes with aryl or alkenyl iodides.[9]

Tetramethyldisiloxane is an inexpensive, commercially available reagent. It reacts with alkynes to generate the alkenyldisiloxanes in situ, which can then react with a variety of iodides bearing different substituent patterns. The processes display very good functional group compatibility and afford products in high yield and with excellent regio- and stereoselectivity (Table 1). A notable characteristic of this protocol is the extremely mild reaction conditions employed. The hydrosilylation was complete at room temperature after 30 min. Most coupling reactions proceeded in 10 min to a few hours at room temperature.

The generality and functional group compatibility were also excellent with regard to the alkynes (Table 2). Free hydroxyl groups and even a remote double bond were compatible and give very good yields and purities.

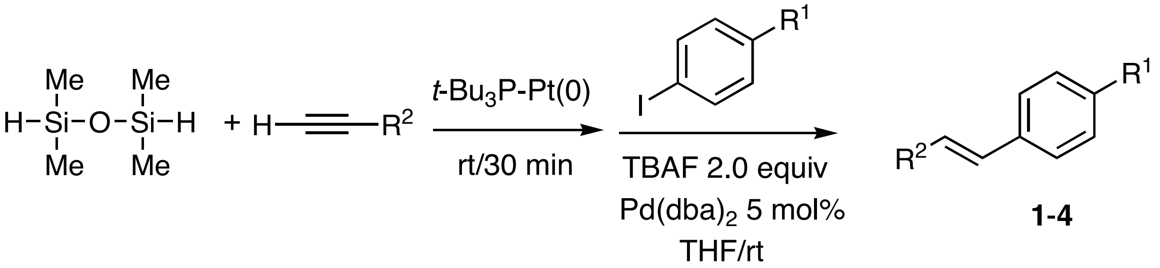
The couplings of reactive iodides (with electron-withdrawing groups) were exothermic. However, the reaction temperature can be modulated by the slow addition of iodides last. These protocols are suitable for larger scale applications as well.

Table 1. One-Pot Hydrosilyation/Cross-Coupling of 1-Heptyne with Aryl Iodides



Entry	Iodide, R^1	Time, min	Product, R^1	Yield, %
1	1-napthyl	10	1-napthyl	82
2	4-$(CH_3CO)C_6H_4$	10	4-$(CH_3CO)C_6H_4$	94
3	4-$(CH_3O)C_6H_4$	10	4-$(CH_3O)C_6H_4$	89
4	3-$(NO_2)C_6H_4$	10	3-$(NO_2)C_6H_4$	85
5	3-$(NO_2)C_6H_4$	60 (1 mol% Pd)	3-$(NO_2)C_6H_4$	89
6	3-$(CH_3)C_6H_4$	10	3-$(CH_3)C_6H_4$	78
7	2-$(CH_3OCO)C_6H_4$	20 h (10 mol% Ph_3As)	2-$(CH_3OCO)C_6H_4$	88
8	2-$(CH_3O)C_6H_4$	10	2-$(CH_3O)C_6H_4$	82

Table 2. One-Pot Hydrosilyation/Cross-Coupling of 1-Alkynes with Aryl Iodides



Entry	Alkyne, R^2	Iodide, R^1	Time, min	Product	Yield, %
1	C_6H_5	4-(CH_3CO)C_6H_4	10	**1a**	89
2	C_6H_5	4-(CH_3O)C_6H_4	10	**1b**	74
3	HO(CH_2)$_3$	4-(CH_3CO)C_6H_4	30	**2a**	82
4	HO(CH_2)$_3$	4-(CH_3O)C_6H_4	60	**2b**	89
5	$C_6H_5C(OH)(CH_3)$	4-(CH_3CO)C_6H_4	24 h	**3a**	72
6	$C_6H_5C(OH)(CH_3)$	4-(CH_3O)C_6H_4	24 h	**3b**	79
7	CH_2=$CHCH_2O(CH_2)_3$	4-(CH_3CO)C_6H_4	10	**4a**	78
8	CH_2=$CHCH_2O(CH_2)_3$	4-(CH_3O)C_6H_4	10	**4b**	76

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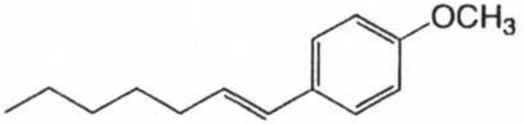
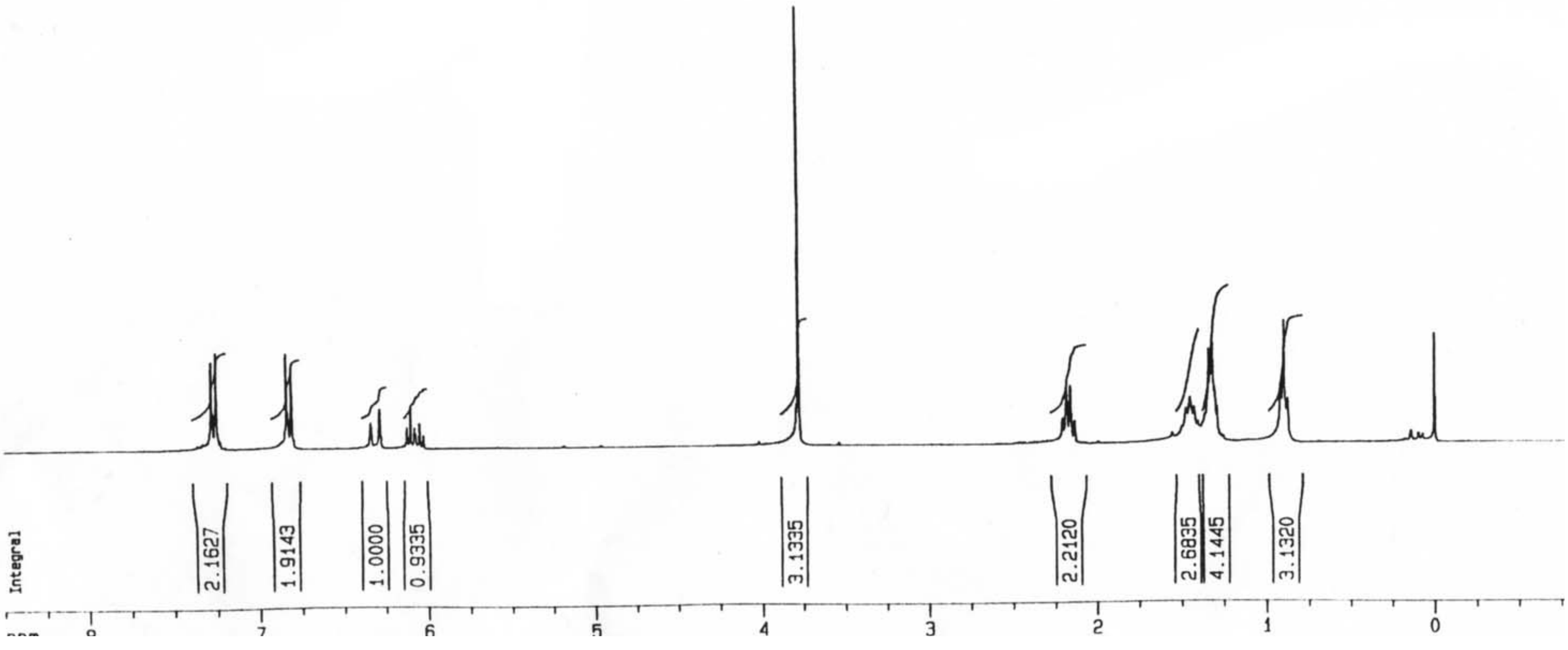
2. Chandra, G.; Lo, P. Y.; Hitchcock, P. B.; Lappert, M. F. *Organometallics* **1987**, *6*, 191-192.
3. Ukai, T.; Kawazura, H.; Ishii Y. *J. Organomet. Chem.* **1974**, *65*, 253-266.
4. Denmark, S. E.; Wehrli, D. *Org. Lett*. **2000**, *2*, 565-568.
5. (a) Miyaura, N.; Yano, T.; Suzuki, A. *Tetrahedron Lett*. **1980**, *21*, 2865-2868. (b) Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314-321. (c) Ishiyama, T.; Nishijima, K.-i.; Miyaura, N.; Suzuki, A. *J. Am. Chem. Soc.* **1993**, *115*, 7219-7225. (d) Baudoin, O.; Guenard, D.; Gueritte, F. *J. Org. Chem*. **2000**, *65*, 9268-9271.
6. Maleczka, R. E., Jr.; Gallagher, W. P.; Terstiege, I. *J. Am. Chem. Soc.* **2000**, *122*, 384-385.
7. Tamao, K.; Kobayashi, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 6051-6054.
8. Takahashi, K.; Minami, T.; Ohara, Y.; Hiyama, T. *Tetrahedron Lett.* **1993**, *34*, 8263-8266.
9. Denmark, S. E.; Wang, Z. *Org. Lett.* **2001**, *3*, 1073-1076.

Appendix
Chemical Abstracts Nomenclature (Registry Number)

1-Heptyne: 1-Heptyne; (628-71-7)
(*E*)-1-Heptenyl-4-methoxybenzene: Benzene, 1-(1*E*)-1-heptenyl-4-methoxy-; (135987-61-0)
4-Iodoanisole: Benzene, 1-iodo-4-methoxy-; (696-62-8)
1,1,3,3-Tetramethyldisiloxane: Disiloxane, 1,1,3,3-tetramethyl-; (3277-26-7)
Tri-(tert-butyl)phosphine: Phosphine, tris(1,1-dimethylethyl)-; (13716-12-6)
Platinum(0)-1,3-divinyl-1,1,3,3-tetramethyldisiloxane complex: Platinum, 1,3-diethenyl-1,1,3,3-tetramethyldisiloxane complex; (68478-92-2)
Tetrabutylammonium fluoride trihydrate: 1-Butanaminium, N, N, N-tributyl, fluoride, trihydrate; (87749-50-6)
$Pd(dba)_2$: Palladium, bis[(1,2,4,5-η)-1,5-diphenyl-1,4-pentadien-3-one]-; (32005-36-0)
Palladium chloride; Palladium chloride ($PdCl_2$); (7647-10-1)
Dibenzylideneacetone (DBA): 1,4-Pentadien-3-one, 1,5-diphenyl-; (538-58-9)


OCH3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1.0000
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3.1335
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4.1445
3.1320
ppm
8
7
6
5
4
3
2
1
0