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Efficient and stereoselective cross-coupling with highly substituted alkenylsilanols

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Abstract

Highly substituted alkenylsilanols (**1**), readily prepared from commercially available simple starting materials, are efficiently coupled with aryl or alkenyl halides in the presence of tetrabutylammonium fluoride (TBAF) and a palladium(0) catalyst. Yields are generally high and the reactions are highly stereoselective and compatible with a wide range of functional groups.

Keywords: Cross-coupling; Alkenylsilanols; Palladium catalysis

1. Introduction

Palladium-catalyzed, cross-coupling of organometallic reagents (Li, Mg, Al, Zn, B, Sn) with a variety of electrophiles is among the most useful of modern organic reactions [1]. For example, the Stille reaction [2] has advanced to such a level that there is hardly any area where of synthesis where it has not been applied [3a]. Nevertheless, the requirement of dealing with toxic organotin reagents and the attendant waste is by no mean a trivial issue. Significant effort has been expended to alleviate this problem [3] and other cross coupling method do exist, but other shortcomings have limited their application [1].

The pioneering efforts of Hiyama [4], Ito [5] and DeShong [6] have demonstrated that organosilicon compounds with heteroatom(s) attached at the silicon are viable nucleophiles in cross-coupling reactions, albeit under relatively harsh condition. In our effort to develop new silicon coupling regents [7], we have already disclosed that silacyclobutanes [7a,7b,7d], silanols [7c], siloxanes [7g,7h] and even silyl hydrides [7f] are reactive agents for cross-coupling with aryl and alkenyl halides. These organosilicon reagents transfer their alkenyl or aryl group to organic acceptors under mild reaction conditions, often at ambient temperature and within a short time [7]. Herein, we report our preliminary result on the synthesis and coupling of more highly substituted and functionalized alkenylsilanols (*E*)- and (*Z*)-**1**, which constitute stereodefined alkenylation reagents [8].

2. Results and discussion

We began by preparing the *Z*-isomer, (*Z*)-**1**, as depicted in Scheme 1. The anti-hydroalumination of 2-butynol (**2**) with Red-Al [9], followed by in-situ trapping with iodine gave (*Z*)-3-iodo-2-butenol cleanly and in high yield. After simple protection, the THP ether (*Z*)-**4** was converted to the corresponding vinyllithium reagent, which in turn was combined with 1,1,3,3,5,5-hexamethyl-1,3,5-trisiloxane (D_3) [10] to give the target silanol (*Z*)-**1** in isomerically pure form.

The synthesis of the stereoisomer (*E*)-**1** was prepared by an independent route as illustrated in Scheme 2. The key intermediate, THP protected vinyl iodide (*E*)-**4**, was prepared starting from ethyl 2-butynoate (**5**) by trans hydroiodination followed by thermal isomerization, separation, DIBAL-H reduction and straightforward protection. Lithiation of (*E*)-**4** with *tert*-butyllithium at −78 °C followed by the addition of D_3 failed to afford any silanol, nor was starting material recovered. Cur-

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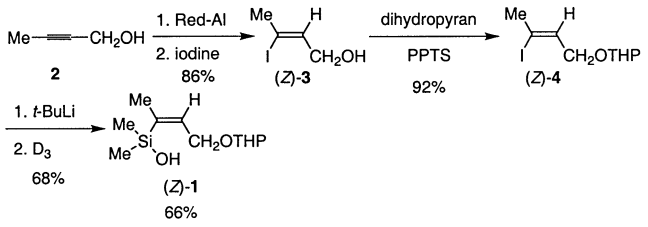


Scheme 1. Preparation of (*Z*)-**1**.

iously, lithiation with *n*-butyllithium [11] at −16 °C followed by reaction with D_3 give the target silanol (*E*)-**1**, in good yield.

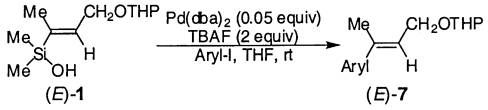
With the stereodefined substrates in hand, we examined their coupling reactions with a selection of aryl iodides under the standard conditions established previously in these laboratories [7c]. We are pleased to find that (*E*)-**1**, (the less congested of the two isomers) coupled with aryl iodides as effectively as simple disubstituted alkenylsilanols. For example, (*E*)-**1** reacted uneventfully with some aryl iodide which showed low reactivity previously [7g], on a preparative scale (Table 1), to afford the (*E*)-allylic alcohols in good yield.

The more hindered silanol (*Z*)-**1**, was next examined. Orienting experiments (Table 2) showed that, in spite of its apparent congestion, coupled with various electrophiles, albeit at substantially lower rates and with attenuated yields compared to most alkenylsilanols previously examined [7a,7b,7c,7d,7e,7f,7g].

Closer inspection of these results, revealed that two factors were responsible for the lower yields. First, despite the already extended reaction times, a small amount of the starting material was present indicating incomplete reaction for many iodides. This can be solved by carefully monitoring the reaction. Second, and more importantly, the product of homocoupling of the aryl iodide was present in nearly all the examples. In the case of entry 6, Table 2, 20% of 2,2′-bithienyl was isolated.

The incomplete consumption and homocoupling of the various iodides (not uncommon in cross-coupling processes) prevented the reactions from affording higher yields of products. To address these issues, we reinvestigated the coupling reaction of (*Z*)-**1** with the simple aryl iodides; iodobenzene and 2-iodothiophene, and the

Table 1
Survey of coupling of aryl iodides with alkenylsilanol (*E*)-**1**



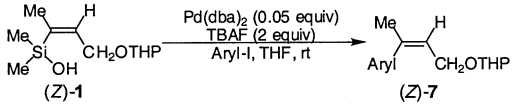
Entry	Aryl	Time (min)	Product	Yield (%) [a]
1	C_6H_5	40	(*E*)-**7a**	91
2	2-naphthyl	200	(*E*)-**7l**	90 [b]
3	(2-MeO)C_6H_4	100	(*E*)-**7c**	77
4	(2-NO_2)C_6H_6	115	(*E*)-**7d**	76

Reaction conditions: 1.1 equivalents of (*E*)-**1**, and 2.0 equivalents of TBAF, and (5 mol% of $Pd(dba)_2$ were employed for 1.0 equivalents of iodide in THF at room temperature. The iodide was added in one portion.

[a] Yields of analytically pure materials.

[b] Isomeric ratio 93/7 by ^{1}H-NMR analysis.

Table 2
Palladium-catalyzed cross-coupling of (*Z*)-**1** with aryl iodides under standard conditions



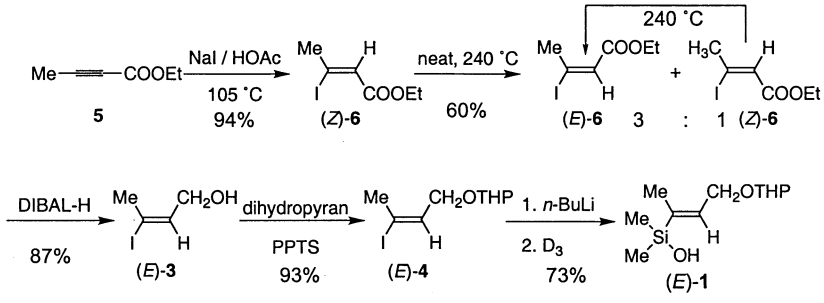
Entry	Aryl	Time (min)	Product	Yield (%) [a]
1	C_6H_5	40	(*Z*)-**7a**	75
2	2-MeC_6H_4	90	(*Z*)-**7b**	79
3	2-$MeOC_6H_4$	600	(*Z*)-**7c**	70
4	4-$MeOC_6H_4$	390	(*Z*)-**7g**	70
5	4-$MeOCC_6H_4$	40	(*Z*)-**7h**	73
6	2-thienyl	300	(*Z*)-**7k**	80 [b]
7	1-naphthyl	140	(*Z*)-**7l**	76

Reaction conditions: (a) (*Z*)-**1** (1.2 equivalents), TBAF (2.4 equivalents), were stirred under nitrogen at room temperature for 10 min, then aryl iodide (1.0 equivalents), $Pd(dba)_2$ (5.5% equivalents) was added successively.

[a] Yields of analytically pure or chromatographic ally homogenous materials.

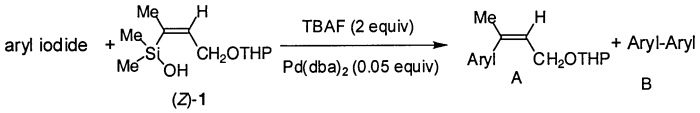
[b] About 20% of 2,2′-bithienyl was also isolated.

results are summarized in Table 3. The survey for optimum conditions showed that portionwise addition



Scheme 2. Preparation of (*E*)-**1**.

Table 3
Optimization of cross-coupling of (*Z*)-**1**



Entry	Aryl	Method of addition	Time	Temperature (°C)	A/B ratio [a]
1	C_6H_5	1 portion	5 h	r.t.	93/7
2	C_6H_5	2 portions [b]	140 min	r.t.	97/3
3	C_6H_5	3 portions [c]	45 min	35	99/1
4	2-thienyl	1 portion	5 h	r.t.	80/20
5	2-thienyl	3 portions	17.5 h	r.t.	88/12

[a] Ratio determined by ^{1}H-NMR analysis.
[b] 2/3 of iodide added initially, final 1/3 added after 20 min.
[c] 1/3 of iodide added every 20 min.

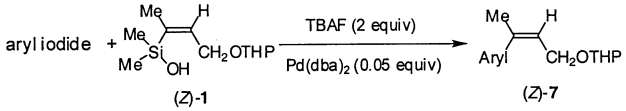
of the iodide is the most effective way to reduce the self coupling [7g]. For iodobenzene compare the results in entries 1, 2 and 3 (Table 3); for 2-iodothiophene, compare entries 4 and 5 (Table 3).

The beneficial effect of added ligands in palladium-catalyzed cross-couplings, particularly triphenylarsine, has found use in reducing byproduct formation and for inhibiting competitive processes [12]. Although, triphenylarsine has a salutary influence on our newly developed, silicon-based coupling as well [7b,7d] in this particular application, the additive seemed to retard the cross-coupling reaction and did not reduce the homocoupling of 2-iodothiophene. In short, portionwise addition of iodides is a simpler solution. Subsequently, addition of iodide in portions and further prolonging the reaction proved to be effective for improving the results with most aryl iodides.

Unfortunately, this variation had no effect on the results from cross-coupling reactions of ethyl 2-iodobenzoate and 2-nitroiodobenzene. Accordingly, we undertook the optimization of these two substrates as being representative of electron deficient aryl iodides. The results are collected in Table 4. Ethyl 2-iodobenzoate reacted sluggishly with (*Z*)-**1** (entry 1). Fortunately, 0.1 equivalents. of triphenylarsine significantly enhanced the rate in this case (entry 2). Not all ligands had a salutary effect however, for example, trifurylphosphine was found to promote protodesilylation of (*Z*)-**1**. The coupling of 2-iodonitrobenzene under standard condition gave substantial amount of nitrobenzene from an intervening reduction process (entry 3). Triphenylarsine was also very effective in suppressing the undesired reduction pathway (entry 4).

With the optimized procedure in hand, the scope of the reaction with respect to the position and the nature of the substituents was explored. The results compiled in Table 5 revealed that the reactions are mild and high yielding. The optimized procedure consistently improved the yields between 4 to 10%. Other noteworthy features include: (1) electron-withdrawing or -donating groups exhibited similar reactivity; (2) steric factors on the aryl iodide did not affect the coupling rate significantly; (3) potentially coordinating groups such a nitro or carboethoxy inhibited the reaction; (4) (*E*)-**1**

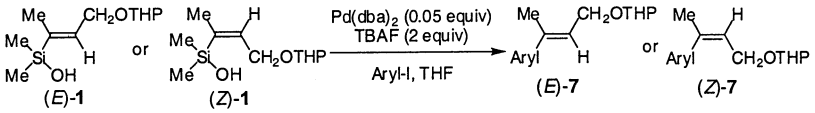
Table 4
Optimization of cross-coupling of (*Z*)-**1**



Entry	Aryl	Additive	Time (h)	Temperature (°C)	Conversion (%) [a]
1	2-(EtO_2C)C_6H_4	None	40	r.t.	17
2	2-(EtO_2C)C_6H_4	Ph_3As [b]	40	r.t.	82
3	2-(NO_2)C_6H_4	None	20	35	100 [c]
4	2-(NO_2)C_6H_4	Ph_3As [b]	13	r.t.	100

[a] Ratio determined by ^{1}H-NMR analysis.
[b] 0.1 equivalents per iodide added.
[c] 11% of nitrobenzene detected.

Table 5
Palladium-catalyzed cross-coupling of (*E*)-**1** and (*Z*)-**1** with aryl iodides [a]

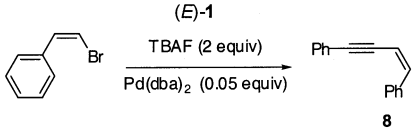


Entry	Silanol	Aryl	Ratio silanol: TBAF:Pd	Time, min (temperature, °C)	Addition mode [b]	Product	Yield (%) [c]
1	(*E*)-**1**	C_6H_5	1.1:2.0:0.05	40 (r.t.)	1 (0)	(*E*)-**7a**	91 [d]
2	(*Z*)-**1**	C_6H_5	1.1:2.0:0.05	147 (r.t.)	3 (30)	(*Z*)-**7a**	85
3	(*Z*)-**1**	2-MeC_6H_4	1.2:2.4:0.055	222 (r.t.) 60 (35)	3 (47)	(*Z*)-**7b**	87
4	(*E*)-**1**	2-$MeOC_6H_4$	1.1:2.0:0.05	100 (r.t.)	1 (0)	(*E*)-**7c**	77
5	(*Z*)-**1**	2-$MeOC_6H_4$	1:1.2:0.06	155 (r.t.) 205 (35)	3 (50)	(*Z*)-**7c**	76
6	(*E*)-**1**	2-$(NO_2)C_6H_4$	1.1:2.0:0.05	115 (r.t.)	1 (0)	(*E*)-**7d**	76
7	(*Z*)-**1**	2-$(NO_2)C_6H_4$	1.1:2.0:0.05 [e]	55 (r.t.) 610 (r.t.)	3 (55)	(*Z*)-**7d**	77
8	(*Z*)-**1**	2-$(MeO_2C)C_6H_4$	1.2:2.0:0.05 [e]	48 h (35)	1 (0)	(*Z*)-**7e**	80
9	(*Z*)-**1**	2-NCC_6H_4	1.1:2.2:0.05	580 (r.t.)	3 (50)	(*Z*)-**7f**	70
10	(*Z*)-**1**	4-$MeOC_6H_4$	1.2:2.4:0.06	160 (r.t.)	3 (50)	(*Z*)-**7g**	81
11	(*Z*)-**1**	4-$(MeOC)C_6H_4$	1.1:2.2:0.054	125 (r.t.)	3 (40)	(*Z*)-**7h**	86
12	(*Z*)-**1**	4-$(NO_2)C_6H_4$	1.2:2.0:0.05	400 (r.t.)	3 (40)	(*Z*)-**7i**	83
13	(*Z*)-**1**	4-$(MeO_2C)C_6H_4$	1.1:2:0.05	510 (r.t.) 150 (35)	3 (40)	(*Z*)-**7j**	82
14	(*Z*)-**1**	2-thienyl	1.3:2.6:0.065	300 (r.t.) 150 (35)	4 (180)	(*Z*)-**7k**	86
15	(*E*)-**1**	1-naphthyl	1.1:2.0:0.05	200 (r.t.)	1 (0)	(*E*)-**7l**	90
16	(*Z*)-**1**	1-naphthyl	1.2:2:0.05	410 (r.t.) 110 (35)	3 (40)	(*Z*)-**7l**	80
17	(*Z*)-**1**	2-pyridyl	1.1:2:0.06	41 h (35)	1 (0)	(*Z*)-**7m**	66

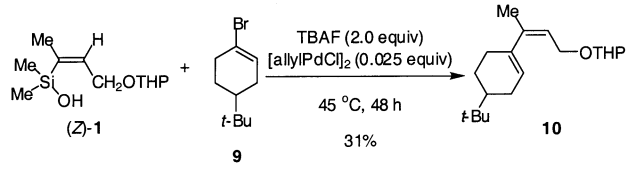
[a] Reaction conditions: **1** (1.0–1.3 equivalents), TBAF (2.0–2.6 equivalents), were stirred under nitrogen at room temperature for 10 min, then aryl iodide (1.0 equivalents), $Pd(dba)_2$ (0.05–0.065 equivalents) was added successively.
[b] Number of equal portions (total addition time, min).
[c] Yield of analytically pure material.
[d] Yield of chromatographically homogenous materials.
[e] Ph_3As (0.1 equivalents) was added with the catalyst.

reacted faster than (*Z*)-**1** in general; (5) the reaction tolerated diverse functionalities such as ester, nitro, cyano and ether; (6) the reaction was not limited to aryl iodides; heteroaryl iodide and polyaryl iodides worked as well; (7) the reaction was stereospecific, with the single exception of 1-iodonaphthalene, which gave a small amount of isomer(s) regardless of the silanol configuration.

The reaction of (*Z*)-**1** with ethyl (*E*)- and (*Z*)-3-iodoacrylate as well as (*E*)- and (*Z*)-2-bromostyrenes, were also examined. Whereas ethyl (*Z*)-2-iodoacrylate was nonproductively consumed, the (*Z*)-2-bromostyrene gave an enyne **8** [13] under standard conditions, Scheme 3. Although, the corresponding (*E*)-2-bromostyrene ethyl (*E*)-3-iodoacrylate reacted smoothly, all efforts to isolate pure products by distillation resulted in polymerization, due to the liability of the dienes. We briefly studied the cross-coupling of trisubstituted alkenyl bromide **9**, Scheme 4. The reaction has not



Scheme 3. Attempted cross-coupling with (*Z*)-**2**-bromostyrene.



Scheme 4. Alkenyl–alkenyl cross-coupling with **9**.

been optimized, but it is still noteworthy that an unactivated bromide was able to react in this case using $[allylPdCl]_2$ as the catalyst.

3. Conclusion

Although, many 3-metallo-2-butenol derivatives, are known; the sp^2–sp^2 coupling with them are limited [14–18]. This study demonstrated that substituted organosilicon compounds can effectively undergo cross-coupling with a wide variety of aryl or vinyl halides stereospecifically and in high yield. This reaction constitutes a highly-efficient and stereoselective method of alkenylation which continues to attract attention [19]. The coupling products represent stereodefined trisubstituted allylic alcohols which are very difficult to access by existing methods.

4. Experimental

4.1. Preparation of dimethyl[(1Z)-1-methyl-3-[(tetrahydro-2H-pyran-2-yl)oxy]-1-propenyl]silanol (Z)-1

In a flame-dried, two-necked flask fitted with a rubber septum and gas inlet tube, was placed vinyl iodide (*Z*)-**4** (7.048 g, 25.0 mmol) followed by 40 ml of anhydrous Et_2O at ambient temperature. The mixture was cooled to −78 °C and a 1.44 M solution of *tert*-butyllithium in C_5H_{12} (37.5 ml, 54 mmol, 2.2 equivalents.) was added dropwise by syringe over 25 min. The mixture was stirred at −78 °C for another 60 min, then a solution of 1,1,3,3,5,5-hexamethylcyclotrisiloxane (D_3) (1.85 g, 8.3 mmol) in 10 ml of anhydrous Et_2O was added over 10 min. The mixture was allowed to warm to ambient temperature and was stirred overnight. The reaction was quenched by the addition of ice-water (5.0 ml) and C_5H_{12} (200 ml). The organic layer was separated, and the aqueous layer was extracted with 100 ml of C_5H_{12}. The combined organic layers were washed with 50 ml of H_2O and were dried over Na_2SO_4. The solvent was then evaporated in vacuo to give a yellow oil, Kugelrohr distillation of which afforded 3.8 g (66%) of (*Z*)-**1** as a colorless oil. An analytical sample was obtained by further purification of a small sample by chromatography (SiO_2, C_5H_{12}/Et_2O, 4/1) and redistillation; bp 100 °C (0.5 mmHg); ^{1}H-NMR (500 MHz) δ 6.14 (m, HC(8), 1 H); 4.74 (dd, $J = 3.0$, 4.1, 1H, HC(2)); 4.30–3.20 (m, 3H, $H_2C(7)$, HO); 3.89 (m, 1H, $H_eC(6)$); 3.56–3.34 (m, 1H, $H_aC(6)$); 1.83 (br s, 3H, $H_3C(10)$), 1.83 (m, 1H, $H_eC(3)$); 1.78–1.75 (m, 1H, $H_eC(5)$); 1.61–1.54 (m, 4H, $H_aC(3)$, $H_aC(5)$, $H_2C(4)$); 0.24 (s, 3H, $H_3C(11/11')$); 0.23 (s, 3H, $H_3C(11'/11)$); ^{13}C-NMR (125.6 MHz) δ 143.92 (C(9)), 136.7.6 (C(8)), 96.35 (C(2)), 65.12 (C(7)), 62.61 (C(6)), 30.56, 25.44, 19.51, 1.13/0.49 (C(11)/C(11′)); IR (neat) 3410 (m), 2946 (s), 1620 (w), 1253 (m), 1116 (m), 1023 (s), 870 (s) cm^{-1}; MS (CI, 70 eV) *m/z* 231[$M^+ + 1$, 2], 213 (4), 197 (1), 175 (2), 159 (3), 143 (4), 129 (27), 85 (100), 75 (8); TLC R_f 0.33 (C_5H_{12}/Et_2O, 3/2, SiO_2); GC t_R (*Z*)-**1** 5.17 min (100%) (HP-5, injector 225 °C, column 300 °C, 15 psi). Anal. Calc. for $C_{11}H_{22}O_3S$: C, 57.35; H, 9.63; Si, 12.19. Found: C, 57.11; H, 9.77; Si, 12.08%.

4.2. Preparation of dimethyl[(1E)-1-methyl-3-[(tetrahydro-2H-pyran-2-yl)oxy]-1-propenyl]silanol (E)-1

In a flame dried two-necked flask fitted with a rubber septum and gas inlet tube, was placed (*E*)-**4** (1.43 g, 5.07 mmol) followed by 40 ml of dry C_6H_{14} at ambient temperature under nitrogen. The mixture was cooled to −16 °C. A 1.4 M solution of *n*-butyllithium in C_5H_{12} (5.43 ml, 7.63 mmol, 1.5 equivalents) was added dropwise through syringe over 5 min. The solution was stirred at −16 °C for another 80 min, before a solution of D_3 (0.56 g, 2.52 mmol, 1.5 equivalents) in 2.0 ml of anhydrous C_6H_{14} was added. The mixture was allowed to warm to ambient temperature and was stirred for 21 h. Then, after several pieces of ice were added, the mixture was poured into a separatory funnel and 50 ml of Et_2O was added. After being thoroughly mixed, the organic layer was separated, and the aqueous layer was extracted with 30 ml of Et_2O. The combined organic layers were washed with 20 ml each of brine and water successively, and were dried over Na_2SO_4. The solvent was then evaporated in vacuo to give a yellow oil (1.10 g), Kugelrohr distillation of which afforded 0.86 g (73%) of (*E*)-**1** as a colorless oil: bp 150 °C (0.2 mmHg); ^{1}H-NMR (500 MHz) δ 5.97 (m, 1H, HC(8)); 4.62 (m, 1H, HC(2)); 4.31 (ddq, $J = 1.1$, 5.4, 13.1 Hz, 1H, HC(7)); 4.10 (ddd, $J = 0.7$, 6.0, 13.1, 1H, HC(7)); 3.85 (m (symmetric)), 1 H, $H_eC(6)$); 3.50 (m (symmetric)), 1H, $H_aC(6)$); 3.0 (bs, 1H, OH); 1.81 (m, 1H); 1.70 (m, 4H, $H_3C(10)$ and HC); 1.57 (m, 2 H); 1.50 (m, 2H); 0.17 (s, 6H, $2H_3C(11)$); ^{13}C-NMR (125.6 MHz) δ 139.10 (C(9)), 136.67 (C(8)), 98.40 (C(2)), 64.32 (C(7)), 62.30 (C(6)), 30.78, 25.59, 19.32, 14.46, −0.974 (C(11)); IR (neat) 3402 (s), 2952 (s), 2872 (s), 2856 (s), 1626 (m), 1454 (m), 1442 (m), 1351 (m), 1251 (s), 1201 (m), 1136 (s), 1118 (s), 1027 (s), 976 (s), 868 (s), 831 (m) cm^{-1}; MS (CI, 70 eV) *m/z* 212 [$M^+ - 18$, 1], 197 (1), 175 (6), 159 (7), 129(12), 101(9), 85(100); TLC R_f 0.38 (C_5H_{12}/Et_2O, 1/1, SiO_2); GC t_R (*E*)-**1** 4.78 (98.0%), unknown 5.12 (2.0%), (HP-5, injector 225 °C, column 300 °C, 15 psi). Anal. Calc. for $C_{11}H_{22}O_3Si$: C, 57.35; H, 9.63. Found: C, 57.12; H, 9.67%.

4.3. Reaction of iodobenzene with (Z)-1. 2-[(Z)-3-phenyl-2-butenyloxy]-tetrahydro-2H-pyran ((Z)-7a)

Silanol (*Z*)-**1** (338 mg, 1.47 mmol, 1.20 equivalents), was dissolved in a 1.0 M solution of TBAF in THF (2.67 ml, 2.67 mmol, 2.0 equivalents) and the mixture was stirred for 10 min at room temperature (r.t.) Iodobenzene (272 mg, 1.33 mmol) was added in three portions over 25-min intervals and $Pd(dba)_2$ (38.4 mg, 0.0668 mmol, 0.050 equivalents) was added following the first portion of iodide. The mixture was stirred at r.t. for a total of 165 min and then was poured into 100 ml of C_5H_{12}/Et_2O, 9/1 in a flask. After being well shaken, the mixture was allowed to settle down, and the organic layer was decanted. The residue was washed with 2×10 ml of C_5H_{12}/Et_2O, 4/1. The combined organic layers were concentrated to afford the crude product as a yellow oil. Purification of the oil by column chromatography (SiO_2, 10 g, C_5H_{12}/Et_2O, 28/1) afforded 271 mg of a colorless oil, Kugelrohr distillation of which afforded 262 mg (85%) of (*Z*)-**7a** as colorless oil; bp 155 °C air bath (0.1 mmHg); ^{1}H-NMR (500 MHz) δ

7.37–7.33 (m, 2H, HC(3′); 7.29–7.26 (m, 1H, HC(4′)); 7.23–7.21 (m, 2H, HC(2′)); 5.73 (m, 1 H, HC(8)); 4.58 (br t, $J = 3.8$, 1H, HC(2)); 4.22 (ddd, $J = 1.3$, 6.5, 11.5, 1H, HC(7)); 3.90 (ddd, $J = 10.9$, 6.5, 11.5, 1H, HC(7)); 3.82 (m, 1H, $H_eC(6)$); 3.47 (m, 1H, $H_aC(6)$); 2.12 (br s, 3H, $H_3C(10)$); 1.87–1.82 (m, 1H, $H_eC(3)$); 1.75–1.69 (m, 1H, $H_eC(5)$); 1.64–1.51 (m, 4H, $H_aC(3)$, $H_aC(5)$, $H_2C(4)$); ^{13}C-NMR (125.6 MHz) δ 141.50, 140.83, 128.30, 128.05, 127.28, 124.00, 98.60 (C(2)), 65.22 (C(7)), 62.38 (C(6)), 30.92, 25.65, 25.63, 19.76; IR ($CHCl_3$) 3009 (s), 2946 (s), 2873 (m), 2855 (m), 1600 (w), 1494 (m), 1442 (m), 1378 (m), 1263 (m), 1119 (s), 1022 (s), 907 (s) cm^{-1}; MS (EI, 70 eV) *m/z* 232 [M$^+$, 1], 217 (4), 199 (1), 148 (2), 131 (94), 117 (22), 85(100); TLC R_f 0.50 (C_5H_{12}/Et_2O, 4/1); GC t_R (*Z*)-**7a** 6.04 min (100%) (HP-5, injector 225 °C, column 270 °C, 15 psi). Anal. Calc. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.63; H, 8.79%.

*4.4. Reaction of 2-iodonitrobenzene with (Z)-**1**. 2-[(Z)-3-(2′-Nitrophenyl-2-butenyloxy]-tetrahydro-2H-pyran ((Z)-**7d**)*

Silanol **(*Z*)-1** (269.7 mg, 1.17 mmol, 1.10 equivalents), was dissolved in a 1.0 M solution of TBAF in THF (2.13 ml, 2.13 mmol, 2.0 equivalents) and the mixture was stirred for 10 min at r.t. Iodonitrobenzene (110 mg) was added followed by $Pd(dba)_2$ (30.6 mg, 0.054 mmol, 0.050 equivalents) and triphenylarsine (31.0 mg, 0.11 mmol, 0.10 equivalents). Two portions of iodide (90 mg and 65 mg, respectively, for a total, 265 mg, 1.06 mmol) were added 20 min and 55 min later. The mixture was stirred at 35 °C for another 610 min. The mixture was poured into 100 ml C_5H_{12}. After being well shaken, it was allowed to settle down, and the organic layer was decanted. The residue was washed with 2×20 ml of C_5H_{12}/Et_2O, 4/1. The combined organic layers were concentrated to afford the crude product as a yellow oil. Purification of the oil by column chromatography (SiO_2, 9 g, C_5H_{12}/Et_2O, 9/1) afforded 261 mg of yellow oil, Kugelrohr distillation of which afforded 226 mg (77%) of (*Z*)-**7d** as a yellow oil; bp 165 °C (air bath, 0.2 mmHg); ^{1}H-NMR (500 MHz) δ 8.00 (dd, $J = 1.3$, 8.1, 1 H, HC(3′)); 7.60 (dt, $J = 1.3$, 7.5, 1H, HC(5′)); 7.45 (ddd, $J = 1.5$, 7.5, 8.1, 1H, HC(4′)); 7.28 (dd, $J = 1.5$, 7.5, 1H, HC(6′)); 5.76 (m, 1H, HC(8)); 4.48 (br t, $J =$ 2.8, 1H, HC(2)); 3.90 (ddd, $J = 1.3$, 6.4, 10.9, 1H, HC(7)); 3.67 (ddd, $J = 3.2$, 8.8, 11.1, 1H, $H_eC(6)$); 3.62 (ddd, $J = 1.1$, 7.5, 10.9, 1H, HC(7)); 3.40–3.36(m, 1H, HC(6)); 2.11 (br s, 3H, $H_3C(10)$); 1.80–1.74 (m, 1H, $H_eC(3)$), 1.68–1.61 (m, 1H, $H_eC(5)$), 1.56–1.46 (m, 4H, $H_aC(3)$, $H_aC(5)$, $H_2C(4)$); ^{13}C-NMR (125.6 MHz) δ 148.33, 137.95, 137.01, 133.37, 130.98, 128.35, 125.09, 124.62, 98.25 (C(2)), 64.60 (C(7)), 62.15 (C(6)), 30.70, 25.56, 25.15, 15.54; IR ($CHCl_3$) 3028 (w), 3026 (w), 3024 (w), 3008 (m), 2947 (s), 2873 (m), 2854 (m), 2854 (m), 1610 (w), 1530 (s), 1454 (w), 1441 (m), 1352 (s), 1323 (w), 1261 (w), 1157 (w), 1118 (m), 1074 (m), 1051 (m), 1022 (s), 980 (m), 904 (m), 868 (w), 856 (w) 1051 (m), 856 (w) cm^{-1}; MS (EI, 70 eV) *m/z* 233 [M$^+ -$44, 5], 176 (25), 146 (10), 130 (30), 85 (100), 67 (17); TLC R_f 0.37 (C_5H_{12}/Et_2O, 3/2, SiO_2); GC t_R (*Z*)-**7d** 8.50 min (100%) (HP5, injector 225 °C, detector 300 °C, column 270 °C, 15 psi). Anal. Calc. for $C_{15}H_{21}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.71; H, 6.79; N, 4.84%.

*4.5. Reaction of 2-iodoanisole with (E)-**1**. 2-[(E)-3-(2′-methoxyphenyl)-2-butenyloxy]-tetrahydro-2H-pyran ((E)-**7c**)*

Silanol (*E*)-**1** (254 mg, 1.10 mmol, 1.10 equivalents), was dissolved in a 1.0 M solution of TBAF in THF (2.0 ml, 2.0 mmol, Two equivalents) and the mixture was stirred for 10 min at r.t. 2-iodoanisole (232 mg, 1.0 mmol) was added followed by $Pd(dba)_2$ (29.0 mg, 0.05 mmol, 0.050 equivalents). The mixture was stirred at r.t. for a total of 100 min and was loaded onto 2.0 g of SiO_2. Purification by column chromatography (SiO_2, 51 g, C_5H_{12}/Et_2O, 24/1) afforded 240 mg yellow oil which contained ca. 5% of dibenzylidene acetone. To this oil was added 5.0 ml C_5H_{12} and the solution was cooled in refrigerator overnight. Yellow needles of crystalline dibenzylidene acetone (8.5 mg) were filtered off. Kugelrohr distillation of the residual oil afforded 202 mg (77%) of (*E*)-**7c** as a colorless oil; bp 140 °C (air bath, 0.3 mmHg); ^{1}H-NMR (500 MHz) δ 7.26 (ddd, $J = 1.7$, 7.7, 8.7, 1 H, HC(5′/4′)); 7.19 (dd, $J = 1.7$, 7.7, 1H, HC(3′/6′)); 6.93 (br dd, $J = 7.7$, 8.7, 1H, HC(4′/5′)); 6.88 (br d, $J = 8.7$, 1H, HC(6′/3′)); 5.67 (qt, $J = 1.1$, 6.6, 1H, HC(8)); 4.74 (t $J = 3.4$, 1 H, HC(2)); 4.33 (dd, $J = 6.0$ 12.5, 1H, HC(7)), 4.27 (dd, $J = 7.1$, 12.5, 1H, HC(7)); 3.96 (ddd, $J = 2.8$, 7.7, 11.2, 1H, $H_eC(6)$), 3.83 (s, 3H, $H_3C(7')$), 3.58 (m, 1H, $H_aC(6)$); 2.05 (br s, 3H, $H_3C(10)$); 1.96–1.86 (m, 1H, $H_eC(3)$); 1.80–1.74 (m, 1H, $H_eC(5)$); 1.67–1.53(m, 4H, $H_aC(3)$, $H_aC(5)$, $H_2C(4)$); ^{13}C-NMR (125.6 MHz) δ 156.83 (C(2′)), 138.93(C(9/1′)), 134.30 (C(1′/9)), 129.79 (C(3′/6′)), 128.46 (C(4′/5′)), 126.13 (C(8)), 120.74 (C(5′/4′)), 110.91 (C(6′/3′)), 98.05 (C(2)), 64.03 (C(7)), 62.50 (C(6)), 55.58 (C(7′)), 30.95 (C(3)), 25.75 (C(4)), 19.79 (C(5)), 17.61 (C(10)); IR (neat) 2943 (m), 1597 (m), 1490 (m), 1249 (m), 1118 (m), 1043 (m) cm^{-1}; MS (EI, 70 eV) *m/z* 262 [M$^+$, 2], 178 (13), 161 (42), 147 (13), 132 (16), 91 (11), 85 (97), 67 (11), 57 (14); TLC R_f 0.42 (C_5H_{12}/Et_2O 4/1, SiO_2); GC t_R (*E*)-**7c** 7.68 min (100%) (HP5, injector 225 °C, detector 300 °C, column 270 °C, 15 psi). Anal. Calc. for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.09; H, 8.48%.

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