Palladium(II) and Copper(I) Cocatalyzed Coupling of Stereodefined Alkenyl(phenyl)iodonium Triflates and Unsaturated Tri-*n*-butylstannanes[†]

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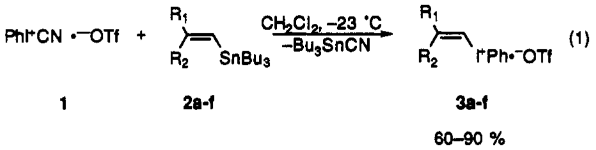
The synthesis of conjugated dienes and enynes via cross-coupling reactions permeates the literature.[1,2] Coupling of aryl and vinyl halides[3] and vinyl triflates[4] with (alkynyl)- and (alkenyl)tri-*n*-butylstannanes under palladium-catalyzed conditions is usually performed in polar solvents (e.g., DMF, THF) at 60–80 °C over a period of 1–8 h. Although the coupling is known to proceed in good yields with retention of vinyl triflate and iodide stereochemistry, the synthesis and purification of the premier coupling partners, simple, stereoisomerically pure vinyl triflates, is nontrivial[5] and coupling with vinyl idodides is often sluggish unless the very toxic trimethylstannane analogs are used.[3] Furthermore, few examples of coupling with unprotected α,β-alkynylcarbonyl compounds have appeared.

Stable, crystalline alkenyl(phenyl)iodonium salts[6] are useful in a plethora of carbon–carbon bond forming reactions by substitution with alkyl- and alkynylcuprates,[7,8] soft enolates, and alkyl- and phenyllithium reagents and in palladium-catalyzed carbonylation.[6–8] Recently, Moriarty reported the palladium-catalyzed coupling of alkenyliodonium salts with olefins.[9] The development of the iodonium transfer reagent **1** allows ready access to stereodefined alkenyl(phenyl)iodonium triflates (**3a–f**) in excellent yields (eq 1).[10] The enormous number of methods for vinylstannane synthesis implies extensive utility for the iodonium products obtained via this method.[11]



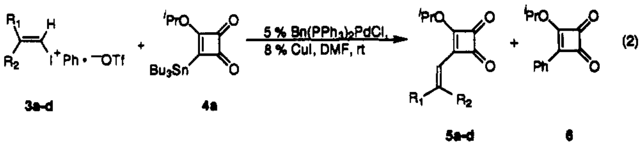
Because of the ubiquity of cross-coupling reactions in synthetic organic chemistry,[1] the coupling of stereodefined, easily prepared iodonium salts with acetylenes to form conjugated enynes and with trisubstituted olefins to form highly substituted dienes would be of great utility. Herein, we report that palladium/copper-catalyzed coupling of trisubstituted alkenyl(phenyl)iodonium triflates with alkynyl- and alkenylstannanes proceeds under exceedingly mild conditions with retention of geometry of the alkenyl ligand of the iodonium salt.

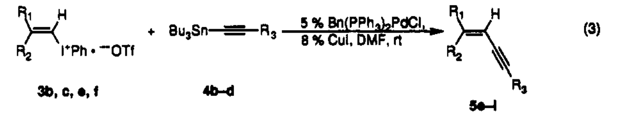
Table I. Palladium/Copper-Cocatalyzed Coupling of Alkenyl(phenyl)iodonium Triflates **3a–e** with Stannanes **4a–d**

entry	iodonium salt	R_1	R_2	stannane	R_3	product	yield (%)[a]
1	**3a**	Me	Me	**4a**		**5a**	70
2	**3b**	^{n}Bu	^{n}Bu	**4a**		**5b**	65
3[b]	**3c**	^{n}Bu	Et	**4a**		**5c**	60
4[b]	**3d**	Et	^{n}Bu	**4a**		**5d**	76
5	**3b**	^{n}Bu	^{n}Bu	**4b**	Ph	**5e**	77
6[b,c]	**3e**	Me	Et	**4b**	Ph	**5f**	64
7[b,c]	**3f**	Et	Me	**4b**	Ph	**5g**	66
8	**3b**	^{n}Bu	^{n}Bu	**4c**	(CO)^{t}Bu	**5h**	66
9	**3c**	^{n}Bu	Et	**4d**	(CO)N$(CH_2)_4$	**5i**	67

[a] Isolated yields of pure compounds based on starting iodonium salts. Typical procedure: iodonium salt (0.60 mmol) was placed in 2 mL of degassed DMF at room temperature followed by the stannane (0.67–0.90 mmol), 5 mol % $Bn(PPh_3)_2PdCl$ (0.031 mmol), and 8 mol % CuI (0.049 mmol). After the mixture was stirred at room temperature for 30 min, 10 mL of saturated NH_4Cl was added and the phases were separated. The organic phase was washed with 3 × 10 mL of 10% KF and dried with $MgSO_4$, and the compound was purified by radial chromatography. [b] Stereochemistry was assigned on the basis of the stereochemistry of the starting alkenyl(phenyl)iodonium triflate and verified by NOE measurements between the vinylic proton and the methylene resonances. [c] Each of the isolated products was determined to be at least 98.5% devoid of the other isomer by capillary GC.

The iodonium coupling reaction (eqs 2 and 3 and Table I) occurs instantaneously at room temperature with 1.0 equiv of alkenyl(phenyl)iodonium triflates (**3a–f**),[10] 1.0–1.5 equiv of (alkynyl)- or (alkenyl)stannane (**4a–d**),[12,13] 5 mol % *trans*-benzyl(chloro)bis(triphenylphosphine)palladium(II),[14] and 8 mol % copper iodide[15] in DMF.[16] Both copper and palladium are necessary for the desired reaction to occur. Table I reveals that this reaction provides good yields with a variety of stannanes including the useful squarate **4a** developed by Liebeskind.[13] Furthermore, it affords stereodefined products (**5c** and **5d**) with retention of alkenyl geometry from the original alkenyl ligand of the iodonium triflate. Reaction of iodonium salts **3e** and **3f** with





[†] Dedicated to Professor John D. Roberts on the occasion of his 75th birthday.

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(14) Palladium(II) catalyst was prepared according to the procedure of Stille: Lau, K. S. Y.; Wong, P. K.; Stille, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 5832.

(15) Copper(I) iodide (99.999%) was purchased from Aldrich Chemical Company and used as received.

(16) Dimethylformamide was purchased from Mallinckrodt Chemical Company and sparged with dry N_2 for 15 min prior to use.

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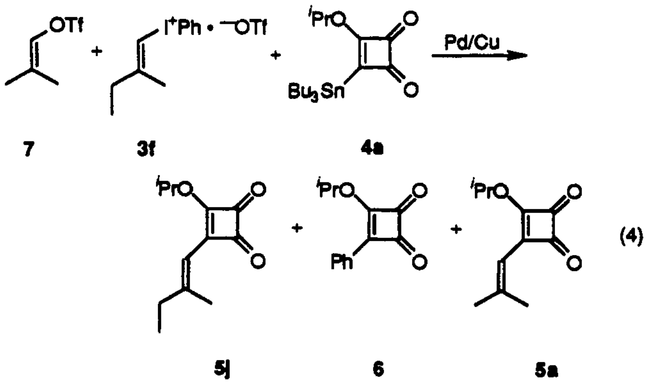
Table II. Competition Studies between Alkenyl(phenyl)iodonium Triflates, Excess Iodobenzene or Stannane **4a**, and Vinyl Triflate **7**

entry[a]	temp (°C)	time (min)	ratio[b] **5j**:**6**:**5a**
1[c]	−23	15	0:8:92
2	−23	15	91:6:3
3	−23	30	88:8:4
4	20	15	71:25:4
5	20	60	63:33:4

[a] Reactions except entry 1) performed with 1.0 equiv of **3f**, 1.0 equiv of vinyl triflate, **7**, and 2.1 equiv of stannane **4a**. [b] Ratio determined by ^{1}H NMR analysis of crude reaction mixtures quenched with NH_4Cl, washed with aqueous KF, and concentrated in vacuo. [c] Ratio (**5a**:**6**) of 92:8 was achieved by reaction (−23 °C, 15 min) of 1.0 equiv of **3a** and 1.0 equiv of **4a** in the presence of 1.0 equiv of added iodobenzene.

stannane **4b** provides another pair of stereoisomers, **5f** and **5g**, in greater than 98.5% isomeric purity. Finally, entries 8 and 9 demonstrate that functionalized alkynylstannanes also effectively couple under these conditions.

In 1990, Liebeskind and Fengl reported that iodobenzene (a byproduct of the current reaction) effectively couples with stannane **4a** under similar conditions.[13] Therefore, a competition study (Table II) was performed between alkenyl(phenyl)iodonium salt **3a**, 1 equiv of stannane **4a**, and 1.0 equiv of *added* iodobenzene at −23 °C (entry 1). Analysis of the crude product mixture revealed that the iodonium salt reacts preferentially, leading to a 92:8 mixture of the desired squarate product **5a** and the phenyl analog **6**. Another study (entries 2–5) was performed with 1.0 equiv of **3f**, 2.1 equiv of stannane **4a**, and 1.0 equiv of vinyl triflate **7** at various times and temperatures (eq 4). Without exception, the squarate resulting from reaction of the alkenyl(phenyl)iodonium triflate was the major product. The two other undesired products (phenyl squarate **6** and vinyl squarate **5a**) each increased in quantity with longer reaction times and higher temperatures. However, under typical reaction conditions with the 1.0–1.1 equiv of **4a** necessary for the reaction and no added iodobenzene, only 0–4% of phenyl byproduct **6** was observed in the synthesis of **5a–d** even at room temperature and reaction times of up to 1 h. Hence, it is likely that the iodobenzene simply reacts after all of the iodonium salt is consumed.



(4)

In summary, we have exploited the electron-deficient character of alkenyl(phenyl)iodonium triflates in an efficient and stereospecific palladium/copper-cocatalyzed cross-coupling with unsaturated tri-*n*-butylstannanes. A variety of stannanes, including simple and functionalized alkynylstannanes, couple in good yields under exceedingly mild conditions and afford stereodefined products. The very mild conditions required also allow for selective coupling of iodonium salts in the presence of other known coupling reagents such as iodobenzene and a simple vinyl triflate.

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Supplementary Material Available: Experimental procedures and data for the preparation of products **5a–i** and ^{1}H and $^{13}C\{^1H\}$ spectra (35 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.