# The Stille Reaction of 1,1-Dibromo-1-alkenes: Preparation of Trisubstituted Alkenes and Internal Alkynes

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The Stille reaction of 1,1-dibromo-1-alkenes **1** with aryl- and vinylstannanes produces different products depending on the reaction conditions. When the reaction is run in toluene or 1,4-dioxane with tris(2-furyl)phosphine (TFP) as the ligand, (*Z*)-bromoalkenes **2** are obtained stereospecifically in good to excellent yields with most substrates. However, 2-aryl-1,1-dibromo-1-alkenes (**1e**,**1g**) having an electron-donating methoxy group in the para- or ortho- position give poor yields. This method has been applied to the one-pot syntheses of stereospecifically trisubstituted alkenes **5**. When the Stille reaction is conducted in a highly dipolar solvent (DMF), monobromides **2** and/or internal alkynes **4** are the products. The less reactive phenylstannane favors the formation of alkynes **4**, regardless of which ligand is used. More reactive organostannanes (vinyl, furyl) require a very electron rich ligand, tris(4-methoxyphenyl)phosphine, for the formation of alkynes **4**. This new method for internal alkyne preparation is general, requires very mild reaction conditions, and gives high yields.

## Introduction

1,1-Dibromo-1-alkenes are easily prepared,[1] and they can provide a convenient and straightforward route for the preparation of stereospecifically trisubstituted alkenes by palladium-catalyzed stepwise coupling of both bromides.[2] The rates of palladium-catalyzed cross-coupling reactions of (*E*)- and (*Z*)-1-bromo-1-alkenes are substantially different.[3] Palladium-catalyzed stereoselective monosubstitutions of 1,1-dihalo-1-alkenes (halo as chloride and bromide) with Grignard, and organozinc reagents,[4] organoalanes,[5] and organoboronic acids[6] have been reported. However, the use of organoaluminum, Grignard and organozinc reagents is limited by their difficulty in preparation and incompatibility with many functional groups. Coupling of vinylboronic acids with 1,1-dibromo-1-alkenes gives good yields with highly toxic thallium(I) hydroxide[6a,b] but only poor to moderate yields with other bases.[6c] Moreover, the coupling of less reactive arylboronic acids with 1,1-dibromo-1-alkenes has not been demonstrated.

The Stille reaction[7] of organostannanes with organohalides has gained wide acceptance in synthetic organic chemistry due to the mild reaction conditions and easy preparation of organostannanes. Because the Stille chemistry is compatible with virtually any functional group, and also because organostannanes are stable to many reaction conditions, the Stille reaction is ideal in synthesis of complex natural products.[8] However, few studies of the Stille reaction of 1,1-dibromo-1-alkenes have been reported despite the advantages this approach may provide over the existing methods.[9] The successful intramolecular cross-coupling of 1,1-dibromo-1-alkenes with organostannanes was reported,[10] and the reaction proceeded with stereoselective coupling of the (*Z*)-bromide with an internal directing group but failed in the absence of the directing group.[10a] More recently, Uneshi and coworkers demonstrated that the (*E*)-bromides in 1,1-dibromo-1-alkenes could be selectively reduced by tributyltin hydride using tetrakis(triphenylphosphine)palladium as the catalyst.[11] Only one example of the intermolecular Stille reaction of 1,1-dibromo-1-alkenes has been reported previously.[12] Specifically, $\beta,\beta$-dibromostyrene and 1-pro-

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(7) Reviews of the Stille reactions: (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. (b) Farina, V.; Krishnamurthy, V.; Scott, W. J. *Org. React.* **1997**, *50*, 1. (c) Mitchell, T. N. In *Metal-catalyzed Cross-coupling Reactions;* Diederich, F., Stang, S., Eds.; Wiley-VCH: Weinheim, Germany, **1998**; Chapter 4.

(8) Examples: (a) Lankacidin C: Kende, A. S.; Koch, K.; Dorey, G.; Kaldor, I.; Liu, K. *J. Am. Chem. Soc.* **1993**, *115*, 9842. (b) Rapamycin: Nicolaou, K. C.; Piscopio, A. D.; Bertinato, P.; Chakrabarty, T. K.; Minowa, N.; Koide, K. *Chem. Eur. J.* **1995**, *1*, 318. (c) Dynemicin A: Shair, M. D.; Yoon, T.; Chao, T.-C.; Danishesky, S. J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2477. (d) Eleutherobin: Chen, X.-O., Zhou, B.; Bhattacharya, S. K.; Gutteridge, C. E.; Pettus, T. R. R.; Danishesky, S. J. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 789.

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(10) (a) Nuss, J. M.; Rennels, R. A.; Levine, B. H. *J. Am. Chem. Soc.* **1993**, *115*, 6991. (b) Torii, S.; Okumoto, H.; Tadokodo, T.; Nishimura, A.; Rashid, M. A. *Tetrahedron Lett.* **1993**, *34*, 2139. (c) Trost, B. M.; Walchli, R. *J. Am. Chem. Soc.* **1987**, *109*, 3487.

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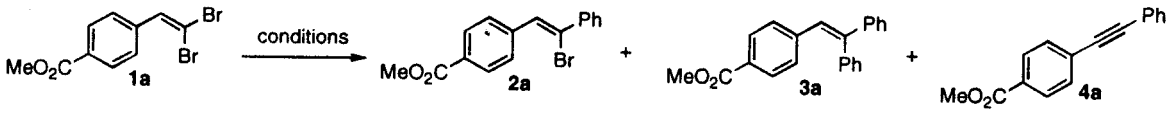
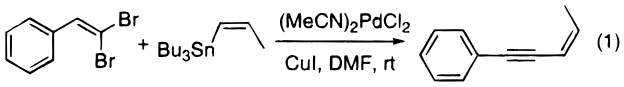
**Table 1. Solvent and Ligand Effects**



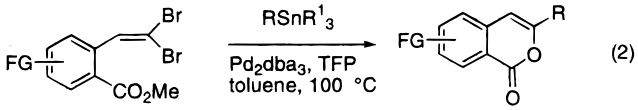

| entry | solvent | ligand | $PhSnMe_3$ (equiv) | base[a] | *T* (°C) | *t* (h) | **1a**:**2a**:**3a**:**4a** (yield, %)[b] |
|---|---|---|---|---|---|---|---|
| 1 | PhMe | TFP | 1.05 | none | 100 | 20 | 0:92:8:0 (98)[c] |
| 2 | PhMe | TFP | 2.2 | none | 105 | 48 | **3a** only (100) |
| 3 | PhMe | $Ph_3P$ | 1.05 | none | 100 | 20 | 77:4:1:18 |
| 4 | PhMe | $Ph_3As$ | 1.05 | none | 100 | 20 | 31:37:32:0 |
| 5 | PhMe | $(o\text{-Tol})_3P$ | 1.05 | none | 100 | 20 | **1a** only (no rxn) |
| 6 | PhMe | dppf | 1.05 | none | 100 | 20 | **1a** only (no rxn) |
| 7 | PhMe | $(4\text{-MeOPh})_3P$ | 1.05 | none | 100 | 20 | **1a** only (no rxn) |
| 8 | Dioxane | TFP | 1.05 | none | 100 | 20 | 0:90:10:0 (93) |
| 9 | MeCN | TFP | 1.05 | none | 100 | 20 | 46:27:7:21 |
| 10 | DMF | TFP | 2.2 | none | 80 | 10 | **4a** only (92) |
| 11 | DMF | TFP | 1.05 | DIPEA | 80 | 10 | **4a** only (91) |
| 12 | DMF | $(4\text{-MeOPh})_3P$ | 1.05 | DIPEA | 80 | 10 | **4a** only (88) |
| 13 | DMF | $Ph_3P$ | 1.05 | DIPEA | 80 | 10 | **4a** only (88) |
| 14 | DMF | MeCN[d] | 1.05 | DIPEA | 80 | 10 | 0:0:26:74 (19%) |
| 15 | DMF | TFP | 1.05 | DIPEA | 80 | 48 | **1a** only (no rxn)[e] |

[a] 1.5 equiv when used. [b] Yields were isolated; product ratios were determined by GC. [c] GC showed that product **3a** appeared early with **2a**, and 1.05 equiv of $PhSnMe_3$ was needed to completely consume **1a**. [d] $Pd(MeCN)_2Cl_2$ (5 mol %) was used without an added ligand; see ref 12. [e] No Pd was added to the reaction; see also ref 12.

penyltributyltin react to give an enyne product in 39% yield (eq 1).




Previously, we reported the synthesis of isocoumarins via a palladium-catalyzed tandem Stille reaction and subsequent annulation of methyl 2-(2′,2′-dibromovinyl)-benzoates (eq 2).[13] In this paper, we report that the Stille




reaction of 1,1-dibromo-1-alkenes (**1**) can occur stereospecifically to produce the desired (*Z*)-monobromides in good yields. More importantly, we also demonstrate that 1,1-dibromo-1-alkenes may form internal alkynes in excellent yields under slightly varied reaction conditions.

## Results and Discussion

**A. Investigation of Reaction Conditions.** The reported unsuccessful intermolecular Stille reaction[12] of 1,1-dibromo-1-alkenes prompted us to carry out a systematic investigation to determine alternative conditions for the proposed reaction (Table 1). Methyl 4-(2′,2′-dibromovinyl)benzoate (**1a**) was chosen as a model substrate to couple with trimethyl(phenyl)tin due to the ease of monitoring the reaction by TLC and to the ease of separating the products by flash chromatography as compared with *β*,*β*-dibromostyrene. The product ratios were determined by gas chromatography using an internal standard (1,3,5-tri-*tert*-butylbenzene).

First, different ligands were examined while stirring the reaction mixture under an atmosphere of nitrogen at 100 °C in toluene. Unless otherwise noted, tris(dibenzylideneacetone)dipalladium ($Pd_2dba_3$, 2.5 mol %) was used as the palladium source, along with 15 mol % of the chosen ligand (7.5% if bidentate). With tris(2-furyl)-phosphine (TFP) or triphenylarsine as the ligand, the coupling proceeded without the formation of alkyne **4a**. TFP efficiently catalyzed the stereospecifical cross-coupling of the (*E*)-bromide with trimethyl(phenyl)tin to give (*Z*)-monobromide **2a** in excellent yield (entry 1, Table 1). The coupling of both (*E*)- and (*Z*)-bromides to form diphenylated product **3a** required a higher temperature and a longer reaction time (entry 2). Triphenylarsine yielded a considerable amount of **3a** in addition to remaining **1a** (entry 4), as the formation of **3a** consumed 2 equiv of trimethyl(phenyl)tin. When triphenylphosphine was used (entry 3), most **1a** remained, and alkyne **4a** was the major product observed. Other ligands (entries 5−7) gave no reaction at all in toluene. Apparently, a "soft" ligand, such as TFP or $Ph_3As$, which facilitates the transmetalation step is required for the reaction to succeed in toluene.[14] TFP is superior to $Ph_3As$ because of the selectivity.

Next, the solvent effect was examined (entries 8−10, Table 1). In 1,4-dioxane, a low polarity solvent, the reaction gave a similar yield and ratio of products to those obtained with toluene. Acetonitrile afforded about equal amounts of alkyne **4a** and monobromide **2a**, along with unreacted **1a** and small amount of diphenylated product **3a**. When DMF, a highly dipolar and good coordinating solvent, was used (entries 10−13), only alkyne **4a** formed. The reaction in DMF required a shorter time and a lower temperature. Because the formation of alkyne **4a** is accompanied by generation of HBr, 2 equiv of trimethyl(phenyl)tin is needed to complete the reaction (entry 10). The addition of *N*,*N*-diisopropylethylamine (DIPEA, entries 11−13) resulted in the requirement of only slightly more than 1 equiv of the stannane.

Other highly dipolar solvents (not reported in Table 1), such as DMSO, HMPA, 1-methyl-2-pyrolidinone (NMP), and *N*,*N*-dimethylacetamide (DMA), also give **4a** as the only product in good yields under similar reaction conditions to entry 11. When the reaction was run in DMF under similar reaction conditions to entry 11, all of the

(13) Wang, L.; Shen, W. *Tetrahedron Lett.* **1998**, *39*, 7625.

(14) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585.

phosphine ligands surveyed (entries 12, 13, and others[15] not listed in Table 1) gave alkyne **4a** in good yields.

Finally, when the reaction was run with $Pd(MeCN)_2Cl_2$, without using an added alternative ligand, as reported in the literature,[12] a poor yield of a 1:3 mixture of **3a** and **4a** was obtained (entry 14). In a control experiment, **1a** remained unchanged after prolonged heating if the reaction was run without palladium but with a ligand (TFP) and DIPEA in DMF (entry 15).

**B. Stereospecifical Monocoupling of 1,1-Dibromo-1-alkenes.** A variety of 1,1-dibromo-1-alkenes **1** (1.0 mmol) were coupled with different stannanes, using 2.5 mol % $Pd_2(dba)_3$ and 15 mol % TFP in toluene (5.0 mL) at 100 °C for 20 h, as shown in Table 2. Most 2-aryl- and 2-alkyl-1,1-dibromo-1-alkenes gave monobromides **2** in good yields, with no to small amount of biscoupled products **3** isolated. Substitutions at different positions of the aromatic ring (entries 4−6) by the electron-withdrawing cyano group did not affect the reaction. However, because the methoxy group at ortho or para position in **1e** or **1g** (entries 7, 9) conjugatively donates electron to the alkene bond, the oxidative insertion by Pd(0) into the C−Br bond becomes more difficult. Consequently, the reactions required more stannane and resulted in lower yields and mixtures of products. On the other hand, the methoxy group at the *meta* position (**1f**) cannot conjugatively donate electrons to the alkene bond, and a satisfactory coupling result was obtained (entry 8).

The significant amounts of diphenylated products **3j**,**n** could be attributed to the weak directing effect of oxygen atoms in **1g**,**j**, as shown in Scheme 1. Coordination of palladium(0) to the oxygen atoms prior to the oxidative insertion leads to the formation of reversed (*E*)-monobromides **2jr** and **2nr**, which were further phenylated to give the minor products **3j**,**n**.

**C. Synthesis of Internal Alkynes.** As shown in entries 11 and 12 of Table 1, when the coupling reactions of dibromides **1** (1.0 mmol) with $PhSnMe_3$ (1.05 mmol) were performed in DMF at 80 °C for 10 h, alkynes **4** were the product. DIPEA (1.5 mmol) was used to neutralize hydrogen bromide generated from the reaction. The results are summarized in Table 3.

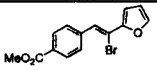
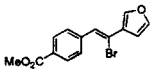
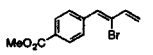
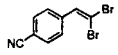
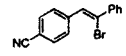
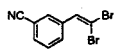
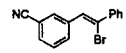
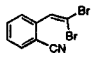
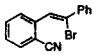
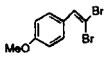
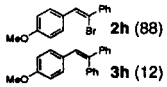
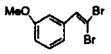
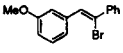
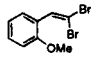
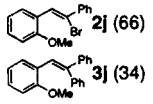
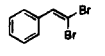
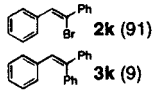
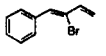
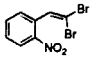
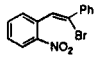
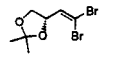
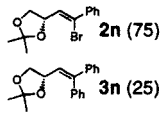
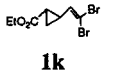
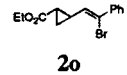
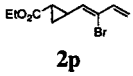
Internal alkynes **4** always resulted when trimethyl(phenyl)tin was used, and the phosphine ligands had little effect on the coupling (entries 11−13, Table 1; entries 17, 18, Table 3). However, when reactive stannanes, such as vinyltributyltin[16] and 2- and 3-furyltributyltin were coupled using the TFP ligand, monobromides **2** were obtained exclusively or partly (entries 1, 3, 5, 19, Table 3) instead of the expected alkynes **4**. It was found that a very electron rich ligand, tris(4-methoxyphenyl)-phosphine, which promotes much slower transmetalation than TFP,[14] suppressed the formation of monobromides **2** completely to give alkynes **4** in good yields. Other palladium ligands, such as triphenylphosphine, tricyclohexylphosphine, dppf, and tri-*o*-tolylphosphine give a mixture of both products **2** and **4** in varied ratios.

Alkyne formation is unaffected by the electronic character or position of substituents on 1,1-dibromoalkenes

(15) Other ligands: triphenyl phosphite; tri-*o*-tolylphosphine; tricyclohexylphosphine; dppp; dppf.

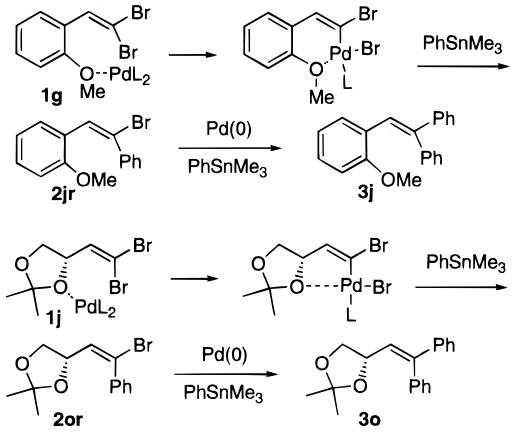
(16) The rate of transmetalation correlates with the electronegativity of the organometallica. The relative rates of selected stannane transmetalations: Labadie, J. W.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6129.

**Table 2. Monosubstitution of 1,1-Dibromo-1-alkenes**

| Entry | Dibromide | $R^1SnR^2_3$ | Product, yield (%) |
|---|---|---|---|
| 1 |  **1a** | 2-FurSnBu$_3$ |  **2b** 80 |
| 2 | **1a** | 3-FurSnBu$_3$ |  **2c** 63 |
| 3 | **1a** | VinSnBu$_3$ |  **2d** 55 |
| 4 |  **1b** | $PhSnMe_3$ |  **2e** 74 |
| 5 |  **1c** | $PhSnMe_3$ |  **2f** 72 |
| 6 |  **1d** | $PhSnMe_3$ |  **2g** 97 |
| 7 |  **1e** | $PhSnMe_3$[a] |  **2h** (88) **3h** (12) 20[b] |
| 8 |  **1f** | $PhSnMe_3$ |  **2i** 83 |
| 9 |  **1g** | $PhSnMe_3$[a] |  **2j** (66) **3j** (34) 18[b] |
| 10 |  **1h** | $PhSnMe_3$ |  **2k** (91) **3k** (9) 89[b] |
| 11 | **1h** | VinSnBu$_3$ |  **2l** 75 |
| 12 |  **1i** | $PhSnMe_3$ |  **2m** 64 |
| 13 |  **1j** | $PhSnMe_3$[c] |  **2n** (75) **3n** (25) 72[b] |
| 14 |  **1k** | $PhSnMe_3$ |  **2o** 63 |
| 15 | **1k** | VinSnBu$_3$ |  **2p** 64 |

[a] 1.5 equiv of $PhSnMe_3$ was used. [b] Ratio was determined by $^1H$ NMR integration. [c] 1.2 equiv of $PhSnMe_3$ was used.

**Scheme 1**

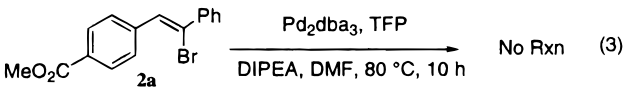



**1**. Thus, 2-aryl-1,1-dibromo-1-alkenes (**1b**−**g**) bearing either the electron-donating methoxy group or the electron-withdrawing cyano group at ortho, meta, and para positions (entries 7−12, Table 3) afforded good yields of the corresponding alkynes. As reported in the literature,[17a] we also observed that a highly dipolar solvent accelerates the Stille reaction (Table 4, entries 1−3). This may explain the observation that, contrary to the formation of monobromides **2h**,**j**, dibromides **1e**,**g** give good yields of alkynes **4h**,**j**, as the solvent effect offsets the conjugative electron donation by the methoxy group to allow the reactions to proceed smoothly.

**D. Synthesis of Trisubstituted Alkenes.** Trisubstituted alkenes **3** and **5** could be synthesized from monobromides **2** by coupling of the remaining bromide (method A, Table 4), and the reactions are faster in DMF than in toluene with similar yields (entries 1, 2). Alternatively, the preparation of **5** could be accomplished by an one-pot process of sequential coupling of (*E*)- and (*Z*)-bromides in **1** with two different stannanes (method B, Table 4) in toluene.

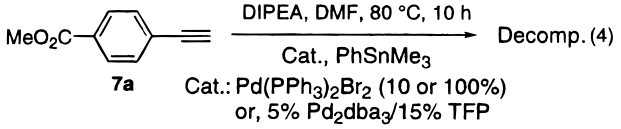
When monobromide **2a** was reacted with trimethyl(phenyl)tin in DMF, products resulting from both the methyl (**5a**) and phenyl transfer (**3a**) were obtained. However, product **3a** was obtained cleanly from the coupling of **2a** with trimethyl(phenyl)tin in toluene (entry 2) or with tributyl(phenyl)tin in DMF (entry 1).[17] Product **5a** was synthesized quantitatively by coupling **2a** with tetramethyltin in DMF (entry 4).

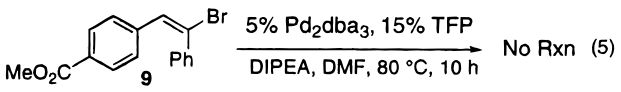
**E. Mechanistic Considerations.** In their coupling of $\beta,\beta$-dibromostyrene with 1-propenyltributyltin (eq 1), Zapta and co-workers reported that the two substrates reacted at room temperature to afford the corresponding enyne without a palladium catalyst or other additives.[12] However, dibromide **1a** did not react with trimethyl(phenyl)tin in DMF in the absence of palladium, even at elevated temperature for prolonged time (entry 15, Table 1). Furthermore, alkynes **4** are not derived from the monobromides **2**, as **2a** remained unchanged when heated with the catalyst (eq 3).




Other possible mechanisms for the formation of alkynes **4** involve the formation of terminal alkyne **7** through a carbenoid intermediate[1,18] (path A) or the formation of alkynyl bromide **8** (path B) from cis $\beta$-hydrogen elimination of intermediate **6** (Scheme 2).

However, these hypotheses are not consistent with the observation illustrated in eqs 4 and 5. The reaction of




alkyne **7a** and trimethyl(phenyl)tin did not yield **4a** even in the presence of one equivalent of bis(triphenylphosphine)palladium(II) dibromide (eq 4). No identifiable product was isolated from the reaction, though alkyne **7a** was totally consumed. On the other hand, when (*E*)-bromoalkene **9**[19] was subjected to the reaction conditions, dehydrobromination did not ocuur as path B suggested (eq 5).

A working hypothesis is proposed in Scheme 3. In a highly dipolar, coordinating solvent such as DMF, complex **6**, formed from initial oxidative insertion by Pd(0) into **1**, may undergo ligand/solvent exchange to form complex **10**.[17b] The Pd−C bond in **6,** and especially in **10**, is polarized by the solvent, which may lead to the formation of palladium carbenoid **11** (path C).[20,21] The highly dipolar solvent also stabilizes complex **11**, which favors its formation. Rearrangement of **11** results in the formation of complex **12**, which loses HBr to form alkynyl palladium species **13**. Alternatively, elimination of HBr from either complex **6** or **10** could also occur to give complex **13** (path D). Coupling of **13** with a stannane affords alkyne **4**.

The rate of transmetalation determines the formation of either monobromides **2** or internal alkynes **4**. When trimethyl(phenyl)tin, a slow transmetalating stannane is used in the Stille reaction in a highly dipolar solvent, alkynes **4** are the product regardless of which ligand is used. When fast transmetalating organostannanes, such as 2-(tributylstannyl)furan and tributyl(vinyl)tin, are used in the reaction, monobromides **2** are formed even in DMF with the TFP ligand (path E). On the other hand, a very electron rich ligand, tris(4-methoxyphenyl)phosphine, promotes much slower transmetalation than TFP and leads to the exclusive formation of alkynes **4** regardless of which stannane is used.

## Conclusions

We determined that the Stille coupling of 1,1-dibromo-

(17) Similar solvent and stannane effects were observed previously: (a) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478. (b) Farina, V.; Krishnan, B.; Marshall, D. R.; Roth, G. P. *J. Org. Chem.* **1993**, *58*, 5434.

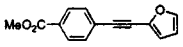
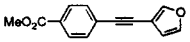
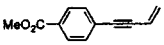
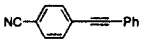
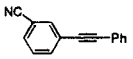
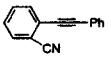
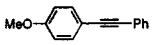
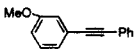
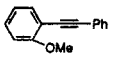
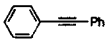
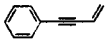
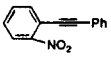
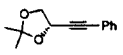
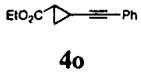
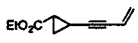
(18) Braun, M. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 430.

(19) (a) Kolodiazhnyi, O. I. *Tetrahedron* **1996**, *52*, 1855. (b) Speziale, A. J.; Ratts, K. W. *J. Org. Chem.* **1963**, *28*, 465.

(20) Palladium(II) carbenoid is well-known in palladium-catalyzed cyclopropanations: (a) Paulissen, R.; Hubert, A. J.; Teyssie, Ph. *Tetrahedron Lett.* **1972**, 1465. (b) Doyle, M. P.; Wang, L. C.; Loh, K.-L. *Tetrahedron Lett.* **1984**, *25*, 4087.

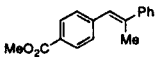
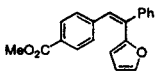
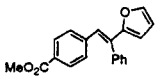
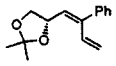
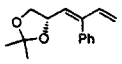
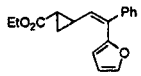
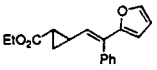
(21) Palladium(0) carbenoid is the intermediate in anomalous cine substitution in the Stille couplings: (a) Busacca, C. A.; Swestock, J.; Johnson, R. E.; Bailey, T. R.; Musza, L.; Rodger, C. A. *J. Org. Chem.* **1994**, *59*, 7553. (b) Farina, V.; Hossain, M. A. *Tetrahedron Lett.* **1996**, *37*, 6997.

**Table 3. Syntheses of Alkynes 4 from 1,1-Dibromoalkenes 1**

| Entry | Dibromide[a] | $R^1SnR^2_3$ | Ligand | Product, yield (%) | |
|---|---|---|---|---|---|
| 1 | **1a** | 2-FurSnBu$_3$ | TFP | **2b** | 75 |
| 2 | **1a** | 2-FurSnBu$_3$ | (4-MeOPh)$_3$P |  **4b** | 91 |
| 3 | **1a** | 3-FurSnBu$_3$ | TFP | **2c** (15); **4c** (58) | |
| 4 | **1a** | 3-FurSnBu$_3$ | (4-MeOPh)$_3$P |  **4c** | 94 |
| 5 | **1a** | VinylSnBu$_3$ | TFP | **2d** | 67 |
| 6 | **1a** | VinylSnBu$_3$ | (4-MeOPh)$_3$P |  **4d** | 92 |
| 7 | **1b** | PhSnMe$_3$ | TFP |  **4e** | 91 |
| 8 | **1c** | PhSnMe$_3$ | TFP |  **4f** | 71 |
| 9 | **1d** | PhSnMe$_3$ | TFP |  **4g** | 93 |
| 10 | **1e** | PhSnMe$_3$ | TFP |  **4h** | 69 |
| 11 | **1f** | PhSnMe$_3$ | TFP |  **4i** | 81 |
| 12 | **1g** | PhSnMe$_3$ | TFP |  **4j** | 70 |
| 13 | **1h** | PhSnMe$_3$ | TFP |  **4k** | 84 |
| 14 | **1h** | VinylSnBu$_3$ | (4-MeOPh)$_3$P |  **4l** | 89 |
| 15 | **1i** | PhSnMe$_3$ | TFP |  **4m** | 57 |
| 16 | **1i** | PhSnMe$_3$ | TFP |  **4n** | 94 |
| 17 | **1k** | PhSnMe$_3$ | TFP |  **4o** | 85 |
| 18 | **1k** | PhSnMe$_3$ | (4-MeOPh)$_3$P | **4o** | 91 |
| 19 | **1k** | VinylSnBu$_3$ | TFP | **2p** | 70 |
| 20 | **1k** | VinylSnBu$_3$ | (4-MeOPh)$_3$P |  **4p** | 77 |

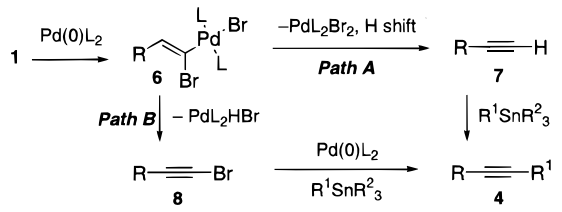
[a] Reaction was performed on a 1.0 mmol scale.

**Table 4. Syntheses of Trisubstituted Alkenes**

| Entry | Halide[a] | Stannane 1 | Stannane 2 | Solvent | Method[b] | $T$ (°C) | $t_1$ (h) | $t_2$ (h) | Product, Yield (%) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | **2a** | $PhSnBu_3$ | | DMF | A | 80 | 10 | | **3a** 95 |
| 2 | **2a** | $PhSnMe_3$ | | PhMe | A | 100 | 40 | | **3a** 100 |
| 3 | **2a** | $PhSnMe_3$ | | DMF | A | 80 | 10 | | **3a** and **5a** (7:3) 100 |
| 4 | **2a** | $Me_4Sn$ | | DMF | A | 80 | 10 | |  **5a** 99 |
| 5 | **2a** | 2-$FurSnBu_3$ | | DMF | A | 80 | 8 | |  **5b** 99 |
| 6 | **1a** | 2-$FurSnBu_3$ | $PhSnMe_3$ | PhMe | B | 100 | 8 | 36 |  **5c** 89 |
| 7 | **1j** | $PhSnMe_3$ | $VinSnBu_3$ | PhMe | B | 100 | 20 | 5 |  **5d** 62 |
| 8 | **1j** | $VinylSnBu_3$ | $PhSnMe_3$ | PhMe | B | 100 | 4 | 36 |  **5e** 51 |
| 9 | **1h** | $PhSnMe_3$ | 2-$FurSnBu_3$ | PhMe | B | 100 | 20 | 10 |  **5f** 61 |
| 10 | **1h** | 2-$FurSnBu_3$ | $PhSnMe_3$ | PhMe | B | 100 | 10 | 36 |  **5g** 70 |

[a] On 1.0 mmol scale. [b] Method A: monobromide **2a** (1.0 mmol) and a stannane (1.1 mmol) were stirred with $Pd_2dba_3$ (0.025 mmol) and TFP (0.15 mmol). Method B: dibromide **1** (1.0 mmol) and stannane 1 (1.05 mmol) were stirred with $Pd_2dba_3$ (0.025 mmol) and TFP (0.15 mmol) in toluene at 100 °C until TLC indicated the disappearance of **1** (reaction time $t_1$). Stannane **2** (1.1 mmol) was added, along with more catalyst (0.025 mmol of $Pd_2dba_3$, 0.15 mmol of TFP), and the reaction was continued at 100 °C (reaction time $t_2$).

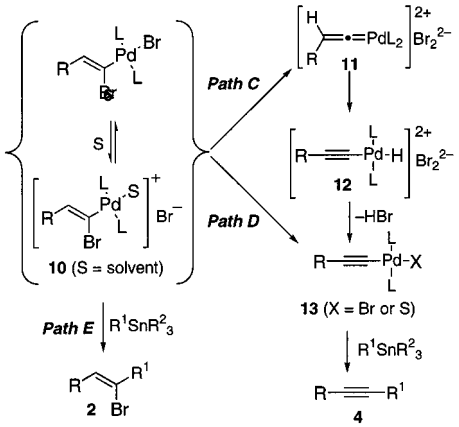
**Scheme 2**




1-alkenes **1** with organostannanes gave good to high yields of monobromides **2** when the reactions were run in low to nonpolar solvents with the TFP ligand. The reaction is less suitable for 2-aryl-1,1-dibromo-1-alkenes bearing strongly electron donating groups at ortho or para positions. This methodology can be applied to the stereospecifical syntheses of trisubstituted alkenes, including synthetically important 1,3-dienes (**2d**,**l**,**q**,**5d**,**e**).

We also developed an alternative method for the preparation of internal alkynes **4.** The formation of alkynes using the Stille reaction of 1,1-dibromo-1-alkenes in a highly dipolar solvent represents a new, general, mild, and high-yielding method to prepare this important class of compounds.

**Scheme 3**




## Experimental Section

**General Methods.** All reagents were commercially available and were used without further treatment. All solvents were commercial anhydrous solvents from Aldrich. $^1$H NMR spectra were recorded at 300 MHz (75 MHz for $^{13}$C) and 400 MHz (100 MHz for $^{13}$C). Elemental analyses were performed by Robertson Microlit Laboratories, Inc., of Madison, NJ. Column chromatography was performed on Merck silica gel 60. All reactions were performed under nitrogen atmosphere.

**General Procedures for the Preparation of Starting Dibromides 1**. To a 0 °C solution of an aldehyde (10.0 mmol) and carbon tetrabromide (10.5 mmol) in dichloromethane (30 mL) was added triphenylphosphine (21.0 mmol) in 4 portions at 3 min intervals. The reaction was then stirred for 1 h at 25 °C. Hexane was added to the reaction mixture with good stirring, and the resulting slurry was filtered through silica gel and rinsed twice with a mixed solvent of hexane and ether (1/1). The crude product after evaporation of the filtrate was then recrystallized from ethyl acetate/hexane (if solid) or purified with column chromatography by dichloromethane/hexane (if liquid). Yields are in the range of 85−100%.

**Methyl 4-(2,2-Dibromovinyl)benzoate (1a):** $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.04 (dt, $J$ = 1.9, 8.4 Hz, 2H), 7.61 (dt, $J$ = 1.8, 8.5 Hz, 2H), 7.52 (s, 1H), 3.91 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 165.9, 139.0, 135.5, 129.4, 129.1, 127.8, 91.4, 51.7. Anal. Calcd for $C_{10}H_8Br_2O_2$: C, 37.54; H, 2.52. Found: C, 37.74; H, 2.63.

**General Procedure for the Preparation of Monobromides 2.** A solution of a starting dibromide **1** (1.0 mmol), tris(dibenzylideneacetone)dipalladium(0) ($Pd_2dba_3$, 0.025 mmol), tris(2-furyl)phosphine (TFP, 0.15 mmol), and a stannane (1.05 mmol) in toluene (5 mL) was flushed with nitrogen twice and heated at 100 °C for 20 h. The reaction mixture was then filtered through silica gel and rinsed with 20% ether in hexane. The filtrate was concentrated and purified by column chromatography. The product could be further purified by recrystallization from ethanol to give analytically pure samples.

**Methyl (*Z*)-4-(2-Bromo-2-phenylvinyl)benzoate (2a):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.04 (td, $J$ = 1.7, 8.5 Hz, 2H), 7.74 (d, $J$ = 8.3 Hz, 2H), 7.62 (m, 2H), 7.35 (m, 3H), 7.20 (s, 1H), 3.89 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 166.6, 140.7, 140.5, 129.4, 129.3, 129.06, 129.03, 128.9, 128.3, 127.7, 126.2, 52.0. Anal. Calcd for $C_{16}H_{13}BrO_2$: C, 60.59; H, 4.13. Found: C, 60.69; H, 4.28.

**General Procedure for the Preparation of Alkynes 4.** A solution of a starting dibromide **1** (1.0 mmol), a stannane (1.05 mmol), *N*,*N*-diisopropylethylamine (DIPEA, 1.50 mmol), $Pd_2dba_3$ (0.025 mmol), and TFP or tris(4-methoxyphenyl)-phosphine (0.15 mmol) in DMF (5 mL) was flushed with nitrogen and heated at 80 °C for 10 h. The reaction mixture was diluted with ether, washed with water, dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography. If necessary, the products were further purified by recrystallization from ethanol to give analytically pure samples.

**Methyl 4-(2-Phenylethynyl)benzoate (4a):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.98 (td, $J$ = 1.7, 8.5 Hz, 2H), 7.55 (td, $J$ = 1.7, 8.5 Hz, 2H), 7.52 (m, 2H), 7.32 (m, 3H), 3.87 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 166.3, 131.6, 131.3, 129.35, 129.33, 128.6, 128.3, 127.9, 122.6, 92.3, 88.5, 52.0. Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found: C, 81.06; H, 5.24.

**General Procedure A for the Preparation of Trisubstituted Alkenes 5 from Monobromide 2a.** A solution of **2a** (1.0 mmol), a stannane (1.1 mmol), $Pd_2dba_3$ (0.025 mmol), and TFP (0.15 mmol) in DMF (5 mL) was flushed with nitrogen and heated at 80 °C for 10 h. The reaction mixture was then diluted with ether, washed with water 3 times, dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography. If necessary, the products were further purified by recrystallization from ethanol to give analytically pure samples.

**Methyl 4-[(*E*)-2-Methyl-2-phenylvinyl]benzoate (5a):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.02 (td, $J$ = 1.7, 8.5 Hz, 2H), 7.49 (m, 2H), 7.39 (d, $J$ = 8.2 Hz, 2H), 7.35 (m, 2H), 7.28 (m, 1H), 6.81 (s, 1H), 3.88 (s, 3H), 2.26 (d, $J$ = 1.2 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.8, 143.4, 142.9, 139.5, 129.4, 128.9, 128.3, 127.9, 127.5, 126.7, 125.9, 51.9, 17.6. Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.81; H, 6.44.

**General Procedure B for the Preparation of Trisubstituted Alkenes 5 from Dibromides 1.** A solution of a starting dibromide **1** (1.0 mmol), the first stannane (1.05 mmol), $Pd_2dba_3$ (0.025 mmol), and TFP (0.15 mmol) in toluene (5 mL) was flushed with nitrogen twice and heated at 100 °C until the starting dibromide was completely consumed. Then, the second stannane (1.1 mmol) was added to the reaction mixture, along with more $Pd_2dba_3$ (0.025 mmol) and TFP (0.15 mmol). The reaction was further heated at 100 °C until the intermediate monobromide was consumed. The reaction mixture was filtered through silica gel and rinsed with 20% ether in hexane. The filtrate was concentrated and purified by column chromatography. If necessary and feasible, the products were further purified by recrystallization from ethanol to give analytically pure samples.

**(4*S*)-2,2-Dimethyl-4-[(*E*)-2-phenyl-1,3-butadienyl]-1,3-dioxolane (5d):** $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.35−7.24 (m, 5H), 6.85 (ddd, $J$ = 0.8, 11.0, 17.4 Hz, 1H), 5.55 (d, $J$ = 8.5 Hz, 1H), 5.36 (td, $J$ = 1.8, 11.0 Hz, 1H), 5.10 (m, 2H), 4.17 (dd, $J$ = 6.4, 8.1 Hz, 1H), 3.63 (t, $J$ = 7.8 Hz, 1H), 1.41 (s, 3H), 1.40 (s, 3H); $^{13}$C NMR (100 MHz, $CD_3OD$) $\delta$ 143.7, 140.0, 132.5, 127.9, 127.7, 127.1, 119.2, 109.0, 73.7, 72.3, 69.1, 25.6, 24.7. Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88; Found: C, 78.25; H, 7.98.

**Acknowledgment.** We thank Mr. Rodger Henry for determining crystal structures of **2a** and **5b**. The authors are grateful to Dr. Kenneth Barr for discussions and suggestions.

**Supporting Information Available:** Elemental analyses and $^1$H NMR and $^{13}$C NMR spectral data for all the new compounds (**1c**,**i**,**k**, **2b**−**j**,**l**−**p**, **3a**, **4b**−**d**,**n**−**p**, **5b**,**c**,**e**−**g**), information about the known compounds (**1b**,**d**−**h**,**j**, **2k**, **3k**, **4a**,**e**−**m**), and X-ray structural data for **2a** and **5b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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