Copper(II) Mediated Homo-Coupling of 1,2-difluorovinylstannanes

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Abstract. The reaction of substituted 1,2-difluorovinylstannanes with anhydrous $Cu(OAc)_2$ in dimethylformamide, under an oxygen atmosphere, at room temperature stereospecifically gives the corresponding symmetrical 1,3-dienes in good to excellent yields. Moisture drastically reduces the yield of homo-coupled product and produces significant amounts of RCF=CFH. The Cu(II) promoted homo-coupling of the fluorinated vinylstannanes is superior to the Cu(I)Cl mediated homo-coupling of the corresponding hydrocarbon vinylstannanes. When 1,2-difluorovinylstannanes are treated with Cu(I)Cl, the reaction is sluggish and significant amounts of RCF=CFH are formed.

INTRODUCTION

The regio- and stereospecific formation of carbon–carbon bonds continues to be an important goal in synthetic organic chemistry. This goal, combined with the incorporation of fluorine at strategic positions in a molecule due to its unique properties, represents a challenge to synthetic chemists. To accomplish this goal, the Pd(0)/CuI co-catalyzed intermolecular cross-coupling of 1,2-difluorovinylstannanes with aryl iodides or fluorinated (and non-fluorinated) vinyl halides[1] has provided a valuable method for the stereospecific preparation of fluorinated acyclic conjugated diene systems.

Though this methodology is quite useful, researchers continue to modify and develop new chemistry for carbon–carbon bond forming reactions. Recent reports have attempted to accomplish similar coupling chemistry without palladium catalysis via the use of stoichiometric amounts of Cu(I) salts to mediate cross-couplings[2] of vinylstannanes with aryl, vinyl, and allyl halides. Falk et al.[3] showed this method to be useful in cross-coupling of α-heteroatom substituted *alkyl*-tributylstannanes with organic halides. Additionally, efficient intramolecular[5] and homo[4]-coupling of a variety of vinylstannanes by employment of stoichiometric amounts of Cu(I)Cl, was demonstrated by Piers et al.[4]

The Cu(II) promoted homo-coupling of fluorinated vinylstannanes is superior to the Cu(I)Cl mediated homo-coupling of the corresponding hydrocarbon vinylstannanes. To our knowledge, there are no examples yet of Cu(II) mediated cross-couplings of vinylstannanes with organic halides. Reports by Kyler,[5] Guibe,[6] Crisp,[7] and Quayle,[8] and their coworkers, have shown that $Cu(NO_3)_2{\cdot}3H_2O$ works very well for self-coupling of a variety of functionalized vinylstannanes. Even $CuCl_2$, a well known halogenating agent, has been utilized for this purpose,[9] including an interesting electro-oxidation method described by Itoh et al.[10] Herein, we describe the anhydrous $Cu(OAc)_2$ mediated stereospecific homo-coupling of 1,2-difluorovinylstannanes, including the scope and limitations of our work, as well as some mechanistic implications and future work.

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EXPERIMENTAL

General

All boiling points are uncorrected. ^{19}F NMR (282.41 HMz), ^{1}H NMR (300.17 MHz), ^{13}C (75.49 MHz) spectra were recorded on a Bruker AC 300-MHz multinuclear spectrometer. All samples were taken in $CDCl_3$ solvent and all chemical shifts are recorded in parts per million downfield (positive) of the standards. ^{19}F NMR spectra are referenced against internal $CFCl_3$, ^{1}H NMR and ^{13}C NMR spectra, against internal tetramethylsilane (TMS). FT-IR spectra were recorded as neat samples on a Nicolet Impact 410 FT-IR, and absorbance frequencies reported in cm^{-1}. GC-MS spectra were obtained at 70 eV, in the electron-impact mode. High resolution mass spectral determinations were made at the University of Iowa High Resolution Mass Spectrometry Facility. GLPC analyses were performed on a 10% OV-101 column with a thermal conductivity detector.

Materials

Anhydrous $Cu(OAc)_2$ was purchased from Acros Chemical and Aldrich Chemical and subsequently stored under nitrogen in a desiccator. DMF was dried over 4Å molecular sieves and consecutively cannulated again over 4Å molecular sieves and stored under nitrogen.

Preparation of (E,E)-5,6,7,8-tetrafluoro-5,7-dodecadiene (trans,trans-n-BuCF=CF–CF=CFBu-n, (1)): A 100 mL round-bottom flask equipped with a septum port and stir bar was charged with 2.72 g (15.0 mmol) of Acros $Cu(OAc)_2$ and 50 mL of benzene. Then the flask was equipped with a Dean–Stark trap, reflux condenser, and N_2 tee. The heterogeneous $Cu(OAc)_2$/benzene mixture was refluxed under a nitrogen atmosphere for 8 h. Afterwards, the water/benzene in the side arm of the Dean–Stark trap was removed; the remaining benzene was distilled off, and the resultant dry $Cu(OAc)_2$ was cooled to room temperature. Then, 45 mL of dry DMF was injected via syringe into the flask containing the $Cu(OAc)_2$ and the mixture stirred until the aqua-blue solution was homogeneous. Then, the DMF solution was purged with oxygen for 10 min to flush the system and 5.73 g (14.0 mmol) of *trans-n*-BuCF=CFSnBu$_3$-*n*[17] was injected via syringe into the flask all at once and the resultant solution was allowed to stir at room temperature for 8 h. Then, the dark green liquid reaction mixture was poured directly onto a silica gel/hexanes packed column (18 inches in length, 1.75 inch diameter) and eluted with hexanes. The product was detected on TLC plates using UV light (254 nm). The resultant fractions were concentrated via rotoevaporation and then were subjected to a partial vacuum to remove hexanes to afford the clear liquid (*E*,*E*)-5,6,7,8-tetrafluoro-5,7-dodecadiene (1.31g, 96% GLPC pure), 79% yield. R_f = 0.75 (hexanes) ^{1}H NMR ($CDCl_3$): δ 0.94 (t, J = 7.3 Hz, 3H), 1.40 (m, 2H), 1.58 (m, 2H), 2.46 (m, 2H)ppm. ^{19}F NMR ($CDCl_3$): δ –137.3 (dm, $^{3}J_{FF}$ = 122.1 Hz, 2F), –164.8 (dm, $^{3}J_{FF}$ = 122.0 Hz, 2F) ppm. ^{13}C NMR ($CDCl_3$): δ 13.69 (s), 26.6 (m), 27.61 (t, $^{3}J_{CF}$ = 2.4 Hz), 138.2 (dm, $^{1}J_{CF}$ = 244.1 Hz), 155.2 (dm, $^{1}J_{CF}$ = 261.5 Hz) ppm. GC-MS: 238 (M$^+$, 30.46), 182 (M$^+$ - *n*-Bu, 13.36), 43 ($CH_3CH_2CH_2^+$, 100). FTIR (neat): 2967.83 (s), (C–H), 1702.80 (m), (C=C), 1224.48 (s), (C-F) cm^{-1}. HRMS: Calcd for $C_{12}H_{18}F_4$: 238.1345; Found: 238.1368.

Preparation of (E,E)-4,5,6,7-tetrafluoro-3,8-dimethyl-4,6-decadiene (trans,trans-sec-BuCF=CF–CF=CFBu-sec, (2)): Similarly, 2.72 g (15.0 mmol) of Acros $Cu(OAc)_2$ was reacted with 5.69 g (13.9 mmol) of *trans-sec*-BuCF=CFSnBu$_3$- *n*[17] in 45 mL of dry DMF to afford 1.15 g (98% GLPC pure) of the clear liquid (*E*,*E*)-4,5,6,7-tetrafluoro-3,8-dimethyl-4,6-decadiene, 69.5% yield, bp 96-98°C/20 mm Hg (lit.[18] bp 77 °C/11 mm Hg). R_f = 0.78 (hexanes) ^{1}H NMR ($CDCl_3$): δ 0.95 (t, J = 7.5 Hz, 3H), 1.16 (d, J = 7.1 Hz, 3H), 1.54 (m, 2H), 2.8 (m, 1H) ppm. ^{19}F NMR ($CDCl_3$): δ –149.7 (dm, $^{3}J_{FF}$ = 121.6 Hz, 2F), –165.4 (dm, $^{3}J_{FF}$= 122.1 Hz, 2F) ppm. ^{13}C NMR ($CDCl_3$): δ 11.78 (d, J = 2.2 Hz), 16.7 (s), 26.22 (dd, J = 3.6 Hz, J = 2.2 Hz), 33.6 (m), 138.4 (dddd, $^{1}J_{CF}$ = 215.8 Hz, $^{2}J_{CF}$ = 61.3 Hz, $^{3}J_{CF}$ = 29.9 Hz, $^{4}J_{CF}$ = 13.8 Hz) ppm. GC-MS: 238 (M$^+$, 37.23), 209 (M$^+$, C_2H_5, 14.10), 153 (100). FTIR (neat): 2961.54 (s), (C–H), 1696.50 (m), (C=C), 1224.48 (s), (C–F) cm^{-1}. HRMS: Calcd for $C_{12}H_{18}F_4$: 238.1345; Found: 238.1344.

Preparation of (E,E)-3,4,5,6-tetrafluoro-2,2,7,7-tetramethyl-3,5-octadiene (trans,trans-^{t}*BuCF=CF–CF=CF*^{t}*Bu, (3))*: Similarly, 2.48 g (13.7 mmol) of Acros $Cu(OAc)_2$ was reacted with 5.32 g (13.0 mmol) *trans*-^{t}BuCF=CFSnBu$_3$-*n*[17] in 39 mL of dry DMF to afford 3.84 g (97% GLPC pure) of white solid (*E*,*E*)-3,4,5,6-tetrafluoro-2,2,7,7-tetramethyl-3,5-octadiene, 59% yield, mp 31–32 °C. R_f = 0.77 (hexanes). ^{1}H NMR ($CDCl_3$): δ 1.26 (s) ppm. ^{19}F NMR ($CDCl_3$): δ –139.5 (dm, $^{3}J_{FF}$ = 125.7 Hz, 2F), –161.4 (dm, $^{3}J_{FF}$ = 124.7 Hz, 2F) ppm. ^{13}C NMR ($CDCl_3$): δ 27.24 (m), 35.22 (m), 138.4 (dm, $^{1}J_{CF}$ = 250.3 Hz), 159.0 (dm, $^{1}J_{CF}$ = 260.2 Hz) ppm. GC-MS: 238 (M$^+$, 7.28), 65 (20.59), 61 (100), 57 (47.65). HRMS: Calcd for $C_{12}H_{18}F_4$: 238.1345; Found: 238.1346.

Preparation of (E,E)-1,2,3,4-tetrafluoro-1,4-bis(triethylsilyl)-1,3-butadiene (trans,trans-Et$_3$*SiCF=CF–CF=CFSiEt*$_3$*, (4))*: Similarly, 1.81 g (10.0 mmol) of Acros $Cu(OAc)_2$ was reacted with 4.37 g (9.36 mmol) *trans*-Et$_3$SiCF=CFSnBu$_3$-*n*[17] in 30 mL of dry DMF to afford 0.87 g (96% GLPC pure) of the light yellow liquid (*E*,*E*)-1,2,3,4-tetrafluoro-1,4-triethylsilyl-1,3-butadiene, 53% yield. R_f = 0.69 (hexanes). ^{1}H NMR ($CDCl_3$): δ 0.78 (q, J = 8.0 Hz, 2H), 1.02 (t, J = 8.1 Hz, 3H) ppm. ^{19}F NMR ($CDCl_3$): δ –152.0 (dm, $^{3}J_{FF}$ = 122.4 Hz, 2F), –159.6 (dm, $^{3}J_{FF}$ = 121.8 Hz, 2F) ppm. ^{13}C NMR ($CDCl_3$): δ 2.44 (s), 7.09 (s), 151.5 (dm, $^{1}J_{CF}$ = 232.4 Hz), 160.5 (dm, $^{1}J_{CF}$ = 284.1 Hz) ppm. FTIR (neat): 2960.46 (s), (C–H), 1623.90 (w), (C=C), 1132.29 (s), (C–F), 1291.04 (m), (Si-CH_2) cm^{-1}. GC-MS: 115 (Et_3Si^+, 4.19), 105 (26.34), 77 (100). HRMS: Calcd for $C_{16}H_{30}F_4Si_2$: 354.1822; Found: 354.1827.

Preparation of (E,E)-1,2,3,4-tetrafluoro-1,4-diphenyl-1,3-butadiene (trans,trans-PhCF=CF–CF=CFPh, (5)): Similarly, 2.72 g (15.0 mmol) of Acros $Cu(OAc)_2$ was reacted with 6.07 g (14.2 mmol) *trans*-PhCF=CFSnBu$_3$-*n*[17] in 45 mL of dry DMF to afford 1.57 g of white solid (*E*,*E*)-1,2,3,4-tetrafluoro-1,4-diphenyl-1,3-butadiene, 80% yield, mp 55–56 °C (lit.[9] mp 57–58 °C), R_f = 0.63 (hexanes). ^{1}H NMR ($CDCl_3$): δ 7.46 (m, 3H), 7.78 (m, 2H) ppm. ^{19}F NMR ($CDCl_3$): δ –142.5 (dm, $^{3}J_{FF}$ = 117.6 Hz, 2F), –159.5 (dm, $^{3}J_{FF}$ = 117.2 Hz, 2F) ppm.

Table 1. Cu(II) salts and solvents used to self-couple 1 and ratios of the products[a]

entry	Cu(II) salt	solvent	diene	reduced olefin	starting material
1	$Cu(NO_3)_2{\cdot}3H_2O$	THF (undried)	0.74	1	–
2	$Cu(NO_3)_2{\cdot}3H_2O$	DMF (dry)	2.5	1	–
3	$Cu(OAc)_2{\cdot}H_2O$	THF (undried)	trace	1	2.25
4	$Cu(OAc)_2{\cdot}H_2O$	DMF (dry)	3	1	–
5	$Cu(OAc)_2$, 98%[b]	DMF (dry)	4.53	1	–
6	$Cu(OAc)_2$, 98%	DMF-d_7 (dry)	5.40	1	–[c]
7	$CuSO_4{\cdot}5H_2O$	DMF (dry)	0.18	1	0.11
8	$CuSO_4$ (anhyd.)	DMF (dry)	–	–	1[d]
9	$CuBr_2$	DMF (dry)	1.29	–	–[e]
10	$CuCl_2$	DMF (dry)	3.80	1	–[f]
11	CuF_2 (anhyd.)	DMF (dry)	–	–	1[g]
12	$Cu(acac)_2$	DMF (dry)	–	–	1[h]
13	$Cu(OOCH)_2{\cdot}4H_2O$	DMF (dry)	1.53	1	–

[a]All reaction times were approximately 1 h; [b]Purchased from Aldrich Chemical Co.; [c]No n-BuCF=CFD was detected; [d]Insoluble in DMF; [e]A significant amount of vinyl bromide was also formed; [f]A significant amount of vinyl chloride was also formed; [g]CuF_2 is not soluble in DMF at room temperature, but did homo-couple vinylstannane at 85 °C after several days' reaction time; [h]Partially soluble in DMF.

^{13}C NMR ($CDCl_3$): δ 126.3 (m), 128.6 (s), 130.2 (s), 139.5 (dm, $^1J_{CF}$ = 238.9 Hz), 150 (dm, $^1J_{CF}$ = 242.6 Hz) ppm. GC-MS: 280 (M^+ + 2, 1.75), 279 (M^+ + 1, 16.97), 278 (M^+, 100), 200 (M^+ –Ph, 68.33). HRMS: Calcd for $C_{16}H_{10}F_4$: 278.0719; Found: 278.0716.

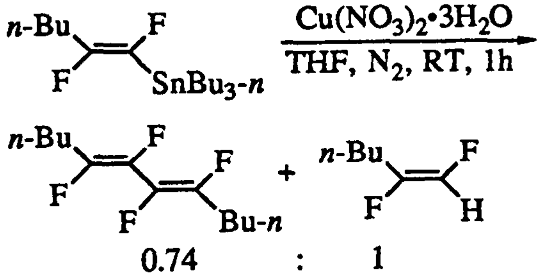
Preparation of (Z,Z)-3,4,5,6-tetrafluoro-2,2-7,7-tetramethyl-3,5-octadiene (cis,cis-^{t}BuCF=CF–CF=CF^{t}Bu, (6)): Similarly, 2.90 g (16.0 mmol) of Acros $Cu(OAc)_2$ was reacted with 6.14 g (15.0 mmol) *cis*-^{t}BuCF=CFSnBu$_3$-*n*[16] in 45 mL of dry DMF to afford 1.10 g of white solid (Z,Z)-3,4,5,6-tetrafluoro-2,2,7,7-tetramethyl-3,5-octadiene, 62% yield, mp 43.5–45 °C. ^1H NMR ($CDCl_3$): δ 1.20 (s) ppm. ^{19}F NMR ($CDCl_3$): δ –122.24 (d, $^3J_{FF}$ = 6.8 Hz, 2F), –125.20 (d, $^3J_{FF}$ = 7.2 Hz, 2F) ppm. ^{13}C NMR ($CDCl_3$): δ 27.08 (s), 34.15 (d, $^2J_{CF}$ = 21.5 Hz) 135.5 (dm, $^1J_{CF}$ = 212.3 Hz), 159.5 (dm, $^1J_{CF}$ = 261.7 Hz) ppm. GC-MS: 239 (M^+ + 1, 5.32), 238 (M^+, 38.89), 182 (M^+ – ^{t}Bu, 15.12), 43 (100). HRMS: Calcd for $C_{12}H_{18}F_4$: 238.1345; Found: 238.1355.

RESULTS

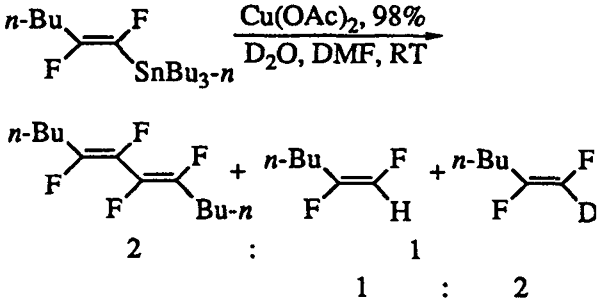
Our initial attempt at the homo-coupling of *trans-n*-BuCF-CFSnBu$_3$-*n* was carried out with Quayle's conditions; namely, 1 mmol of vinylstannane in THF (20 mL) and 1 mmol of $Cu(NO_3)_2{\cdot}3H_2O$ under N_2.[8] In Quayle's report, the dryness of THF was not mentioned; we used THF without prior drying. After 1 h reaction time, we observed (via ^{19}F NMR) the complete consumption of vinylstannane and formation of diene and *trans-n*-BuCF=CFH (reduced olefin) in a 0.74:1 ratio (Scheme 1). A variety of Cu(II) salts in various solvents were studied via this model reaction to ascertain the best conditions to maximize the diene product and minimize the reduced olefin product. From the results summarized in Table 1, some important observations can be ascertained.

Contrary to what Quayle and coworkers[8] reported, the best combination for our substrate was dry DMF and Aldrich $Cu(OAc)_2$, 98%.[11] A typical procedure included the following steps: a 50 mL round-bottom flask with a side arm was equipped with a magnetic stir bar, and the side arm fitted with a septum. The flask was charged with one mmol of a Cu(II) salt, fitted with a nitrogen tee, and placed under a N_2 atmosphere. Then, 15 mL of dry DMF was syringed into the flask and the slurry stirred. When the solution became homogeneous, 1 mmol of vinylstannane was syringed into the reaction mixture and the reaction mixture stirred at room temperature for 1 h.

When the results of homo-coupling employing $Cu(OAc)_2{\cdot}H_2O$ vs. $Cu(OAc)_2$, 98%, are compared, the monohydrated species gave considerably more reduced product. Presumably, the reduced olefin formation is due to the presence of water in the Cu(II) salt. To test this assumption, a simple experiment was conducted:



Scheme 1



Scheme 2

the $Cu(OAc)_2$, 98%/DMF solution was charged with excess D_2O and then vinylstannane was syringed into the reaction mixture. After approximately 20 min, all starting material had been consumed and a 2:1 ratio of homo-coupled to reduced olefin, respectively, was detected via ^{19}F NMR. The ratio of *trans*-*n*-BuCF=CFD/*trans*-*n*-BuCF=CFH was 2:1 (Scheme 2). We independently synthesized *trans*-*n*-BuCF=CFD[21] and spiked the NMR sample with the deuterated olefin. The deuterated olefin product signals overlapped perfectly. The small amount of *trans*-*n*-BuCF=CFH that was initially detected is likely due to H_2O in the commercial $Cu(OAc)_2$, 98%. Note also, in Table 1, entry #6, that when DMF-d_7 was employed as the solvent, no *trans*-*n*-BuCF=CFD was detected in the ^{19}F NMR spectrum of the reaction mixture. Therefore, the proton source is either water or acetic acid, but not DMF. In contrast, the addition of water in Piers' hydrocarbon vinylstannane reaction mixtures does not have a detrimental effect on the oxidative coupling, and the conversion to 1,3-dienes is very high.[4c]

Since water is detrimental to our copper(II) mediated homo-coupling, several methods were evaluated to suppress reduced olefin formation. We initially added various drying agents to the initial $Cu(OAc)_2$, 98%/DMF solution prior to the addition of vinylstannane. Molecular sieves, dicyclohexylcarbodiimide (DCC), and magnesium sulfate were all tried as desiccants under various conditions, but no diminution in reduced olefin formation was evident via ^{19}F NMR analysis after addition of the vinylstannane.

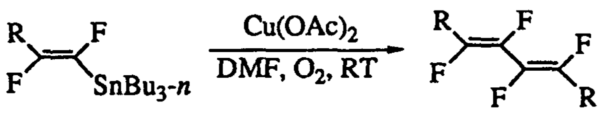
Next, we attempted to dry the $Cu(OAc)_2$ by removing the water via the H_2O/benzene azeotrope. In our initial attempt, we charged Aldrich $Cu(OAc)_2$, 98%/ DMF, and benzene into the reaction flask equipped with a Dean–Stark trap, and the mixture refluxed overnight. Then, the benzene was distilled off and the DMF/$Cu(OAc)_2$ solution cooled to room temperature. *trans*-$Et_3SiCF=CFSnBu_3$-*n* was injected and the reaction mixture stirred at room temperature for 3 h. ^{19}F NMR analysis revealed a 1.87:1 ratio of diene to reduced olefin.

When this experiment was repeated, DMF was excluded from the H_2O/benzene azeotrope. After refluxing overnight, the benzene was distilled off, leaving behind dry Aldrich $Cu(OAc)_2$. The dry $Cu(OAc)_2$ was cooled to room temperature, dry DMF injected, and the slurry stirred until the reaction mixture was homogeneous. Then, *trans*-$Et_3SiCF=CFSnBu_3$-*n* was injected. After 40 min, ^{19}F NMR analysis of the reaction mixture showed complete consumption of starting material and a ratio of 6.11:1 diene to reduced olefin. When we repeated this experiment using Acros anhydrous $Cu(OAc)_2$, the ratio improved to 9:1. On the basis of these results, we utilized the Acros material for scale-up reactions.

Typically, when these self-coupling reactions were completed, the reaction mixture contained a brown precipitate, presumably Cu°, that had been formed from copper(II) acetate reduction. To suppress reduced olefin formation, a non-stoichiometric amount of Acros $Cu(OAc)_2$ (not dried via benzene azeotrope) was employed under an oxygen atmosphere to minimize water contamination of the $Cu(OAc)_2$, and to oxidize any reduced copper formed in the reaction. When 10 mole % of Acros $Cu(OAc)_2$ was used to homo-couple *trans*-*n*-$BuCF=CFSnBu_3$-*n* under O_2, the starting material was never completely consumed. When 30 mole % of Acros $Cu(OAc)_2$ was used to homo-couple *trans*-$Et_3SiCF=CFSnBu_3$-*n*, all the vinylstannane was consumed and the self-coupled:reduced olefin ratio increased to 11:1. Although the non-stoichiometric amounts of Acros $Cu(OAc)_2$ under O_2 worked well at decreasing the amount of reduced olefin, reaction times were significantly longer, especially when the reaction size was increased.

In summary, we found that the best conditions for fastest reaction times and suppression of reduced olefin formation were as follows: dry a stoichiometric amount of Acros anhydrous $Cu(OAc)_2$ via the H_2O/benzene azeotrope method (under N_2). After all of the benzene is removed by distillation, cool the dry $Cu(OAc)_2$ to room temperature, inject dry DMF, purge the system with oxygen, and finally, inject the vinylstannane into the oxygen-saturated reaction mixture.

Although we had found successful conditions for this reaction (Scheme 3), isolation of the homo-coupled product after a standard workup[22] and column chromatography gave diminished yields. When the reaction



Scheme 3

Table 2. Yield of homo-coupled product vs. isolation procdure

compd. #	substrate	yield[a,b]	yield[a,c]
1	*trans*-*n*-BuCF=CFSnBu$_3$-*n*	46%	79%
2	*trans*-*sec*-BuCF=CFSnBu$_3$-*n*	41%	70%
3	*trans*-*tert*-BuCF=CFSnBu$_3$-*n*	37%	59%
4	*trans*-Et$_3$SiCF=CFSnBu$_3$-*n*	–	53%
5	*trans*-PhCF=CFSnBu$_3$-*n*	–	80%
6	*cis*-*tert*-BuCF=CFSnBu$_3$-*n*	–	62%

[a]isolated yields; [b]standard workup via extraction; [c]via direct column elution.

mixture (which is now homogeneous due to the oxygen atmosphere) was poured directly onto a silica gel/hexanes packed column and eluted, isolated yields improved dramatically. Table 2 illustrates this trend.

An interesting side note is that the *trans,trans*-dienes were UV active and easily visualized on TLC plates, whereas the *cis,cis*-diene that we prepared was not UV active. It appears that there are severe steric interactions between the *tert*-butyl groups of the *cis,cis*-diene forcing the π orbitals out of conjugation.

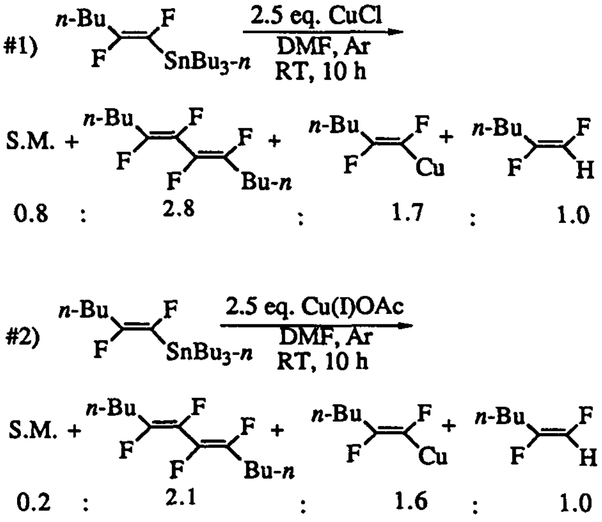
DISCUSSION

Farina, Liebeskind, and coworkers[12] first reported the nature of the "copper effect" in Stille-type palladium/CuI co-catalyzed cross-couplings. They proposed that organo-stannanes undergo a transmetalation with CuI to produce an organocopper reagent and *n*-Bu$_3$SnI, the latter being detected by ^{119}Sn NMR. It has also been suggested that this reaction is reversible.[2b,4b] Piers et al.[4b,c] also confirmed the formation of Cu° after oxidative coupling.

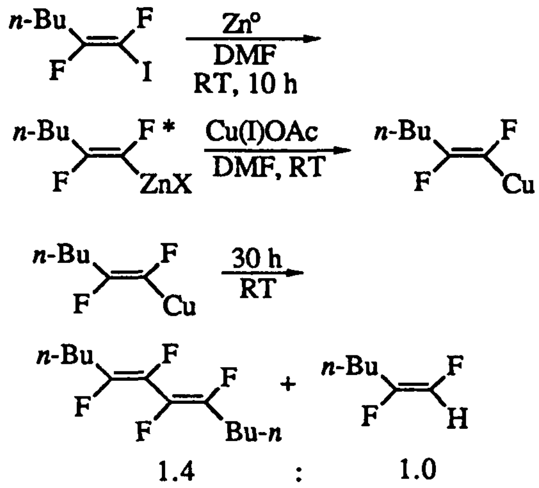
We attempted to duplicate Piers' CuCl-mediated homo-coupling method by employing 2.5 equiv of CuCl in dry DMF under an argon atmosphere to homo-couple *trans*-*n*-BuCF=CFSnBu$_3$-*n*. After 10 h reaction time (Scheme 4, #1), ^{19}F NMR analysis of the reaction mixture showed a significant amount of unreacted vinylstannane and two signals assigned to the vinyl-copper(I) intermediate.[13a] We repeated this experiment using 2.5 equiv of cuprous acetate (Scheme 4, #2). ^{19}F NMR analysis of the reaction mixture also showed significant amounts of the vinylcopper(I) intermediate, unreacted vinylstannane, and an unknown side product. While Piers' report of excess Cu(I)-mediated homo-coupling of hydrocarbon vinylstannanes is quite successful, this method is inferior for the homo-coupling of fluorinated vinylstannanes due to incomplete reaction, even after long reaction times.

Preparation of the vinylcopper(I) intermediate was achieved via the exchange reaction between Cu(I)OAc and a pre-generated vinylzinc reagent (Scheme 5). The ^{19}F NMR chemical shifts of the assigned vinylcopper(I) reagent formed from the vinylzinc reagent corresponded exactly to the chemical shifts observed from the ^{19}F NMR spectrum of the reactions described in Scheme 4. As illustrated in Scheme 5, the vinylcopper(I) reagent prepared via exchange with Cu(I)OAc is not indefinitely stable; it is consumed after 30 h and forms the homo-coupled product (preferentially) and reduced olefin.

We propose that the mechanism of the homo-coupling reaction changes when oxygen is available to oxidize the copper intermediate. For example, when *trans*-*n*-BuCF=CFSnBu$_3$-*n* is homo-coupled with previously dried Cu(OAc)$_2$ (carried out under N$_2$) and the reaction

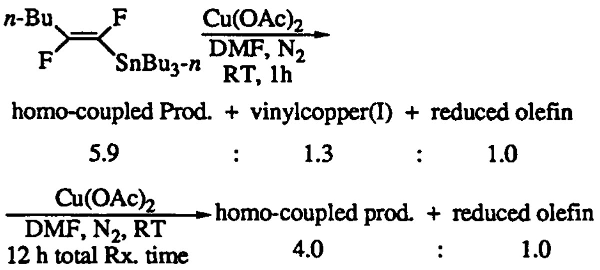


Scheme 4



*75% zinc reagent, 25% reduced olefin

Scheme 5

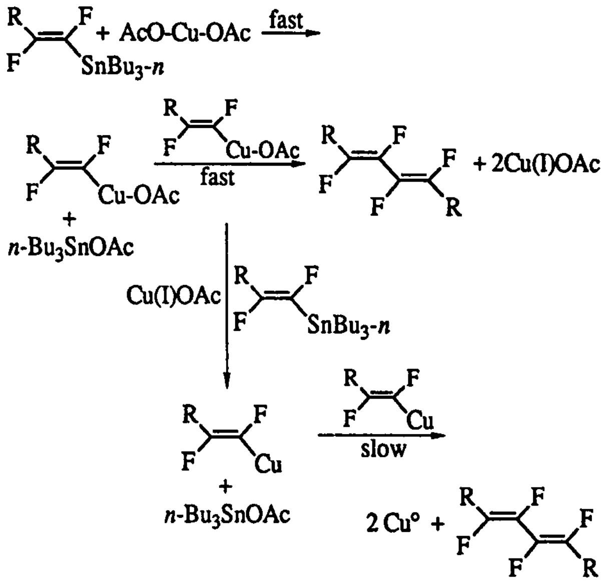


Scheme 6

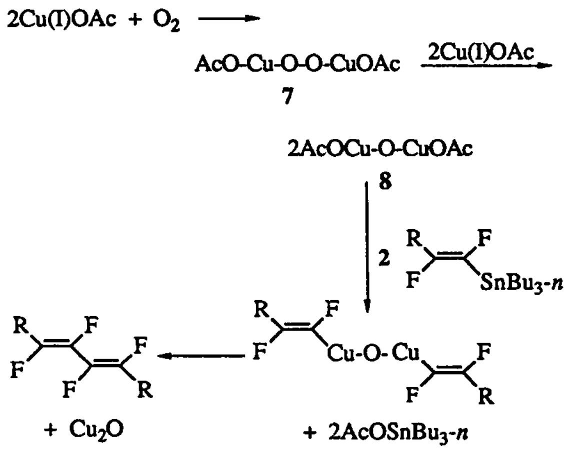
mixture analyzed by ^{19}F NMR after 1 h reaction time, all of the vinylstannane was consumed and only vinylcopper(I) reagent, homo-coupled diene, and reduced olefin were present (Scheme 6). The vinyl-copper(I) intermediate observed in the ^{19}F NMR spectrum exhibits the same ^{19}F NMR chemical shifts as the vinylcopper(I) species outlined in Schemes 4 and 5. As Scheme 6 illustrates, we once again observed the familiar slow competition reaction of vinylcopper(I) reagent to produce homo-coupled product and reduced olefin. It appears that once a significant amount of $Cu(OAc)_2$ has been reduced to Cu(I)OAc, the Cu(I)OAc begins to compete with $Cu(OAc)_2$ for reaction of vinylstannane. It is reaction of the vinylcopper(I) species generated in situ that must be the rate-limiting step in the homo-coupling reaction. ^{119}Sn{^{1}H} NMR studies[20] show n-Bu_3SnOAc (broad singlet, 0.0 ppm) as the only tin-containing side product in the reaction mixture after complete consumption of the vinylstannane. The presence of n-Bu_3SnOAc was confirmed when the NMR sample was spiked with an authentic sample of n-Bu_3SnOAc. We propose that the Cu(II) mediated homo-coupling, carried out under nitrogen, initially proceeds through a vinylcopper(II) intermediate, followed by reductive coupling to produce homo-coupled product and two moles of Cu(I)OAc. The Cu(I)OAc generated in situ can further react with vinylstannane to produce a vinylcopper(I) intermediate that produces homo-coupled diene, reduced olefin, and, presumably, Cu° (Scheme 7).

When an O_2 atmosphere is employed for the homo-coupling reaction, we propose that any Cu(I)OAc formed in solution is reoxidized to a copper(II) species that homo-couples the vinylstannane faster than the vinylstannane can be reduced. Whether it is Cu(I)OAc or the vinylcopper(I) intermediate that is actually oxidized is not yet known.

Few reports on the reaction of cuprous acetate and oxygen have appeared in the literature. Wolf and coworkers[14] showed that the reaction of cuprous acetate with O_2 was found to exhibit a 4:1 Cu(I)OAc/O_2 stoichiometry (Scheme 8).



Scheme 7



Scheme 8

Karlin and coworkers[15] have shown that at ambient temperatures, Cu(I) complexes proceed either through a μ-peroxy-**7** or a μ-η-η-peroxy-dicopper(II) intermediate followed by a disproportionation reaction with Cu(I)OAc to form oxo-dicopper(II) species **8**. Scheme 8 illustrates our proposed oxidation pathway using the μ-peroxy-dicopper(II) intermediate. This proposed mechanism is consistent with Wolf's stoichiometry, and although it is intuitively obvious that dioxygen reoxidizes Cu(I)OAc generated in situ from the reduction of $Cu(OAc)_2$, the exact mechanism of the reaction is unknown. Future work will explore the homo-coupling process with perfluorinated vinylstannanes, as well as multi-olefinic stannanes, and continue our mechanistic studies.

CONCLUSIONS

Successful homo-coupling of fluorinated vinylstannanes, with retention of stereochemistry, is readily accomplished with copper(II) acetate. Unlike hydrocarbon vinylstannanes, the presence of water has a detrimental effect on the homo-coupling of fluorinated vinylstannanes and significantly increases the amount of reduced olefin. The reaction tolerates alkyl, phenyl, and trialkylsilyl groups. It is important that copper(II) salts be utilized to mediate the reaction. When copper(I) salts are employed, excessive reaction times and increased reduced olefin formation dominate the homo-coupling reaction.

ACKNOWLEDGMENT

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(13) (a) ^{19}F NMR: δ –131.0 (dt, $^3J_{FF}$ = 107.0 Hz, $^3J_{FH}$ = 21.9 Hz, 1F), –145.0 (d (broad), $^3J_{FF}$ = 107.0 Hz, 1F) ppm relative to $CFCl_3$. (b) ^{19}F NMR: δ –151.1 (m (broad), 1F), –156.0 (s (broad), 1F) ppm relative to $CFCl_3$.

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(20) ^{119}Sn{^1H} NMR (134.19 MHz) spectra were obtained on a Bruker WM 360-MHz multinuclear spectrometer. Reaction mixtures (in DMF) were referenced against internal tetramethyltin (TMT).

(21) This compound was prepared by Normant's method in which D_2O was substituted for H_2O. Tellier, F.; Sauvetre, R.; Normant, J.F. *J. Organomet. Chem.* **1989**, *364*, 17–28. ^{1}H NMR ($CDCl_3$): δ 0.89 (t, J = 7.1 Hz, 3H), 1.33 (sextet, J = 7.3 Hz, 2H), 1.48 (m, 2H), 2.31 (dm, $^3J_{HF}$ = 22.9 Hz, 2H) ppm. ^{19}F{^1H} NMR (neat): δ –160.8 (d, $^3J_{FF}$ = 128.2 Hz, $^3J_{FD}$ = 0.0 Hz, 1F), –184.6 (dt, $^3J_{FF}$ = 128.5 Hz, $^2J_{FD}$ = 11.6 Hz, 1F) ppm. ^{19}F NMR (neat): δ –160.8 (dt, $^3J_{FF}$ = 128.2 Hz, $^3J_{FH}$ = 22.7 Hz, 1F), –184.6 (dtt, $^3J_{FF}$ = 128.5 Hz, $^2J_{FD}$ = 11.6 Hz, $^4J_{FH}$ = 5.1 Hz, 1F) ppm. ^{13}C NMR ($CDCl_3$): δ 13.8 (s), 22.4 (s), 26.0 (d, $^2J_{CF}$ = 22.9 Hz), 28.0 (d, $^3J_{CF}$ = 2.4 Hz), 156.3 (dd, $^1J_{CF}$ = 239.2 Hz, $^2J_{CF}$ = 39.8 Hz, $^2J_{CD}$ = 0.0 Hz), 139.5 (ddt, $^1J_{CF}$ = 236.4 Hz, $^2J_{CF}$ = 67.1 Hz, $^1J_{CD}$ = 30.6 Hz) ppm.

(22) Our standard workup consisted of addition of aqueous HCl solution to the reaction mixture and extraction with ether. Then the organic layer was dried over anhydrous $MgSO_4$, followed by the evaporation of solvents.