

Homocoupling of Polyfluorovinylstannanes Mediated by a Novel Combination of CuCl/2,2'-Dipyridyl. Stereospecific Synthesis of Polyfluorinated Alka-2,4-dienes[†]

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A new homocoupling methodology mediated by a novel combination of CuCl-2,2'-dipyridyl and its application to the synthesis of substituted polyfluorinated alka-2,4-dienes are described.

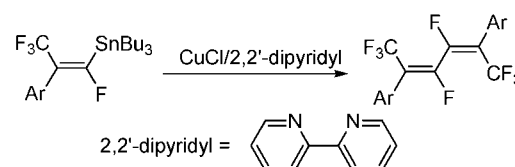
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Introduction

Stille reaction, which is known as the cross-coupling reaction between organostannanes and organic electrophiles, has become a widely employed synthetic tool in organic synthesis for the construction of carbon-carbon single bond,¹ particularly in the synthesis of naturally occurring compounds.² But the homocoupling reaction of vinylstannanes is still limited. Intramolecular CuCl mediated oxidative coupling of alkenyltrimethylstannane has been reported³ and applied to the synthesis of carbocyclic 1,3-diene systems including 5-, 6-, 7- and 8-membered rings. Intramolecular coupling methodology mediated by Cu(NO₃)₂ has been applied to the synthesis of macrocycle.⁴ Intermolecular CuCl-mediated coupling of alkenyltrimethylstannane also has been reported affording substituted conjugated dienes.⁵ Very recently a very stable strained cyclophane has been synthesized in moderate yield using the copper-catalyzed coupling of 1,8-bis[4-(tributylstannyl)phenyl]naphthalene.⁶ However, to the best of our knowledge, there is no paper concerning the homocoupling of fluorinated vinylstannanes. The lower reactivity of fluorinated vinylstannanes in coupling reaction than that of the corresponding nonfluorinated vinylstannanes is obviously due to its strong electron-withdrawing effect of fluorine.⁷ As part of our continuing investigation on the synthetic utility of organometallic and organophosphorus compounds in organic synthesis,⁸ herein we report a novel combination of CuCl/2,2'-bipyridyl system which is a very effective reagent for mediating the homocoupling of polyfluorinated vinylstannanes giving polyfluorinated alka-2,4-dienes, which would be expected to be useful intermediates in the synthesis of fluorine-containing biologically active compounds.

The reaction is shown in Scheme 1.

Scheme 1



In our initial study, in the absence of 2,2'-bipyridyl, the copper(I) chloride mediated homocoupling reaction of (*Z*)- α -fluoro- β -trifluoromethylvinylstannane (**1**) has been tried. The reaction was sluggish. After the reaction mixture was stirred at 20 °C in DMF for 24 h, TLC showed that a lot of starting material was unreacted. The reaction proceeded best in DMF with 2,2'-bipyridyl as ligand.

A typical experimental procedure is described as follows: To a solution of (*Z*)-3,3,3-trifluoro-2-(4-methylphenyl)-1-fluoro-1-tributylstannylprop-1-ene^{8a} (**1a**, 150 mg, 0.3 mmol) in DMF (4 mL) were added CuCl (45 mg, 0.45 mmol) and 2,2'-dipyridyl (70 mg, 0.45 mmol) with stirring. The reaction mixture was stirred under 25 °C for 24 h. Then ethyl ether (40 mL) was added. The ether solution was washed with saturated KF solution (6 × 10 mL) and dried over anhydrous Na₂SO₄. After removal of the solvent under reduced pressure, the residue was column chromatographed on silica gel eluting with petroleum ether (60—90 °C) to afford the desired product **2a** (78 mg, 64%).⁹ Other polyfluorinated alka-2,4-dienes were prepared by using the same method. The results are summarized in Table 1.

On the basis of F and CF₃ coupling constants across the double bond reported in the literature,¹⁰ if the

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Table 1 Preparation of polyfluorinated alka-2,4-dienes

Compound	Ar	Yield ^a	m.p. ^b /°C
2a	4-CH ₃ C ₆ H ₄	64	74—76
2b	3-CH ₃ C ₆ H ₄	82	Oil
2c	4-CH ₃ OC ₆ H ₄	62	94—96
2d	2-CH ₃ OC ₆ H ₄	60	79—81
2e	4-F-C ₆ H ₄	75	Oil
2f	4-Cl-C ₆ H ₄	66	100—102
2g	4-Br-C ₆ H ₄	82	115—116

^a Isolated yields after purification by silica gel chromatography.

^b Petroleum ether (60—90 °C) was used as recrystallization solvent

trifluoromethyl group was *trans* with respect to the F group, the ⁴J_{FF*trans*} ranged from 7 to 13 Hz, while for those *cis* with respect to the F group, the ⁴J_{FF*cis*} ranged from 21 to 31 Hz. In **2a**, ⁴J_{FF} is equal to 7.5 Hz, hence the configuration of the products **2a** could be ascertained as the 2*E*,4*E*-isomer. Similarly the other compounds can also be ascertained as the 2*E*,4*E*-isomers.

In summary, we have developed a new and convenient methodology for the synthesis of substituted polyfluorinated alka-2,4-dienes, which would be useful polyfluorinated building blocks for the synthesis of fluorine-containing biologically active compounds. The detailed application of these building blocks in organic synthesis is being pursued.

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- Analytic data are given for representative compound **2a**: m.p. 74—76 °C (petroleum ether, 60—90 °C); ¹H NMR (CDCl₃-TMS) δ: 7.28—7.23 (m, 8H), 2.40 (d, *J*=2.1 Hz, 6H); ¹⁹F NMR (CDCl₃-TFA) δ: -16.1 (t, *J*=7.5 Hz, 6F), 18.3—18.8 (m, 2F); IR (KBr) ν: 1640, 1510, 1330, 1310, 1230, 1170, 1130, 1100, 960 cm⁻¹; MS *m/z* (%): 406 (M⁺, 7), 391 (3), 337 (99), 314 (50), 268 (91), 253 (25), 233 (24), 92 (100). Anal. calcd for C₂₀H₁₄F₈ (406.32): C 59.12, H 3.47; found C 59.24, H 3.36.
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