Palladium-Catalyzed Cross-Coupling Reactions of 3-Tributylstannylsulfolene

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Abstract: 3-Tributylstannylsulfolene (**1**) undergoes palladium-catalyzed cross-coupling reactions with aryl and vinyl halides, cyclohex-1-enyl triflates and acyl chlorides in moderate to excellent yield, thereby allowing rapid entry to a diverse range of 3-substituted sulfolenes, species known to be reliable precursors to 3-substituted 1,3-dienes.

1,3-Dienes are known to be valuable reagents in organic synthesis, particularly in the Diels-Alder reaction,[1] but also in a variety of other [4+2] cycloadditions and in a range of varied transformations.[2] 3-Sulfolenes are well-known synthetic equivalents of 1,3-dienes, and have frequently been utilized in synthetic manipulations, primarily due to their enhanced stability compared to dienes.[3]

We recently reported the preparation of sulfolene (**1**) as a stable precursor to 3-tributylstannylbuta-1,3-diene;[4] given the known propensity of alkenylstannanes to undergo a variety of palladium-catalyzed cross-coupling reactions (which have been grouped together as 'Stille reactions'[5]), we wished to explore the possibility of using (**1**) in such reactions, offering a more convenient alternative to the method of Franck-Neumann *et al.*, who performed Stille couplings upon the iron tricarbonyl complex of 3-tributylstannylbuta-1,3-diene (the diene itself being too unstable to undergo such reactions).[6] Palladium catalysis has previously been employed before to prepare aryl sulfolenes, *via* Heck reactions, but the previous methods suffer from several drawbacks. For instance, in the 'traditional' Heck reaction of aryl iodides with sulfolene itself,[7] successful reaction could not be realized with aryl iodides bearing *ortho*-substituents, or strongly electron-withdrawing substituents (such as the nitro group). In the Heck reaction of diazonium salts with sulfolene,[8] only aryl groups may be transferred, due to the instability of non-aromatic diazonium species. In this letter, we delineate the preliminary results of our investigations, which indicate that in the presence of palladium(0) catalysts, stannylsulfolene (**1**) reacts with aryl and vinyl iodides, aryl and vinyl triflates, and acyl chlorides, thus offering a more general technique for synthesis of 3-substituted sulfolenes. The data are summarized in Table 1.

Thus, (**1**) undergoes efficient coupling with a range of aryl and alkenyl iodides and bromides,[9] but reacts in rather poorer yield with acyl chlorides.[10] Cyclohexen-1-yl triflates[11] also undergo reaction in moderate yield, but under milder conditions. Of particular note are the successful reactions with electron-deficient and *ortho*-substitued arenes (entries 6 and 3, respectively). (The lower yield in reaction of *o*-methoxyiodobenzene [entry 5] being due to the electron-richness of the arene, rather than steric encumbrance[4a]).

The extrapolation and optimization of these primary data is currently underway in our laboratories.

Acknowledgements

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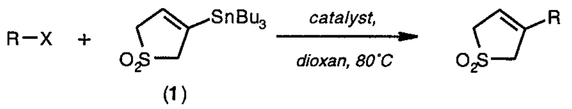
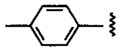
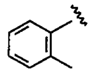
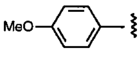
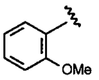
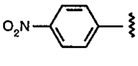
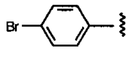
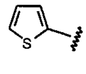
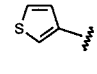
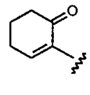
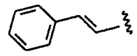
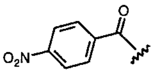
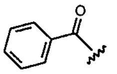
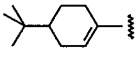
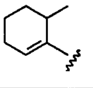
TABLE - PALLADIUM-CATALYZED CROSS COUPLING REACTIONS OF 3-TRIBUTYLSTANNYLSULFOLENE (1)



Entry	R	X	Catalyst	Yield
1	Ph	I	$Pd(PPh_3)_4$	86%
2		I	$Pd(PPh_3)_4$	52%
3		I	$(DPPE)_2Pd$	82%
4		Br	$(DPPE)_2Pd$	82%
5		I	$(DPPE)_2Pd$	36%
6		Br	$(DPPE)_2Pd$	86%
7		Br	$(DPPE)_2Pd$	39%
8		I	$Pd(PPh_3)_4$	64%
9		I	$(DPPE)_2Pd$	61%
10		I	$Pd(PPh_3)_4$	79%
11		Br	$(DPPE)_2Pd$	71%
12		Cl	$BnClPd(PPh_3)_2$	45%[#]
13		Cl	$BnClPd(PPh_3)_2$	47%[#]
14		OTf	$(DPPE)_2Pd$	57%[¶]
15		OTf	$(DPPE)_2Pd$	63%[¶]

[#]reaction performed in chloroform; [¶]reaction perfomed at room temp.

References

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2. See, for instance, Nakamura, A.; Mashima, K.; *J. Organomet. Chem.*, **1995**, *500*, 261.
3. For recent reports of the synthetic utility of 3-sulfolenes, see: Subramanian, T.; Meenakshi, S.; Dange, S.Y.; Bhat, S.V.; *Synth. Comm.*, **1997**, *27*, 2557; Vicente, M.G.H.; Tome, A.C.; Walter, A.; Cavaleiro, J.A.S.; *Tetrahedron Lett.*, **1997**, *38*, 3639; Leonard, J.; Fearnley, S.P.; Hague, A.B.; Wong, G.; Jones, M.F.; *Tetrahedron Lett.*, **1997**, *38*, 3067; Suzuki, T.; Fuchii, H.; Takayama, H.; *J. Chem. Soc., Perkin Trans. 1*, **1996**, 2699; Tso, H.H.; Chandrasekharam, M.; *Tetrahedron Lett.*, **1996**, *37*, 4189; Lee, Y.S.; Ryu, E.K.; Yun, K.Y.; Kim, Y.H.; *Synlett*, **1996**, 247; Chou, S.S.P.; Chao, M.H.; *J. Chin. Chem. Soc.*, **1996**, *43*, 53; Padmakumar, R.; Subramanian, T.; Bhat, S.V.; *Org. Prep. Proc. Int.*, **1995**, *27*, 463; Tso, H.H.; Yang, N.C.; Chang, Y.M.; *J. Chem. Soc., Chem. Commun.*, **1995**, *13*, 1349; Kasatkin, A.N.; Prokopenko, Y.A.; Khabihov, A.M.; Tolstikov, G.A.; *Russ. Chem. Bull.*, **1994**, *43*, 101; Hoffmann, R.; Mattay, J.; Banning, A.; Rodewald, U.; Moller, M.M.; *J. Prakt. Chem.*, **1994**, *336*, 343; Chou, S.S.P; Lee, C.S.; Cheng, M.C.; Tai, H.P.; *J. Org. Chem.*, **1994**, *59*, 2010; Ando, K.; Takayama, H.; *Heterocycles*, **1994**, *37*,1417; Ghabrial, S.S.; *Phosphorus, Sulfur, Silicon And Related Elements*, **1993**, *84*,17; Polunin, E.V.; Maloshitskaya, O.A.; Kashin, A.N.; *Mendeleev Comm.*, **1993**, *6*, 254; Chou, T.S.; Tsai, C.Y.; *J. Chin. Chem. Soc.*, **1993**, *40*, 581; Chou, T.S.; Chang, R.C.; *Heterocycles*, **1993**, *36*, 2839.
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5. (a.) Stille, J.K.; *Ang. Chem. Int. Ed. Engl.*, **1986**, *29*, 508; (b.) Mitchell, T.N.; *Synthesis*, **1992**, 803.
6. Colson, P-J.; Sedrati, M.; Franck-Neumann, M.; *Tetrahedron Lett.*, **1989**, *30*, 2393.
7. Harrington, P.J.; DiFiore, K.A.; *Tetrahedron Lett.*, **1987**, *28*, 495.
8. Sengupta, S.; Bhattacharyya, S.; *Synth. Comm.*, **1996**, *26*, 231.
9. General procedure for coupling of aryl and alkenyl halides with (**1**):
   3-tri-*n*-Butylstannyl-2,5-dihydrothiophene-1,1-dioxide (121 mg, 0.30 mmol) was dissolved in dioxan (3 mL) under a nitrogen atmosphere. To the stirred solution was added the requisite halide (0.30 mmol) and *trans*-benzyl(chloro)*bis*(triphenylphosphine) palladium(II) (26mg, 0.03mmol) or *tetrakis*(triphenylphosphine) palladium(0) (34 mg, 0.03 mmol). The resulting solution was heated at 80°C for twelve hours under an atmosphere of nitrogen. After this time tlc (petroleum ether/ether [8 :2]) showed that the starting materials had been consumed. The solvent was removed *in vacuo* and the crude product redissolved in aqueous methanol (90% v/v, 5 mL). This solution was washed with petroleum ether (3x20mL) to remove the bulk of the tin side-products. The methanolic solution was concentrated *in vacuo*, and the crude product purified by flash chromatography.
10. General procedure for coupling of acyl chlorides with (**1**):
    3-tri-*n*-Butylstannyl-2,5-dihydrothiophene-1,1-dioxide (54 mg, 0.13 mmol) was dissolved in chloroform (3 mL). To the stirred chloroform solution was added freshly distilled acyl chloride (0.13 mmol) and *trans*-benzyl(chloro)*bis*(triphenylphosphine)-palladium(II) (10mg, 0.01mmol). The resulting solution was heated at 80°C for twelve hours under an atmosphere of carbon monoxide. After this time tlc (petroleum ether/ether [8 :2]) showed that the starting materials had been consumed. The pure products were then obtained as described above.
11. General procedure for coupling of alkenyl triflates with (**1**):
    3-tri-*n*-Butylstannyl-2,5-dihydrothiophene-1,1-dioxide (86 mg, 0.21 mmol) was dissolved in *N,N*-dimethylformamide (800 nitrogen atmosphere. The requisite triflate (0.21 mmol), *bis*[1,2-*bis*(diphenylphosphino)ethane]palladium(0) (9.5 mg, 0.01 mmol) and lithium chloride (45 mg, 1.06 mmol) were added *via* a solid-addition tube, and the resulting solution was stirred at room temperature for 48 hours. After this time tlc (petroleum ether/ether [8 :2]) showed that the starting materials had been consumed. The pure products were then obtained as described above.