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POTASSIUM TRIISOPROPYLSILANETHIOLATE: VINYL AND ARYL SULFIDES THROUGH PD-CATALYZED CROSS COUPLING

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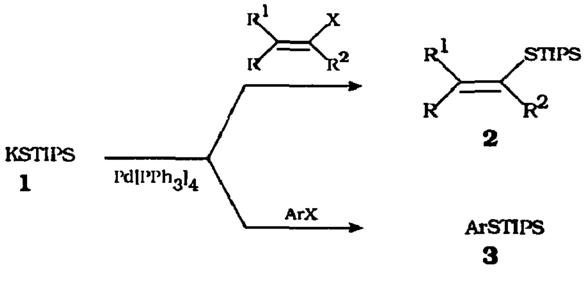
Abstract: *Vinyl and aryl halides are efficiently converted, under Pd catalysis, with KSTIPS (**1**) to the corresponding silyl sulfides (**2**, **3**). The naphthyl derivative was easily hydrolyzed to the mercaptan **4**, or alkylated or alkenylated to provide unsymmetrical sulfides (**5**, **6**).*

A common feature of many natural products and pharmaceuticals, the sulfide functionality is also important in chemical synthesis.[3] While numerous synthetic methods have been successfully employed to introduce this functionality into organic substrates, none appear more convenient than the known Pd-catalyzed coupling of vinyl halides with arylthiolates.[4] However, the introduction of a silylthio, rather than ArS, group, would enable the silyl group to be subsequently replaced by a variety of alternative substituents, a feature which would markedly enhance the versatility of this approach to unsymmetrical sulfides.

Recently, we have discovered that triisopropylsilanethiol (HSTIPS) can be readily prepared from TIPSCl and LiSH (98%) and converted to its stable, crystalline potassium salt, **1**, (95%) with KH.[5] The reagent is a powerful nucleophile which is readily alkylated by both 1° and 2° halides and tosylates to provide silyl alkyl sulfides cleanly. The unusual resistance of these TIPS derivatives to both hydrolysis and cleavage by organometallic reagents suggested that **1** might possess the necessary stability to undergo the coupling process previously observed only for the arylthiolates. Thus, nine representative alkenyl and aryl halides were selected, and all were found to be efficiently silanethiolated to produce the corresponding alkenyl (**2**) or aryl (**3**) silyl sulfides under the Pd-catalyzed conditions.[6]



These results, which are presented in Table 1, reveal that the reaction proceeds with complete retention of configuration in the case of the vinyl derivatives examined (*cf.* entries 2 and 3) and give good to excellent product yields even on a small reaction scale. Electron-withdrawing groups enhance the rate of coupling of **1** with aryl bromides (*cf.* entries 5,7,8). No reaction of **1** with *p*-$BrC_6H_4NO_2$ occurs in 6 h at 25 °C in the absense of the Pd catalyst.

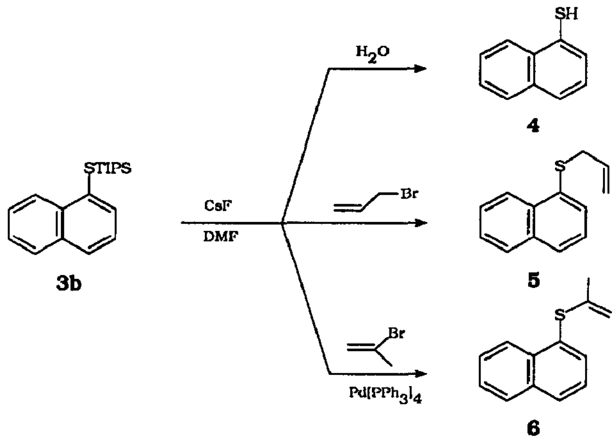
We chose to demonstrate the versatility of these silyl sulfides by effecting the deprotection of

Table 1. Alkenyl and Aryl Silyl Sulfides from **1**.

entry	R, R^1, R^2	Ar	X	time (h)	Product	yield
1	Me, Me, H	-	Br	36	**2a**	84
2	*n*-Pr, H, H	-	I	2	**2b**	66
3	H, *n*-Pr, H	-	I	2	**2c**	89
4	H, H, Me	-	Br	1.5	**2d**	92
5	-	Ph	Br	2	**3a**	77
6	-	1-Naph	Br	5	**3b**	61
7^a	-	$C_6H_4(NO_2$-*p*)	Br	0.25	**3c**	93
8^a	-	C_6H_4(OMe-*p*)	Br	12	**3d**	68
9^a	-	2-Py	Br	12	**3e**	79

[a] The aryl bromide was refluxed 1 h with the catalyst prior to the addition of **1**.[4]

3b (CsF/DMF 8 h, 25 °C) followed by its hydrolysis to **4** (73%). Alternatively, the intermediate thiolate is alkylated with allyl bromide to give **5** (65%) or coupled with isopropenyl bromide to provide **6** (55%),[7] all of which are very clean reactions. However, we were unable to prepare **6** from **2d** and 1-bromonaphthalene under similar conditions, suggesting that stable thio-enolates are required for a successful cross coupling process.



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6. Representative procedure: To a well-stirred solution of $Pd(PPh_3)_4$ (0.070 g, 0.6% mole), *cis*-1-iodo-1-pentene (0.411 g, 2.1 mmol) in C_6H_6 (10 mL) was added **1** (0.457 g, 2 mmol) in THF (2-4 mL). After 2 h at reflux, H_2O (10 mL) and hexanes (10 mL) were added. The organic layer was washed with H_2O (2 x 10 mL), dried over Na_2SO_4, concentrated and the residue was loaded onto an alumina (3 g) column and flash chromatographed with hexanes. Concentration affords 0.459 g (89%) of **2c**. ^{1}H NMR ($CDCl_3$) δ 0.93 (t, J = 7.2 Hz, 3H), 1.12 (d, J = 7.2 Hz, 18 H), 1.26 (m, 3H), 1.43 (sext, J = 7.2 Hz, 2H), 2.25 (dq, J = 7.5, 1.1 Hz, 2H), 5.69 (dt, J = 9.1, 7.2 Hz, 1H), 5.98 (dt, J = 9.1, 1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 12.7, 18.4 (TIPS), 13.8, 22.1, 30.7, 117.4, 134.2; IR (TF) 1610 cm^{-1}; MS m/z (rel abundance) 258 (M^+, 29), 215 (86).
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