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PALLADIUM - CATALYZED REACTIONS OF TRIALKYLSTANNYL PHENYL SULFIDES WITH ALKENYL BROMIDES. A NEW DIASTEREOSELECTIVE SYNTHESIS OF (E)-1-ALKENYL PHENYL SULFIDES

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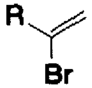
Summary: *The reaction of easily available stereoisomeric mixtures of 1-alkenyl bromides with molar excesses of trialkylstannyl phenyl sulfides takes place readily in the presence of $Pd(PPh_3)_4$ to afford diastereoselectively (E)-1-alkenyl phenyl sulfides in excellent yields.*

Vinyl sulfides are quite interesting reagents which undergo a variety of synthetically useful transformations. They undergo [2+2]- and [4+2]- cycloadditions[1] and are converted to alkenes by the Ni-catalyzed cross-coupling with alkyl, aryl and alkenyl Grignard reagents[2]. Moreover, these compounds, which are synthetically equivalent to carbonyl groups[3], may be easily transformed into the corresponding sulfoxides[4].

Since aryl sulfides have been recently prepared in good yields by Pd-catalyzed reactions of tributylstannyl alkyl or aryl sulfides with aryl bromides[5], it appeared interesting to extend this procedure to the synthesis of vinyl phenyl sulfides. First, we examined the reaction of trialkylstannyl phenyl sulfides (*1*)[6] with 2-bromo-1-alkenes (*2*), in the presence of catalytic amounts of $Pd(PPh_3)_4$, but unsatisfactory results were obtained.

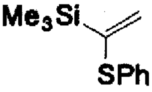
$R^1_3Sn-SPh$

1a R = CH_3
1b R = C_4H_9



2a R = $SiMe_3$
2b R = C_5H_{11}

For instance, *reaction of 1-(bromovinyl)trimethylsilane (1a) (69.9 mmol) with* a solution of *2a* (69.9 mmol) and $Pd(PPh_3)_4$ (3 mol %) in benzene (70 ml) at 80° C for 40 h gave in 88 % yield a mixture of 1-(trimethylsilyl)-1-(phenylthio)ethene (*3*) and (E)/(Z)-2-(trimethylsilyl)-1-(phenylthio)ethene (*4*)[7] in a 76/24 ratio. Analogously, reaction of *2b* with *1b* in toluene at 110° C for 4.5 h, in the presence of 3 mol % of $Pd(PPh_3)_4$, afforded in 99 % yield a mixture of the alkenyl phenyl sulfides *5* and *6*, in a 77.3/22.7 ratio.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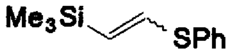
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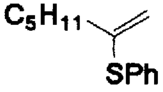
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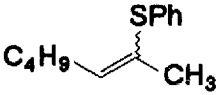
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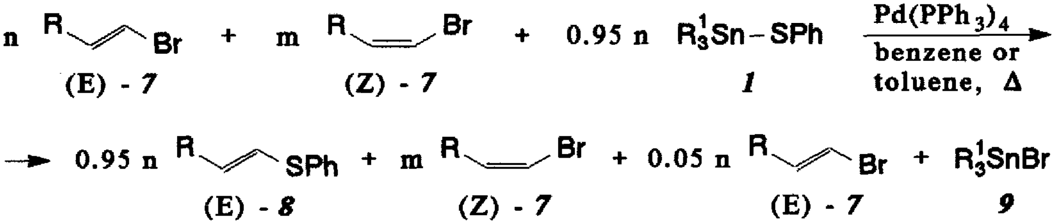
Since steric hindrance could be an important factor in this type of coupling reactions, we examined the reactivity of 1-alkenyl bromides (*7*) which are less hindered than the corresponding 2-bromo-1-alkenes. We found that in this case the cross-couplings proceed cleanly and efficiently. Moreover, we observed that (E)- and (Z)-1-bromo-1-alkenes exhibit differing reactivity towards *1*, and, in particular, that (E)-*7* undergoes stereospecific Pd-mediated cross-coupling faster than the corresponding (Z)-stereoisomers[8]. Thus, the following simple and convenient highly diastereoselective procedure for the synthesis of (E)-1-alkenyl phenyl sulfides (*8*), starting from easily available diastereomeric mixtures of *7*[9], was developed.



A stereoisomeric mixture of *7*, containing n equiv of the (E)-stereoisomer, was reacted under argon with a benzene or toluene solution of 0.95 n equiv of *1*, in the presence of 3-4 mol % of $Pd(PPh_3)_4$. The mixture was stirred at the appropriate temperature for the required length of time (see Table 1), during which it became red. The reaction mixture was quenched with 5 N NaOH, washed with water, and extracted with ether. The ether extracts were filtered, dried, and concentrated *in vacuo*. The residue was dissolved in hexane and filtered. The hexane solutions of *8* prepared from *1a* were concentrated and purified by MPLC on a silica gel column, followed by distillation. The hexane solutions of *8* prepared from *1b* were washed with aq KF and filtered to remove tributyltin fluoride. The filtrates were concentrated *in vacuo* and purified by MPLC on a silica gel column. (E)-1-Alkenyl phenyl sulfides (*8*), having 96 - 99 % stereoisomeric purity, were obtained in 70 - 91 % yields. The experimental conditions and the results of the coupling reaction between a variety of (E)/(Z)-1-alkenyl bromides (*7*)[10] and *1* are summarized in Table 1.

In conclusion, the procedure described here, which represents the first example of a diastereoselective C-S bond formation, provides a highly stereoselective route to (E)-1-alkenyl phenyl sulfides starting from easily available starting materials. Owing to its simplicity, this procedure competes favourably with some established stereospecific[11] or stereoselective methods[12] for preparing these interesting synthetic intermediates. One of these, i.e. (E)-2-(trimethylsilyl)-1-(phenylthio)ethene

(*8a*), which has been previously employed to synthesize 5-mercaptophenyl cyclopenten-2-ones[13], may be conveniently employed to synthesize stereospecifically pure (E)-1-trimethylsilyl-1-alkenes (*11*) in good yields. In fact, reaction of *8a* with 2 mol equiv of a Grignard reagent, in the presence of catalytic amounts of $NiCl_2(dppe)$, affords *11* in 64 - 77 % yields.

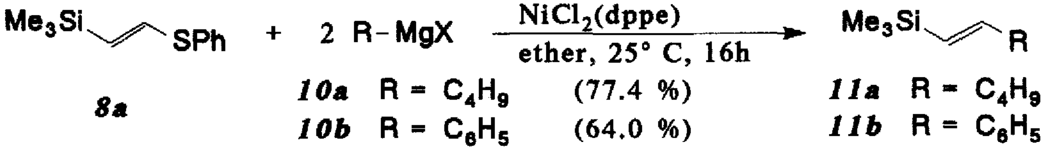
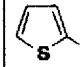


TABLE 1

Diastereoselective Synthesis of (E)-1-Alkenyl Phenyl Sulfides [a)]

1-Alkenyl halide			Trialkylstannyl phenyl sulfide		Solvent	Temp	Reaction time	Product		
7	R	(E)/(Z) ratio	*1*	R^1		(°C)	(h)	(E) - *8*	Yield (%)	Stereoisom. purity (%)
7a	Me_3Si	87/13	*1a*	CH_3	benzene	40	2	*8a*[b)]	91	>99.0
7b	C_5H_{11}	83/17	*1b*	C_4H_9	toluene	65	6	*8b*[c)]	70	>98.0
7c	C_6H_5	89/11	*1b*	C_4H_9	toluene	110	2	*8c*[c)]	91	98.5
7d		68/32	*1b*	C_4H_9	toluene	60	3	*8d*[c)]	85	98.4
7e	C_6H_{13}	64/36	*1b*	C_4H_9	toluene	50	7.5	*8e*[c)]	84	98.0

a) All reactions were carried out using 3-4 mol % of $Pd(PPh_3)_4$ and a *1*/(E)-*7* 1/0.95 molar ratio; b) *8a* = (E)-*4* ; c) distillation of *8b*- *8e* caused a significant stereomutation.

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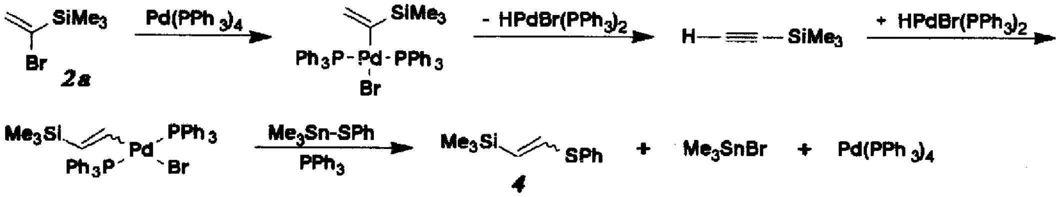
6. Tributylstannyl phenyl sulfide (***1b***) and trimethylstannyl phenyl sulfide (***1a***) were prepared by reaction of THF solutions of C_6H_5SLi with Bu_3SnCl or Me_3SnCl, respectively, at 65 °C for 5 h.

7. The formation of compound ***4*** can be rationalized as follows:



8. For earlier work concerning the Pd-catalyzed diastereoselective cross-coupling between stereoisomeric mixtures of 1-alkenyl bromides and organometallics, see: *a*) R. Rossi, A. Carpita, P. Piccardi, in *"Pesticide Chemistry: Human Welfare and the Environment"*, J. Miyamoto, P. C. Kearney Eds., Pergamon Press, Oxford, 1981, p 129; *b*) R. Rossi, A. Carpita, *Tetrahedron Lett.*, ***27***, 2529 (1986); *c*) A. Carpita, R. Rossi, *Tetrahedron Lett.*, ***27***, 4351 (1986); *d*) B. P. Andreini, A. Carpita, R. Rossi, *Tetrahedron Lett.*, ***27***, 5533 (1986); *e*) B. P. Andreini, A. Carpita, R. Rossi, *Tetrahedron Lett.*, ***29***, 2239 (1988); *f*) B. P. Andreini, M. Benetti, A. Carpita, R. Rossi, *Gazz. Chim. Ital.*, ***118***, 469 (1988).
9. (E)/(Z)-2-(Bromovinyl)trimethylsilane (***7a***) and (E)/(Z)-1-bromo-2-phenylethene (***7c***) are commercially available (Fluka). Stereoisomeric mixtures of 1-bromo-1-heptene (***7b***) and 1-bromo-1-octene (***7e***) were prepared according to the general method described in Ref. ***8a***. (E)/(Z)-1-Bromo-2-(2-thienyl)ethene (***7d***) was prepared from thiophene-2-carboxaldehyde according to the procedure described by: T. Hirao, T. Masunaga, Y. Oshiro, T. Agawa, *J. Org. Chem.*, ***46***, 3745 (1981).
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