Aromatic Allylsulfenylation with *in Situ* Generated Allyl Thiols under the Heck Conditions

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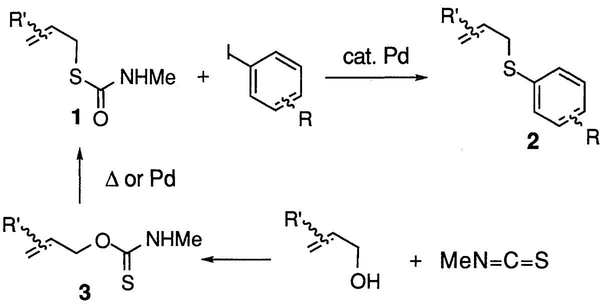
By the catalysis of palladium(0), *S*-allyl thiocarbamates **1** react with aryl iodides and vinyl bromides to give allyl aryl sulfides and allyl vinyl sulfides, respectively, in good yields.

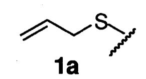
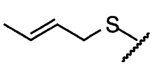
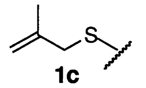
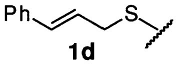
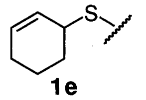
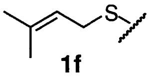
Owing to the synthetic utilities, palladium-catalyzed substitution of aromatic halides with carbon and heteroatom nucleophiles has been a strong concern of organic chemists from synthetic[1] and mechanistic points[2] of view. As for the aromatic sulfenylation, there have appeared two methods that utilize either alkali metal salts of aromatic and aliphatic thiols[3a] or aromatic and aliphatic thiostannanes.[3b,c] One successful example of the allylsulfenylation of phenyl iodide has appeared.[3c]

Here we report that *S*-allyl thiocarbamates **1** serve as a convenient allylsulfenylation reagent of variously substituted aromatic iodides under the Heck arylation conditions (Scheme 1) and furnish allyl aryl sulfides **2** in good yields. A wide structural variety of **1** can be prepared in good yields straightforwardly from the corresponding allylic alcohols via a thermal or a palladium catalyzed rearrangement of *O*-allyl thiocarbamates **3** (Scheme 1).[4] Thus, the present palladium-catalyzed allylsulfenylation of aromatic iodides is the first, practical method that enables one to prepare allyl aryl sulfides avoiding the use of allylthiostannanes[3c] and allyl thiols, being notorious for their stink, instability (radical polymerization and autoxidation), and/or toxicity.



Scheme 1.

Table 1. Palladium-catalyzed synthesis of allyl phenyl sulfides **2** from *S*-allyl thiocarbamates **1** and phenyl iodide

run	allylic moiety of **1**	reaction condition[a]						% isolated yiled of **2** (R = H)
			Pd cat.	ligand	base	additive	time (h)	
1	 **1a**	**B**	$Pd(OAc)_2$	PPh_3	K_2CO_3	$Bu_4N^+I^-$	3	**2a**: 50
2		**C**	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	none	3	**2a**: 57
3	 **1b**	**A**	$Pd(OAc)_2$	PPh_3	K_2CO_3	none	24	**2b**: 60
4		**B**	$Pd(OAc)_2$	PPh_3	K_2CO_3	$Bu_4N^+I^-$	3	**2b**: 77[b]
5		**C**	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	none	4	**2b**: 62
6		**D**	$Pd(OAc)_2$	PPh_3	none	none	46	**2b**: ---[c]
7		**E**	$Pd(PPh_3)_4$	none	K_2CO_3	none	8	**2b**: 55
8	 **1c**	**A**	$Pd(OAc)_2$	PPh_3	K_2CO_3	none	12	**2c**: 59
9		**B**	$Pd(OAc)_2$	PPh_3	K_2CO_3	$Bu_4N^+I^-$	3	**2c**: 62
10	 **1d**	**B**	$Pd(OAc)_2$	PPh_3	K_2CO_3	$Bu_4N^+I^-$	21	**2d**: 77
11	 **1e**	**B**	$Pd(OAc)_2$	PPh_3	K_2CO_3	$Bu_4N^+I^-$	3	**2e**: 87
12	 **1f**	**B**	$Pd(OAc)_2$	PPh_3	K_2CO_3	$Bu_4N^+I^-$	4	**2f**: 75

[a] **1** (1.0 mmol), phenyl iodide (1.3 mmol), palladium catalyst (0.1 mmol), ligand (0.3 mmol), base (1.3 mmol), additive (1.0 mmol) in dioxane (5 cm^3) at 373 K under N_2. [b] 73% isolated yield of **2b** under conditons **B** with a reduced amount of catalyst [$Pd(OAc)_2$ (0.05 mmol), PPh_3 (0.15 mmol), K_2CO_3 (1.3 mmol), $Bu_4N^+ I^-$ (1.0 mmol) at 373 K for 22 h]. [c] Less than 5% of **2b** with 67% recovery of **1b**.

In order to optimize the reaction conditions, the reaction of *S*-(*E*)-crotyl thiocarbamate **1b** and phenyl iodide was examined extensively (runs 3-7, Table 1). The reactivity and the yield greatly depended on the kind of ligands, bases, and additives. Conditions **A**, using $Pd(OAc)_2$ and PPh_3 in a molar ratio of 1 to 3 (run 3, Table 1), were slightly more satisfactory than a typical Heck conditions (conditions **E**), using tetrakis(triphenylphosphine)palladium as a catalyst (run 7, Table 1).[3] Phosphine ligands other than PPh_3 were ineffective: Examinations of run 3 using either $P(o\text{-Tol})_3$ (0.3 equivalents) or $P(OMe)_3$ (0.2 equivalents) in place of PPh_3 resulted in the formation of **2b** in less than 8%. In the absence of a base, the reaction was very slow, and even after prolonged reaction, the most part of the starting **1b** remained (run 6). Tetrabutylammonium iodide, in combination with K_2CO_3, remarkably accelerated the reaction and improved the yield (conditions **B**, run 4, Table 1). The similar acceleration and improvement of the yield were observed by the use of Cs_2CO_3 alone as a base (conditions **C**, run 5, Table 1).

Throughout this study, reactions were undertaken with 0.1 equivalents of palladium catalyst, however, the amount may be reduced to 0.05 equivalents without serious deterioration in yields (see footnote b, Table 1).

Other allylic thiocarbamates **1a**, **1c**-**f** were examined under thus optimized conditions **A**-**C**. Results summarized in Table 1 indicate that the present aromatic allylsulfenylation is general for a wide structural variety of **1**. The reason for the apparently lower yields of **2a**, as compared with those of other **2**, is not clear. Deterioration in yields owing to a further arylation of **2a** at the double bond is unlikely, since **2d**, the double bond arylation product of **2a**, was not detected at all (^{1}H NMR and VPC).

Table 2. Palladium-catalyzed synthesis of aryl (*E*)-crotyl sulfides **2** from *S*-(*E*)-crotyl thiocarbamate **2b** and aryl iodides

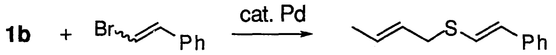
aryl iodides	conditions B^a			conditions C^a		
(R)	run	time (h)	% yield	run	time (h)	% yield
o-OMe	1	18	69	14	4	25
m-OMe	2	3	72	15	3	80
p-OMe	3	22	65	16	5	14
o-Me	4	4	83	17	3	71
m-Me	5	5	71	18	3	35
p-Me	6	4	71	19	3	37
H	7	3	77	20	4	62
o-CO_2Me	8	3	82	21	3	85
m-CO_2Me	9	5	82	22	3	94
p-CO_2Me	10	3	78	23	3	96
m-F	11	6	69	24	4	69
m-NO_2	12	3	77	25	2	59
p-NO_2	13	3	76	26	1	80

[a] See Table 1 for conditions **B** and **C**.

Next, we examined the allylsulfenylation of aryl iodides bearing electron-donating and -attracting substituents at the *o*-, *m*-, and *p*-positions. The results summarized in Table 2 clearly indicate that conditions **B** are satisfactorily applicable to all the aryl iodides examined irrespective of the electronic nature of substituents and their substitution positions (runs 1-13, Table 2). On the other hand, conditions **C**, in general, are superior to conditions **B** for the sulfenylation of aryl iodides with electron-attracting substituents (runs 21-26, Table 2), while inferior for the sulfenylation of aryl iodides with electron-donating groups (runs 14-19, Table 2).

The present allylsulfenylation may proceed through the following sequence of reactions: In the presence of base, **1** fragments into methyl isocyanate and a thiolate.[5] Arylpalladium iodide, generated by an oxidative addition of aryl iodide to Pd(0), reacts with the thus formed allyl thiolate selectively at the sulfur atom to give an (allylthio)arylpalladium(II) intermediate, which undergoes reductive elimination to provide **2** and regenerate palladium(0) species,[2b] whereby remaining the double bonds of allyl thiolates and the starting materials **1** as well as the products **2** intact. The selective arylation of **1** at the sulfur atom makes sharp contrast to the selective arylation of *O*-allyl carbamates, the oxygen analogs of **1**,[6] at the double bonds.

The allylsulfenylation of vinyl bromides[7] nicely proceeds under the similar conditions (equation 1): (*E*)-crotyl (*E*)-β-styryl sulfide was obtained selectively in 53% isolated yield by the reaction of a mixture of (*E*)- and (*Z*)-β-bromostyrene (1.3 equivalents, 5.3:1) and **1b** under condition **A** (373 K, 3 h). No products of the subsequent thia-Claisen rearrangement[8] were detected.



(1)

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References and Notes

1 M. Meller, *Angew. Chem. Int. Ed. Engl.*, **34**, 1316 (1995); A. S. Guram and S. L. Buchwald, *J. Am. Chem. Soc.*, **116**, 7901 (1994).

2 a) F. Paul, J. Patt, and J. F. Hartwig, *J. Am. Chem. Soc.*, **116**, 5969 (1994). b) D. Baranano and J. F. Hartwig, *J. Am. Chem. Soc.*, **117**, 2937 (1995).

3 a) T. Migita, T. Shimizu, Y. Asami, J. Shiobara, Y. Kato, and M. Kosugi, *Bull. Chem. Soc. Jpn.*, **53**, 1385 (1980). b) M. Kosugi, T. Ogata, M. Terada, H. Sano, and T. Migita, *Bull. Chem. Soc. Jpn.*, **58**, 3657 (1985). c) M. J. Dickens, J. P. Gilday, T. J. Mowlem, and D. A. Widdowson, *Tetrahedron*, **47**, 8621 (1991).

4 E.g., **1a** (76% from *O*-allyl thiocarbamate; 10 mol% of $Pd(PPh_3)_4$, rt, 3 h in THF), **1b** (84% from *O*-α-methylallyl thiocarbamate; 373 K, 7 h, neat), **1c** (86% from *O*-β-methylallyl thiocarbamate; 10 mol% of $Pd(PPh_3)_4$, rt, 1 h in THF). Results of detailed synthetic and mechanistic study of the present rearrangement will be reported elsewhere. All products showed satisfactory spectral (^{1}H NMR, IR, MS) and analytical data.

5 Generation of allyl thiolates seems likely: the reaction of **1b** (1.0 mmol) and benzyl bromide (1.1 mmol) [K_2CO_3 (1.1 mmol), dioxane, 373 K, 26 h] gave benzyl crotyl sulfide in 76% yield.

6 K. Ono, K. Fugami, S. Tanaka, and Y. Tamaru, *Tetrahedron Lett.*, **35**, 4133 (1994).

7 S.-I. Murahashi, M. Yamamura, K. Yanagisawa, N. Mita, and K. Kondo, *J. Org. Chem.*, **44**, 2408 (1979); A. Carpita, R. Rossi, and B. Scamuzzi, *Tetrahedron Lett.*, **30**, 2699 (1989); A. G. Martinez, J. O. Barcina, A. de F. Cerezo, and L. R. Subramanian, *Synlett*, **1994**, 561.

8 K. Kondo and I. Ojima, *J. Chem. Soc., Chem. Commun.*, **1972**, 62.