JOC Article

Unsymmetrical Diaryl Sulfones and Aryl Vinyl Sulfones through Palladium-Catalyzed Coupling of Aryl and Vinyl Halides or Triflates with Sulfinic Acid Salts

Sandro Cacchi,*,† Giancarlo Fabrizi,† Antonella Goggiamani,† Luca M. Parisi,† and Roberta Bernini‡

Dipartimento di Studi di Chimica e Tecnologia delle Sostanze Biologicamente Attive, Università degli Studi "La Sapienza", P. le A. Moro 5, 00185 Rome, Italy, and Dipartimento A.B.A.C., Università degli Studi della Tuscia, Via S. Camillo De Lellis, 01100 Viterbo, Italy

sandro.cacchi@uniroma1.it

Received April 19, 2004

The palladium-catalyzed reaction of sulfinic acid salts with a wide variety of aryl and vinyl halides or triflates provides unsymmetrical diaryl sulfones and aryl vinyl sulfones in good to excellent yields. The reaction is strongly influenced by the presence of $^{n}Bu_4NCl$, and the use of Xantphos, a rigid bidentate ligand with a wide natural bite angle, was found to be crucial for the success of the reaction. With neutral, electron-rich, and electron-poor aryl iodides best results were obtained by using $Pd_2(dba)_3$, Xantphos, Cs_2CO_3, and $^{n}Bu_4NCl$, in toluene at 80 °C. Two general procedures were employed with aryl bromides and triflates: sodium *p*-toluenesulfinate, $Pd_2(dba)_3$, Xantphos, Cs_2CO_3, 120 °C, in toluene with $^{n}Bu_4NCl$ (procedure A: neutral, electron-rich, and slightly electron-poor aryl bromides or triflates) and without $^{n}Bu_4NCl$ (procedure B: electron-poor aryl bromides or triflates). With vinyl triflates best results were obtained at 60 °C omitting $^{n}Bu_4NCl$.

Introduction

The aryl sulfone fragment is present in a number of compounds exhibiting important biological activities. For example, sulfone derivatives were found to be potent, selective, and orally active cyclooxygenase-2 (COX-2) inhibitors[1] and to exhibit high antifungal and antibacterial activities.[2] Diaryl sulfones have been shown to possess antitumor activities.[3] Recently, diaryl[4] and aryl heteroaryl[5] sulfones have been shown to inhibit the HIV-1 reverse transcriptase and to represent an emerging class of substances able to address the toxicity and resistance problems of nucleoside inhibitors. They also exhibit interesting chemical properties[6] and are useful intermediates in organic synthesis.[7] Because of this, diaryl sulfones are important synthetic targets, and

† Università degli Studi "La Sapienza".

‡ Università degli Studi della Tuscia.

(1) (a) Ducharme, Y.; Gauthier, J. Y.; Prasit, P.; Leblanc, Y.; Wang, Z.; Leger, S.; Therien, M. US 5474995; *Chem. Abstr.* **1995**, *124*, 201998. (b) Ducharme, Y.; Gauthier, J. Y.; Prasit, P.; Leblanc, Y.; Wang, Z.; Leger, S.; Therien, M. WO 9500501, 1995; *Chem. Abstr.* **1995**, *124*, 55954. (c) Prasit, P.; Wang, Z.; Brideau, C.; Chan, C.-C.; Charleson, S.; Cromlish, W.; Ethier, D.; Evans, J. F.; Ford-Hutchinson, W.; Gauthier, J. Y.; Gordon, R.; Guay, J.; Gresser, M.; Kargman, S.; Kennedy, B.; Leblanc, Y.; Léger, S.; Mancini, J.; O'Neill, G. P.; Ouellet, M.; Percival, M. D.; Perrier, H.; Riendeau, D.; Rodger, I.; Tagari, P.; Thérien, M.; Vockers, P.; Wong, E.; Xu, L.-J.; Young, R. N.; Zamboni, R.; Boyce, S.; Rupniak, N.; Forrest, M.; Visco, D.; Patrick, D. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1773. (d) Catella-Lawson, F.; Mcadam, B.; Morrison, B. W.; Kapoor, S.; Kujubu, D.; Antes, L.; Lasseter, K. C.; Quan, H.; Gertz, B. J.; Fitzgerald, G. A. *J. Pharmacol. Exp. Ther.* **1999**, *289*, 735. (e) Ehrich, E. W.; Dallob, A.; De Lepeleire, I.; Van Hecken, A.; Riendeau, D.; Yuan, W.; Porras, A.; Wittreich, J.; Seibold, J. R.; De Schepper, P.; Mehlisch, D. R.; Gertz, B. J. *Clin. Pharmacol. Ther.* **1999**, *65*, 336. (f) Langman, M. J.; Jensen, D. M.; Watson, D. J.; Harper, S. E.; Zhao, P.-L.; Quan, H.; Bolognese, J. A.; Simon, T. J. *J. Am. Med. Assoc.* **1999**, *282*, 1929.

(2) (a) Richards, I. C.; Thomas, P. S. *Pestic. Sci.* **1990**, *30*, 275. (b) Wolf, W. M. *J. Mol. Struct.* **1999**, *474*, 113. (c) Otzen, T.; Wempe, E. G.; Kunz, B.; Bartels, R.; Lehwark-Yvetot, G.; Hänsel, W.; Schaper, K.-J.; Seydel, J. K. *J. Med. Chem.* **2004**, *47*, 240. See also: *The Merck Index*, 13th ed.; Merck: Rahway, NJ; Monograph nos. 23, 24, 75, 2847, 3013, 3365, 4476, 7015, 7236, 8785, 8962, 9013, 9014, 9058, 9079, 9273, on CD-ROM.

(3) (a) Jones, T. R.; Webber, S. E.; Varney, M. D.; Reddy, M. R.; Lewis, K. K.; Kathardekar, V.; Mazdiyasni, H.; Deal, J.; Nguyen, D.; Welsh, K. M.; Webber, S.; Johnson, A.; Matthews, D. A.; Smith, W. W.; Janson, C. A.; Bacquet, R. J.; Howland, E. F.; Booth, C. L. J.; Ward, R. W.; Herrmann, S. M.; White, J.; Bartlett, C. A.; Morse, C. A. *J. Med. Chem.* **1997**, *40*, 677. (b) Dinsmore, C. J.; Williams, T. M.; O'Neill, T. J.; Liu, D.; Rands, E.; Culberson, J. C.; Lobell, R. B.; Koblan, K. S.; Kohl, N. E.; Gibbs, J. B.; Oliff, A. I.; Graham, S. L.; Hartman, G. D. *Biorg. Med. Chem. Lett.* **1999**, *9*, 3301.

(4) (a) McMahon. J. B.; Gulakowsky, R. J.; Welslow, O. S.; Schoktz, R. J.; Narayanan, V. L.; Clanton, D. J.; Pedemonte, R.; Wassmundt, F. W.; Buckheit, R. W., Jr.; Decker, W. D.; White, E. L.; Bader, J. P.; Boyd, M. R. *Antimicrob. Agents Chemother.* **1993**, *37*, 754. (b) Williams, T. M.; Ciccarone, T. M.; MacTough, S. C.; Rooney, C. S.; Balani, S. K.; Condra, J. H.; Emini, E. A.; Goldman, M. E.; Greenlee, W. J.; Kauffman, L. R.; O'Bnen, J. A.; Sardana, V. V.; Schleif, W. A.; Theoharides, A. D.; Anderson, P. S. *J. Med. Chem.* **1993**, *36*, 1291. (c) Neamati, N.; Mazumder, A.; Zhao, H.; Sunder, S.; Burke, Terrence, R., Jr.; Schultz, R. J.; Pommier, Y. *Antimicrob. Agents Ch.* **1997**, *41*, 385.

(5) (a) Artico, M.; Silvestri, R.; Massa, S.; Loi, A. G.; Corrias, S.; Piras, G.; La Colla, P. *J. Med. Chem.* **1996**, *39*, 522. (b) Artico, M.; Silvestri, R.; Pagnozzi, E.; Bruno, B.; Novellino, E.; Greco, G.; Massa, S.; Ettorre, A.; Loi, A. G.; Scintu, F.; La Colla, P. *J. Med. Chem.* **2000**, *43*, 1886.

(6) (a) Fumio, H.; Mitsuru, K. JP Patent 61271271, 1986; *Chem. Abstr.* **1987**, *106*, 213572. (b) Keiichi, S.; Toru, O.; Aki, S. JP Patent 04120050, 1992; *Chem. Abstr.* **1992**, *117*, 150703. (c) Mitchell, M. A.; Tomida, M.; Padias, A. B.; Hall, H. K., Jr.; Lackritz, H. S.; Robello, D. R.; Willand, C. S.; Williams, D. J. *Chem. Mater.* **1993**, *5*, 1044. (d) Toshiaki, T.; Takeshi Y. JP Patent 2001260544, 2001; *Chem. Abstr.* **2001**, *135*, 264604.

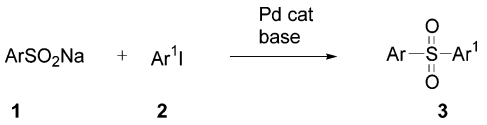
(7) Simpkins, N. S. *Sulfones in Organic Synthesis*; Pergamon Press: Oxford, 1993.

10.1021/jo0493469 CCC: $27.50
Published on Web 07/16/2004

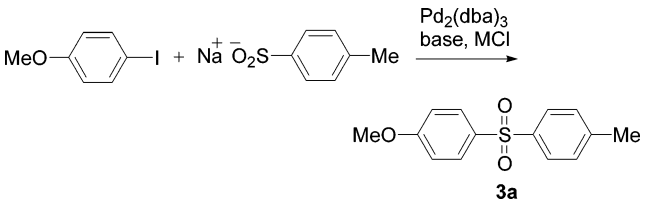
numerous procedures for their preparation have been described, including the oxidation of the corresponding sulfides,[8] the sulfonylation of arenes,[9,10] the reaction of organomagnesium halides[11] or organolithium compounds[12] with sulfonate esters, and the copper-mediated displacement reaction of nonactivated aryl iodides with arenesulfinates.[13] All these procedures, however, have their own drawbacks: the oxidation process is limited by the availability of sulfides, the sulfonylation approach suffers from the formation of mixtures of isomeric products and inefficiency with arenes bearing strongly electron-withdrawing substituents, the employment of organometallic reagents does not tolerate many functionalities, and the copper-mediated displacement uses an excess of copper iodide complicating the workup in large scale preparations. Recently, a copper-catalyzed procedure for the coupling of sulfinate salts and aryl iodides has been developed.[14] However, it does not achieve full conversion of aryl bromides and sulfone products are obtained in low yields when aryl bromides are used. Improved methods for the preparation of sulfone derivatives are therefore highly desirable.

Direct palladium-catalyzed replacement of the C_{aryl}−X (X = I, Br, OTf) bond by a C_{aryl}−SO_2 bond is, to our knowledge, unprecedented. This is in sharp contrast to analogous processes involving the substitution of the C_{aryl}−X bond with an C_{aryl}−heteroatom bond[15] such as C_{aryl}−N, C_{aryl}−PR_2, C_{aryl}−$PO(OR)_2$, and C_{aryl}−SR bonds,

SCHEME 1



SCHEME 2



which have been used extensively in organic synthesis. In attempting to extend the target scope of the C_{aryl}−heteroatom bond-forming technology and to develop a new more convenient synthesis of unsymmetrical sulfones, we observed and previously communicated[16] that the palladium-catalyzed coupling of aryl halides or triflates and arenesulfinates can provide an extremely efficient route to unsymmetrical diaryl sulfones (Scheme 1).

We wish at this time to report full details on this very useful straightforward synthetic approach to this class of compounds.

Results and Discussion

Initial attempts focused on exploring the feasibility of the transformation. *p*-Iodoanisole and the commercially available sodium *p*-toluenesulfinate were used as the model system (Scheme 2). Reactions were carried out using $Pd_2(dba)_3$ as the precatalyst and the following reaction variables were examined: the presence or absence of phosphine or carbene ligands, the base, the added salt, the solvent, and the reaction temperature. All the reactions were conducted on a 0.35 mmol scale in 2 mL of solvent under argon, using 1.2 equiv of sodium *p*-toluenesulfinate, 0.025 equiv of $Pd_2(dba)_3$, 0.05 equiv of bidentate ligand or 0.1 equiv of monodentate ligand, 1.5 equiv of base, and 1.2 equiv of $^nBu_4NCl$ or lithium chloride (when added). Some results from that study are summarized in Table 1.

Essentially no sulfone product was formed after 6 h at 80 °C in a variety of solvents (DMSO, DMF, DME, dioxane, toluene), adding or omitting $^nBu_4NCl$, in the presence or absence of Cs_2CO_3, K_2CO_3, or Li_2CO_3, with a variety of monodentate and bidentate phosphine ligands such as PPh_3, (*o*-tol)$_3$P, (2-furyl)$_3$P, (*p*-MeO-C_6H_4)$_3$P (tmpp), [2,4,6-(MeO)$_3$-C_6H_2]$_3$P (ttmpp), (*p*-Cl-C_6H_4)$_3$P, BINAP [2,2′-bis(diphenylphosphino)-1,1′-binaphthyl], MOP [2-(diphenylphosphino)-2′-methoxy-1,1′-binaphthyl], dppp [1,1′-bis(diphenylphosphino)propane], dppb [1,1′-bis(diphenylphosphino)butane], and with 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride, which has been shown to generate in situ, in the presence of Cs_2CO_3 as the base, the corresponding carbene ligand.[17]

(8) (a) Schank, K. In *The Chemistry of Sulfones and Sulfoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; Wiley: New York, 1988; Chapter 7. (b) Greenhalgh, R. P. *Synlett* **1992**, 235. (c) Reddy, R. S.; Reddy, J. S.; Kumar, R.; Kumar, P. *J. Chem. Soc., Chem. Commun.* **1992**, 84. (d) Hanna, N. B.; Bhattacharya, B. K.; Robins, R. K.; Avery, T. L.; Revankar, G. R. *J. Med. Chem.* **1994**, *37*, 177. (e) Aldea, R.; Alper, H. *J. Org. Chem.* **1995**, *60*, 8365. (f) Bosch, E.; Kochi, J. K. *J. Org. Chem.* **1995**, *60*, 3172. (g) Arterburn, J. B.; Nelson, S. L. *J. Org. Chem.* **1996**, *61*, 2260. (h) Reddy, T. I.; Varma, R. S. *Chem. Commun.* **1997**, 471. (i) Varma, R. S.; Saini, R. K.; Meshram, H. M. *Tetrahedron Lett.* **1997**, *38*, 6525.

(9) Electrophilic aromatic substitution of arenes with arenesulfonic acids in the presence of strong acids: (a) Graybill, B. M. *J. Org. Chem.* **1967**, *32*, 2931. (b) Ueda, M.; Uchiyama. K.; Kano, T. *Synthesis* **1984**, 323.

(10) Electrophilic aromatic substitution of arenes with arenesulfonyl halides: (a) Truce, W, E.; Klinger,T, C.; Brand. W. W. In *Organic Chemistry of Sulfur*; Oae, S., Ed.; Plenum Press: New York, 1977. (b) Nara, S. J.; Harjani, J. R.; Salunkhe, M. M. *J. Org. Chem.* **2001**, *66*, 8616. (c) Frost, C. G.; Hartley, J. P.; Whittle, A. J. *Synlett* **2001**, 830. (d) Bandgar, B. P.; Kasture, S. P. *Synthetic Commun.* **2001**, *31*, 1065. Marquié, J.; Laporterie, A.; Dubac, J.; Roques, N.; Desmurs, J.-R. *J. Org. Chem.* **2001**, *66*, 421.

(11) Gilman, H.; Beaver, N. J.; Meyers, C. H. *J. Am. Chem. Soc.* **1925**, *47*, 2047.

(12) Baarschers, W. H. *Can. J. Chem.* **1976**, *54*, 3056.

(13) Suzuki, H.; Abe, H. *Tetrahedron Lett.* **1995**, *36*, 6239.

(14) Baskin, J. M.; Wang, Z. *Org. Lett.* **2002**, *4*, 4423.

(15) For a recent review on the palladium-catalyzed reaction of aryl halides with soft nonorganometallic nucleophiles, see: (a) Prim, D.; Campagne, J. M.; Joseph, D.; Andrioletti, B. *Tetrahedron* **2002**, *58*, 2041. For some recent references on the substitution of C_{aryl}−halogen bonds with C_{aryl}−N bonds, see: (b) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 6043. (c) Maes, B. U. W.; Loones, K. T. J.; Jonckers, T. H. M.; Lemiere, G. L. F.; Dommisse, R. A.; Haemers, A. *Synlett* **2002**, 1995. (d) Urgaonkar, S.; Nagarajan, M.; Verkade, J. G. *J. Org. Chem.* **2003**, *68*, 452. (e) Ferreira, I. C. F. R.; Queiroz, M.-J. R. P.; Kirsch, G. *Tetrahedron* **2003**, *59*, 3737. For some recent references on the substitution of C_{aryl}−halogen bonds with C_{aryl}−PR_2 bonds, see: (f) Brauer, D. J.; Hingst, M.; Kottsieper, K. W.; Liek, C.; Nickel, T.; Tepper, M.; Stelzer, O.; Sheldrick, W. S. *J. Organomet. Chem.* **2002**, *645*, 14. For recent references on the substitution of C_{aryl}−halogen bonds with C_{aryl}−SR bonds, see: (g) Menger, F. M.; Azov, V. A. *J. Am. Chem. Soc.* **2002**, *124*, 11159. (h) Brown, M. J.; Carter, P. S.; Fenwick, A. E.; Fosberry, A. P.; Hamprecht, D. W.; Hibbs, M. J.; Jarvest, R. L.; Mensah, L.; Milner, P. H.; O'Hanlon, P. J.; Pope, A. J.; Richardson, C. M.; West, A.; Witty, D. R. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 3171.

(16) (a) Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Parisi, L. M. *Org. Lett.* **2002**, *4*, 4719. (b) Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Parisi, L. M. *Synlett* **2003**, 361.

(17) Zhang, C.; Huang, J.; Trudell, M. L.; Nolan, S. P. *J. Org. Chem.* **1999**, *64*, 3804.

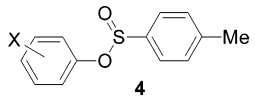
TABLE 1. Bases, Additives, and Solvents in the Reaction of *p*-Iodoanisole with Sodium *p*-Toluenesulfinate in the Presence of $Pd_2(dba)_3$ and Xantphos To Give *p*-Methoxyphenyl Tolyl Sulfone 3a[a]

entry	solvent	base	salt	time (h)	yield % of *p*-methoxyphenyl tolyl sulfone **3a**[b]
1	toluene		$^nBu_4NCl$	24	49
2	toluene	Cs_2CO_3		8	70
3	toluene			24	*c*
4[d]	toluene	Cs_2CO_3		36	
5[d]	toluene			48	
6	toluene	Cs_2CO_3	$^nBu_4NCl$	1	90[e]
7	toluene	Li_2CO_3	$^nBu_4NCl$	6	70
8	toluene	K_2CO_3	$^nBu_4NCl$	6	58
9	toluene	Rb_2CO_3	$^nBu_4NCl$	6	76
10	toluene	AcOK	$^nBu_4NCl$	6	55
11	toluene	Cs_2CO_3	LiCl	48	31
12	toluene	Cs_2CO_3	$^nBu_4NCl$	24	80[f]
13	toluene	Cs_2CO_3	$^nBu_4NCl$	4	81[g]
14	DME	Cs_2CO_3	$^nBu_4NCl$	2	79
15	dioxane	Cs_2CO_3	$^nBu_4NCl$	2	81
16	DMSO	Cs_2CO_3	$^nBu_4NCl$	24	9[h]
17	DMF	Cs_2CO_3	$^nBu_4NCl$	24	22[i]
18	DMF	Cs_2CO_3		24	29[j]
19	DMF	Li_2CO_3	$^nBu_4NCl$	24	20[k]
20	DMF		$^nBu_4NCl$	24	21[l]

[a] Unless otherwise stated, reactions were carried out on a 0.35 mmol scale, under argon, in 2 mL of solvent using 1 equiv of *p*-iodoanisole, 1.2 equiv of sodium *p*-toluenesulfinate, 0.025 equiv of $Pd_2(dba)_3$, 0.05 equiv of Xantphos, 1.5 equiv of base, and 1.2 equiv of $^nBu_4NCl$ or LiCl (when added). [b] Yields are given for isolated products. [c] *p*-Iodoanisole was recovered in 83% yield. [d] In the absence of Xantphos. [e] 81% in 6 h, under the same conditions, with toluenesulfinic acid lithium salt. [f] At 40 °C. [g] At 60 °C. [h] *p*-Iodoanisole was recovered in 70% yield. [i] *p*-Iodoanisole was recovered in 45% yield. The ester **4a** was isolated in 9% yield. [j] *p*-Iodoanisole was recovered in 52% yield. The ester **4a** was isolated in 4% yield. [k] *p*-Iodoanisole was recovered in 47% yield. The ester **4a** was isolated in 5% yield. [l] *p*-Iodoanisole was recovered in 47% yield. The ester **4a** was isolated in 3% yield.

Only after switching to Xantphos [9,9-dimethyl-4,6-bis-(diphenylphosphino)xanthene],[18] a rigid bidentate ligand with a wide natural bite angle,[19] did the desired sulfone product, **3a**, form in moderate yield within 24 h at 80 °C in the presence of $^nBu_4NCl$ (Table 1, entry 1). Compound **3a** was isolated in 70% yield in 8 h in the presence of Cs_2CO_3 omitting $^nBu_4NCl$ (Table 1, entry 2), whereas no sulfone product was observed omitting both Cs_2CO_3 and $^nBu_4NCl$ (Table 1, entry 3). The yield increased to 90% in 1 h by adding both Cs_2CO_3 and $^nBu_4NCl$[20,21] (Table 1, entry 6). At lower temperatures, 40 and 60 °C, **3a** is still isolated in high yield, but longer reaction times are required (Table 1, entries 12 and 13). From these studies, at least with our model reaction, it appears that the best base for this substitution reaction is Cs_2CO_3. Lower reaction rate and/or yield were observed with Li_2CO_3 (Table 1, entry 7), K_2CO_3 (Table 1, entry 8), Rb_2CO_3 (Table 1, entry 9) and AcOK (Table 1, entry 10). The use of $^nBu_4NCl$ is clearly superior to LiCl (Table 1, compare entry 6 with entry 11). Use of more polar solvents such as dioxane and DME proved less satisfactory whereas in DMSO and DMF yields were very low. In DMF, formation of small amounts of the ester **4a** (X = *p*-OMe), generated through the competitive *O*-arylation of the ambident sulfinate anion, was also observed.

The use of $Pd(OAc)_2$ (0.05 equiv) as the precatalyst was also attempted and, in the presence of Xantphos, Cs_2CO_3, and $^nBu_4NCl$, in toluene at 80 °C, sulfone **3a** was isolated in a satisfactory 78% yield after 6 h. Interestingly, employing Pd/C (5%) under the same conditions afforded the desired sulfone in 69% yield after 20 h. Most probably, the active species is a soluble Pd−Xantphos complex which is formed via leaching of palladium into solution.[22] Accordingly, no sulfone product was observed after 20 h when the same reaction was carried out omitting Xantphos.



4

As indicated in Table 2, a wide variety of neutral, electron-rich, and electron-poor aryl iodides were converted into the corresponding unsymmetrical diaryl sulfones, usually in high yields, under the best conditions developed so far [$Pd_2(dba)_3$, Xantphos, Cs_2CO_3, $^nBu_4NCl$, toluene, 80 °C]. The reaction tolerates important functional groups, amenable to further functionalization. For example, the high I/Br selectivity observed with *p*-bromoiodobenzene (Table 2, entry 14) allows a ready access to amino derivatives[23] as shown in Scheme 3. The *aryl-sulfonyl-phenyl-piperidine* motif is present in compounds prepared as β3 adrenergic receptor agonists.[24] Only *p*-iodoacetophenone, among the substrates that we have investigated, produced a complex reaction mixture (most probably as the result of ketone arylation processes)[25] that we have not further investigated (Table 2,

(18) Kranenburg, M.; van der Burgt, Y. E. M.; Kramer, P. C. J.; van Leeuwen, P. W. N. M.; Goubitz, K.; Fraanje, J. *Organometallics* **1995**, *14*, 3081. For recent reviews on the use of Xantphos ligands in transition metal-catalyzed reactions, see: van Leeuwen, P. W. N. M.; Kramer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem Rev.* **2000**, *100*, 2741. Kramer, P. C. J.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *Acc. Chem. Res.* **2001**, *34*, 895.

(19) Casey, C. P.; Whiteker, G. T. *Isr. J. Chem.* **1990**, *30*, 299.

(20) For the influence of halide additives on Pd(0)-catalyzed reactions, see: (a) Jeffery, T *J. Chem. Soc., Chem. Commun.* **1984**, 1287. (b) Scott, J. W.; Crisp, G. T.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4630. (c) Amorese, A.; Arcadi, A.; Bernocchi, E.; Cacchi, S.; Cerrini, S.; Fedeli, W.; Ortar, G. *Tetrahedron* **1989**, *45*, 813. (d) Larock, R. C.; Leung, W.-Y.; Stolz-Dunn, S. *Tetrahedron Lett.* **1989**, *30*, 6629. (e) Loupy, A.; Tchoubar, B. *Salt Effects in Organic and Organometallic Chemistry*; VCH: Weinheim, 1992; pp 254−272. (f) Jeffery, T.; Gallang, J. C. *Tetrahedron Lett.* **1994**, *35*, 4103. (g) Herrmann, W. H.; Brossmer, C.; Öfele, K.; Reisinger, C.-P.; Priermeier, T.; Beller, M.; Fisher, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1844. (h) Cacchi, S.; Fabrizi, G.; Marinelli, F.; Pace, P. *Tetrahedron* **1996**, *52*, 10225. (i) Jeffery, T. *Tetrahedron* **1996**, *52*, 10113. (j) Goodson, F. E.; Wallow, T. I.; Novak, B. M. *J. Am. Chem. Soc.* **1997**, *119*, 12441. (k) Cook, G. R.; Shanker, P. S. *Tetrahedron Lett.* **1998**, *39*, 4991. (l) Roesch, K. R.; Larock, R. C. *Org. Lett.* **1999**, *1*, 1551. (m) Wang, Z.; Zhang, Z.; Lu, X. *Organometallics* **2000**, *19*, 775. (n) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Pace, P. *Eur. J. Org. Chem.* **2000**, 4099. (o) Zhang, Z.; Lu; X.; Xu, Z.; Zhang, Q.; Han, X. *Organometallics* **2001**, *20*, 3724. (p) Larock R. C.; Reddy, C. K. *J. Org. Chem.* **2002**, *67*, 2027. For a recent review, see: (q) Amatore, C.; Jutand, A. *Acc. Chem. Res.* **2000**, *33*, 314.

(21) For the influence of halide additives on divalent palladium-catalyzed reactions, see: (a) Bäckvall, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1980**, *102*, 393. (b) Bäckvall, J. E.; Åkermark, B.; Ljunggren, S. O. *J. Am. Chem. Soc.* **1979**, *101*, 2411. (c) Simone, D. O.; Kennelly, T.; Brungard, N. L.; Farrauto, R. J. *Appl. Catal.* **1991**, *70*, 87. (d) Francis, J. W.; Henry, P. M. *J. Mol. Catal. A Chem.* **1995**, *99*, 77. (e) Harrington, P. J. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: New York, 1995; Vol. 12, pp 797, 904. (f) Widenhoefer, R. A.; Buchwald, S. L. *Organometalllcs* **1996**, *15*, 2755. (g) Bäckvall, J. E. In *Metal-Catalyzed Cross-Coupling Reactions;* Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; pp 339−385.

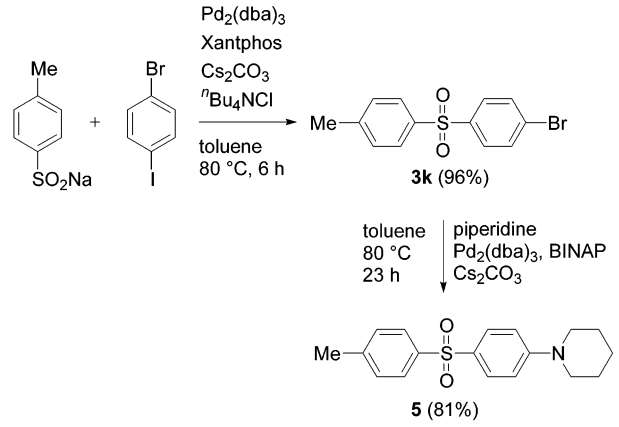
(22) Novák, Z.; Szabó, A.; Répási, J.; Kotschy, A. *J. Org. Chem.* **2003**, *68*, 3327.

TABLE 2. Palladium-Catalyzed Synthesis of Diaryl Sulfones from Aryl Iodides 2 and Sodium *p*-Toluenesulfinate 1[a]

entry	aryl iodide **2**	time (h)	diaryl sulfone **3** yield[b] (%)
1	*p*-MeO-C_6H_4-I	1	90, **a**
2	*m*-MeO-C_6H_4-I	1	88, **b**
3	*o*-MeO-C_6H_4-I	24	
4	*p*-Me-C_6H_4-I	6	96, **c**
5	*m*-Me-C_6H_4-I	1	93, **d**
6	*o*-Me-C_6H_4-I	24	
7	3,5-Me_2-C_6H_3-I	1	85, **e**
8	PhI	1	90, **f**
9	*p*-F-C_6H_4-I	1	89, **g**
10	*m*-F-C_6H_4-I	5	90, **h**
11	*o*-F-C_6H_4-I	24	
12	*p*-Cl-C_6H_4-I	3	81, **i**
13	*m*-CF_3-C_6H_4-I	24	46, **j**
14	*p*-Br-C_6H_4-I	1	67, **k**
15	*p*-EtO_2C-C_6H_4-I	6	65, **l**
16	*p*-MeCO-C_6H_4-I	7	
17	*p*-O_2N-C_6H_4-I	1	72, **m**

[a] Reactions were conducted on a 0.35 mmol scale in starting aryl iodides in toluene (2 mL) at 80 °C under argon using 1.2 equiv of **1**, 0.025 equiv of $Pd_2(dba)_3$, 0.05 equiv of Xantphos, 1.5 equiv of Cs_2CO_3, and 1.2 equiv of $^nBu_4NCl$. [b] Yields are given for isolated products.

SCHEME 3



entry 16). Lowering the temperature to 60 °C resulted in a substantial slower reaction. No sulfone product was, however, formed after 20 h, *p*-iodoacetophenone was recovered in only 5% yield, and formation of significant amount of tar was observed. The presence of substituents close to the C−I bond was found to hamper the reaction (Table 2, entries 3, 6, and 11).

Extension of the procedure to include aryl bromides and triflates, a target of obvious interest for academic and industrial applications, was then attempted. Using the reaction of sodium *p*-toluenesulfinate and 4-bromo biphenyl as a model system, we were pleased to find that the desired sulfone derivative **3o** could be obtained in 87% isolated yield after 24 h under the same conditions [$Pd_2(dba)_3$, Xantphos, Cs_2CO_3, $^nBu_4NCl$, in toluene], increasing the temperature to 120 °C (Table 3, entry 2). Even in this case the addition of $^nBu_4NCl$ proved crucial for the success of the reaction. Compound **3o** was isolated in only 18% yield when sodium *p*-toluenesulfinate and 4-bromobiphenyl were treated under the same conditions omitting $^nBu_4NCl$ (Table 3, entry 3; see also Table 4, compare entries 3 and 5 with, respectively, entries 4 and 6).

When the procedure was extended to electron-poor aryl bromides, a dramatic decrease in efficiency was observed. In fact, subjecting *m*-nitrophenyl bromide to the same conditions afforded the corresponding sulfone in only 20% yield (Table 3, entry 6). In addition, the toluenesulfinic acid ester **4t** (X = *m*-NO_2) was isolated in 17% yield along with *n*-butyl *p*-toluenesulfinate (15% yield), generated through a nucleophilic substitution reaction involving sodium *p*-toluenesulfinate and $^nBu_4NCl$. We then went back and reexamined the influence on the reaction outcome of some variables, such as ligands, the amounts of sulfinate salts, and the added salts. Using other bidentate phosphine ligands such as dppf [1,1′-bis-(diphenylphosphino)ferrocene] only trace amounts of sulfone were obtained and the yield of the ester **4t** increased to 43% (Table 3, entry 7). Increasing the sulfinate salt to aryl bromide molar ratio produced only a moderate increase of the yield (Table 3, entry 9) and the employment of other ammonium salts did not provide any beneficial effect. The use of both $^nBu_4NBr$ and $^nBu_4NI$ produced low yields of the sulfone derivative and almost equimolar amounts of the sulfinic acid ester (Table 3, entries 12 and 13). Surprisingly, the best result in terms of yield and reaction time was obtained by omitting the ammonium salt (Table 3, entry 14). None of the sulfinic acid ester was observed under these conditions and the sulfone derivative was isolated in 89% yield. The negative effect of $^nBu_4NCl$ on the reaction yield observed with *m*-nitrophenyl bromide resulted to be quite general with electron-poor aryl bromides and triflates. A variety of aryl donors of this type afforded sulfone products in low yields in the presence of $^nBu_4NCl$ (Table 4, entries 19, 21, 27, 30, 32, and 35) or, in any case, lower than without $^nBu_4NCl$ (Table 4, entry 15).

Therefore, two general procedures were employed when the reaction was extended to include other aryl bromides and triflates:[26] procedure A (with neutral, electron-rich, and slightly electron-poor aryl bromides or triflates)—sodium *p*-toluenesulfinate, $Pd_2(dba)_3$, Xantphos, Cs_2CO_3, $^nBu_4NCl$, 120 °C, toluene; procedure B (with electron-poor aryl bromides or triflates)—sodium *p*-toluenesulfinate, $Pd_2(dba)_3$, Xantphos, Cs_2CO_3, 120 °C, toluene. Under these conditions, the reaction gives unsymmetrical diaryl sulfones in good to high yields with

(23) For some reviews on the substitution of the C_{aryl}−X bond with a C_{aryl}−N bond, see: (a) Hartwig, J. F. *Synlett* **1997**, 329. (b) Baranano, D.; Mann, G.; Hartwig, J. F. *Curr. Org. Chem.* **1997**, *1*, 287. (c) Hartwig, J. F. *Acc. Chem. Res.* **1998**, *31*, 852. (d) Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805. (e) Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046. (f) Hartwig, J. F. *Pure Appl. Chem.* **1999**, *71*, 1417. (g) Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem.* **1999**, *576*, 125. See also: (h) Prim, D.; Campagne, J.-M.; Joseph, D.; Andrioletti, B. *Tetrahedron* **2002**, *58*, 2041.

(24) Sum, F.-W.; Malamas, M. S. WO 2002006274, 2002; *Chem. Abstr.* **2002**, *136*, 134678.

(25) Fox, J. M.; Huang, X.; Chieffi, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 1360. (b) Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 1473. (c) Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Zappia, G. *Org. Lett.* **2001**, *3*, 2539.

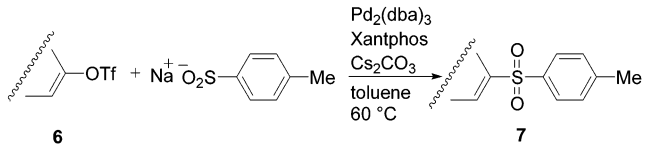
(26) For other reactions in which electron-rich and electron-poor substrates require different conditions, see, for example: (a) Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805. (b) Yin, J.; Buchwald, L. S. *Org. Lett.* **2000**, *2*, 1101. (c) Reference 23c. (d) Rutherford, J. F.; Rainka, M. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 15168.

TABLE 3. Optimization for Neutral and Electron-Poor Aryl Bromides[a]

entry	aryl bromide	ligand	salt	base	*T* (°C)	time (h)		yield %[b]		S/O arylation ratio
1	*p*-Ph-C_6H_4-Br	Xantphos	^{n}Bu$_4$NCl	Cs_2CO_3	100	24	**3o**	11	**4o**	
2		Xantphos	^{n}Bu$_4$NCl	Cs_2CO_3	120	2		87		
3		Xantphos		Cs_2CO_3	120	24		18[c]		
4		Xantphos	^{n}Bu$_4$NCl		120	24				
5		Xantphos			120	24				
6	*m*-O_2N-C_6H_4-Br	Xantphos	^{n}Bu$_4$NCl	Cs_2CO_3	120	24	**3t**	20	**4t**	17[d] 1.17
7		dppf	^{n}Bu$_4$NCl	Cs_2CO_3	120	24		traces		43
8		dppf	^{n}Bu$_4$NCl	Cs_2CO_3	120	24		traces		30[e]
9		Xantphos	^{n}Bu$_4$NCl	Cs_2CO_3	120	24		27[f]		
10		Xantphos	^{n}Bu$_4$NCl		120	24		26		30 0.87
11		Xantphos	^{n}Bu$_4$NCl		120	24		27		33[g] 0.82
12		Xantphos	^{n}Bu$_4$NBr	Cs_2CO_3	120	22		19		20 0.93
13		Xantphos	^{n}Bu$_4$NI	Cs_2CO_3	120	27		28		22 1.23
14		Xantphos		Cs_2CO_3	120	8		89		
15		Xantphos		Cs_2CO_3	120	24		73[h]		

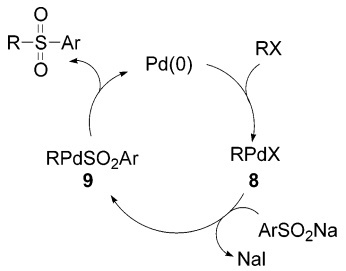
[a] Unless otherwise stated, reactions were carried out on a 0.35 mmol scale under an argon atmosphere using 1 equiv of bromide, 1.2 equiv of sodium *p*-toluenesulfinate, 0.025 equiv of $Pd_2(dba)_3$, 0.05 equiv of ligand, 1.5 equiv of Cs_2CO_3, and 1.2 equiv of ammonium salt in 2 mL of toluene at 120 °C. [b] Yields are given for isolated products. [c] 4-Bromobiphenyl was recovered in 74% yield. [d] *n* Butyl *p*-toluenesulfinate was isolated in 15% yield. [e] The reaction was carried out by using $Pd(OAc)_2$. [f] **1**/aryl bromide = 2:1. [g] In DMF. [h] The reaction was carried out using *p*-Me-C_6H_4-SO_2Li.

SCHEME 4



6 **7**

SCHEME 5



many neutral, electron-rich and electron-poor aryl and heteroaryl bromides or triflates and tolerates a variety of functional groups, including ether, cyano, aldehyde, and nitro groups. The best results obtained during this study are summarized in Table 4.

Finally, the procedure was extended to vinyl triflates to prepare aryl vinyl sulfones (Scheme 4). Vinyl sulfones have been recently shown to act as inhibitors of SrtA, a transpeptidase required for cell wall protein anchoring and virulence in *Staphylococcus aureus*.[27] Our preparative results are shown in Table 5. Even in this case, omitting ^{n}Bu$_4$NCl appears to play a beneficial effect on the reaction outcome (Table 5, compare entry 1 with entry 2). Reactions were run at 60 °C. At 80 °C complex reaction mixtures were obtained, at least with 4-phenylcyclohex-1-en-1-yl triflate, the compound we used as the model triflate. Interestingly, the vinyl triflate **6f**, containing an acetyl fragment at the C-17, gave the corresponding sulfone derivative in 70% yield (Table 5, entry 7) though the reaction failed with *p*-iodoacetophenone (Table 2, entry 16), most probably because of ketone arylation processes.[25] The higher acidity of the methyl protons of aromatic methyl ketones,[28] favoring the formation of enolate nucleophiles, can account for this result.

This synthesis of unsymmetrical sulfones presumably proceeds via the following basic steps (the ligand has been omitted for clarity): (a) oxidative addition of the organic halide or triflate to Pd(0), (b) selective nucleophilic displacement of the halide or triflate of the resultant organopalladium intermediate **8** by the sulfur atom of the ambident sulfinate anion to give the sulfonylpalladium intermediate **9**, and (c) reductive elimination of a Pd(0) species to give the sulfone product and regenerate the palladium catalyst (Scheme 5).

Xantphos has been proved to be crucial for the success of the reaction. Though the reasons for such a beneficial influence of this ligand are not straightforward to elucidate and we have not investigated this point, it is likely that the close proximity of the oxygen to the palladium center (with the possibility of assisting the displacement of the leaving group from palladium)[29] and/or the known ability of chelating diphosphines with large bite angle to promote the product-forming reductive elimination step[30] play an important role.

As to the role of ^{n}Bu$_4$NCl in controlling the reaction outcome, it is conceivable that this ammonium salt acts as a source of chloride ions,[31] whose effect is to stabilize palladium species as proposed by Amatore and Jutand.[20q] Furthermore, the large ammonium cation can stabilize halide ligated zerovalent or divalent palladium-centered complexes.[32] ^{n}Bu$_4$NCl is superior to LiCl in this respect. However, the fact that with electron-poor aryl bromides the best results in terms of yield and *S*/*O* arylation ratio

(27) Frankel, B. A.; Bentley, M.; Kruger, R. G.; McCafferty, D. G. *J. Am. Chem. Soc.* **2004**, *126*, 3404.

(28) The pK_a values for acetophenone and acetone in dimethyl sulfoxide solutions are, respectively, 24.7 and 26.5: Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.

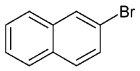
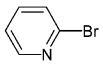
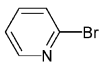
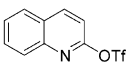
(29) Guari, Y.; van Stijdonck, G. P. F.; Boele, M. D. K.; Reek, J. N. H.; Kamer, P. C. J.; Van Leeuwen, P. W. N. M. *Chem. Eur. J.* **2001**, *7*, 475.

(30) For a recent review on wide bite angle diphosphines in transition-metal catalysis, see: Kamer, P. C. J.; Van Leeuwen, P. W. N. M.; Reek, J. N. H. *Acc. Chem. Res.* **2001**, *34*, 895.

(31) For a recent review on halide effects in transition metal catalysis, see: Fagnou, K.; Lautens, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 26.

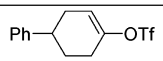
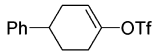
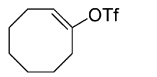
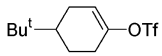
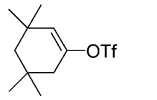
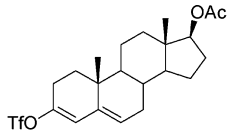
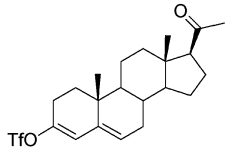
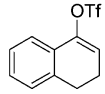
(32) Amatore, C.; Jutand, A.; Suarez, A. *J. Am. Chem. Soc.* **1993**, *115*, 9531.

TABLE 4. Synthesis of Unsymmetrical Diaryl Sulfones through the Palladium-Catalyzed Reaction of Sodium *p*-Toluenesulfinate 1 with Aryl and Heteroaryl Bromides or Triflates 2[a]

entry	aryl/heteroaryl bromide or triflate **2**	procedure	time (h)	yield %[b,c] of **3**	
1	*p*-MeO-C_6H_4-Br	A	24	**3a**	93
2	*p*-MeO-C_6H_4-Br	B	24	**3a**	46
3	*p*-MeO-C_6H_4-OTf	A	22	**3a**	89
4	*p*-MeO-C_6H_4-OTf	B	22	**3a**	72
5	*p*-Me_2N-C_6H_4-Br	A	20	**3n**	72
6	*p*-Me_2N-C_6H_4-Br	B	20	**3n**	26
7	*m*-MeO-C_6H_4-Br	A	2	**3b**	90
8	*p*-Me-C_6H_4-Br	A	2.5	**3c**	93
9	*m*-Me-C_6H_4-Br	A	2	**3d**	92
10	3,5-Me_2-C_6H_3-Br	A	2	**3e**	82
11	PhBr	A	7	**3f**	91
12	PhOTf	A	7	**3f**	82
13	*p*-F-C_6H_4-Br	A	19	**3g**	74 (21)
14	*p*-F-C_6H_4-Br	B	24	**3g**	73
15	*m*-F-C_6H_4-Br	A	24	**3h**	73
16	*m*-F-C_6H_4-Br	B	24	**3h**	80
17	*m*-CF_3-C_6H_4-Br	A	10	**3j**	73
18	*p*-NO_2-C_6H_4-Br	B	5	**3m**	78 (7)
19	*p*-NO_2-C_6H_4-Br	A	5	**3m**	57
20	*p*-NO_2-C_6H_4-OTf	B	20	**3m**	57 (19)
21	*p*-NO_2-C_6H_4-OTf	A	20	**3m**	traces
22	*p*-Ph-C_6H_4-Br	A	2	**3o**	87
23	*p*-Ph-C_6H_4-ONf	A	6	**3o**	71
24	*p*-Bu^t-C_6H_4-Br	A	24	**3p**	67
25		A	8	**3q**	80
26	*p*-CN-C_6H_4-Br	B	7	**3r**	85
27	*p*-CN-C_6H_4-Br	A	24	**3r**	35 (14)
28	*p*-CN-C_6H_4-OTf	B	22	**3r**	67
29	*m*-CN-C_6H_4-Br	B	7	**3s**	85
30	*m*-CN-C_6H_4-Br	A	24	**3s**	40 (23)
31	*m*-NO_2-C_6H_4-Br	B	8	**3t**	89
32	*m*-NO_2-C_6H_4-Br	A	24	**3t**	20 (17)
33	*p*-CHO-C_6H_4-Br	B	37	**3u**	65
34		B	24	**3v**	52
35		A	24	**3v**	28
36		B	4	**3w**	31

[a] Reaction conditions (0.35 mmol scale, 2 mL of toluene): (procedure A) 1.0 equiv of organic bromide or triflate, 1.2 equiv of sodium *p*-toluenesulfinate, 0.025 equiv of $Pd_2(dba)_3$, 0.05 equiv of Xantphos, 1.5 equiv of Cs_2CO_3, 1.2 equiv of $^nBu_4NCl$, toluene, 120 °C, under argon; (procedure B) same molar ratios, solvent, and temperature of procedure A omitting $^nBu_4NCl$. [b] Yields are given for isolated products. [c] Figures in parentheses refer to isolated sulfinic esters **4**.

TABLE 5. Synthesis of Vinyl Aryl Sulfones 7 through the Palladium-Catalyzed Reaction of Sodium *p*-Toluenesulfinate 1 with Vinyl Triflates 6[a]

entry	vinyl triflate **6**		time (h)	yield % of **6**[b]	
1		**6a**	20	**7a**	75
2		**6a**	20	**7a**	53[c]
3		**6b**	24	**7b**	31
4		**6c**	16	**7c**	69
5		**6d**	16	**7d**	80
6		**6e**	24	**7e**	67
7		**6f**	9	**7f**	70
8		**6g**	24	-	[d]

[a] Unless otherwise stated, reactions were carried out on a 0,35 mmol scale under the following conditions: 1.0 equiv of bromide or triflate, 1.2 equiv of sodium *p*-toluenesulfinate, 0.025 equiv of $Pd_2(dba)_3$, 0.05 equiv of Xantphos, 1.5 equiv of Cs_2CO_3, toluene, 60 °C, under argon. [b] Yields are given for isolated products. [c] In the presence of 1.2 equiv of $^nBu_4NCl$. [d] The starting triflate was recovered in 66% yield.

have been obtained in the absence of $^nBu_4NCl$, whereas its presence is required to achieve the best results with electron-rich aryl bromides, appears to call for further considerations.

The rationalization that may be advanced to account for the observed dichotomy of behavior has its origin in differential ion-pairing effects. In the presence of $^nBu_4NCl$, a tetrabutylammonium sulfinate salt can be generated in situ, which is expected to exist as a relatively loose ion-pair in toluene. Furthermore, addition of a salt increases the solvent polarity and a more polar solvent can favor the formation of a loose ion pair. With arylpalladium bromides containing electron-poor aryl fragments, a charge controlled reaction may become an important reaction pathway. In fact, the palladium atom of the arylpalladium intermediate possesses a substantial cationic character (the effect of the electron-withdrawing substituent on the aromatic ring combines with the electron-withdrawing effect of bromine) and can show a tendency to react with the more electronegative site of the ambident sulfinate nucleophile.[33] Sulfinate esters may form as significant side products. In the absence of $^nBu_4NCl$, sodium sulfinate is likely to exist as a tight ion-

pair. The oxygen is shielded by the associated metal atom and the reaction of the ambident sulfinate nucleophile with the palladium intermediate involves preferentially the sulfur atom. In this case, sulfones are by far the main reaction products. In general, a similar reasoning can account for the behavior of aryl and vinyl triflates.

With aryl iodides, the presence of iodide in the coordination sphere of palladium most probably limits the cationic character of palladium and the reaction of the sulfinate anion with the arylpalladium intermediate is primarily controlled by the softer character of the sulfur atom, in the presence or absence of $^{n}Bu_4NCl$, with electron-rich and electron-poor aryl iodides.

To sum up, it seems that this new palladium-catalyzed transformation is a useful route for the synthesis of unsymmetrical diaryl sulfones and aryl vinyl sulfones, providing an attractive complement to existing methods. Sulfones are usually isolated in good to high yields and, although substituents close to the oxidative addition site hamper the reaction, the method merits attention due to the tolerance of a wide range of substituents, the simplicity of the experimental procedure, and the use of readily available starting materials.

Acknowledgment. This work was carried out in the framework of the National Project "Stereoselezione in Sintesi Organica. Metodologie ed Applicazioni" supported by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Rome. We are also greatly indebted to the University "La Sapienza" for financial support of this research.

Supporting Information Available: Experimental procedure and a complete description of product characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0493469

(33) For the behavior of the ambident sulfinate anion with hard and soft electrophiles, see: (a) Meek, J. S.; Fowler, J. S. *J. Org. Chem.* **1968**, *33*, 3422. See also: (b) Grossert, J. S.; Dubey, P. K.; Elwood, T. *Can. J. Chem.* **1985**, *63*, 1263. (c) Schank, K.; Weber, A. *Synthesis* **1970**, 367.