Catalytic Coupling of Aryl Sulfonates with sp^2-Hybridized Nitrogen Nucleophiles: Palladium- and Nickel-catalyzed Synthesis of *N*-Aryl Sulfoximines

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Dedicated to Professor Dr. B. Giese, Basel, with best wishes on the occassion of his 60th birthday

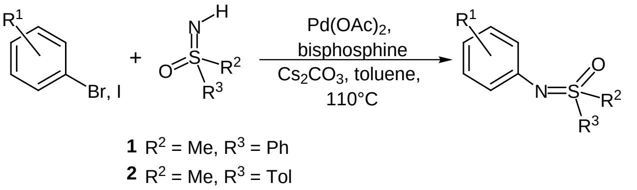
Abstract: Several sulfoximines have been arylated in good to high yield by palladium catalysis using aryl nonaflates and aryl triflates. Moreover, the successful synthesis of *N*-aryl sulfoximines from aryl tosylates is described using a Ni(COD)$_2$/BINAP catalyst.

Key words: palladium, nickel, sulfoximines, cross-coupling, aryl sulfonates

Palladium-catalyzed processes which employ aryl or vinyl sulfonates[1] are becoming increasingly attractive, because they are easily accessible from the corresponding phenols and ketones, respectively, thus allowing an entirely different class of substrates – other than aryl or vinyl halides – to be utilized as starting materials. For example, aryl triflates have been widely used in Heck[2] and Suzuki-Miyaura[3] type couplings and more recently, they have also been employed in the palladium-catalyzed synthesis of aryl amines.[4] An important improvement for the latter transformation was achieved when NaO*t*-Bu – which was responsible for the formation of large amounts of hydrolytic byproducts of the aryl triflate[5] – was replaced by cesium carbonate. This mild base led to both an increased functional group tolerance and a dramatically decreased rate of the hydrolysis of the triflate precursors.[6] Compared to aryl triflates, the corresponding nonaflates are even more attractive substrates because they display a higher reactivity and a more pronounced stability towards hydrolysis.[7] Despite of all of these positive characteristics of aryl sulfonates, palladium-catalyzed aminations of aryl sulfonates with sp^2-hybridized nitrogen nucleophiles other than benzophenone imine are still rare.[8]

Recently, we established a novel method for the catalytic *N*-arylation of sulfoximines with aryl bromides and aryl iodides which has already been applied by Harmata and Parvi in the synthesis of benzothiazines.[9,10] In this protocol Pd(OAc)$_2$/BINAP serves as catalyst and cesium carbonate acts as base allowing for mild reaction conditions and broad functional group tolerance (Scheme 1).

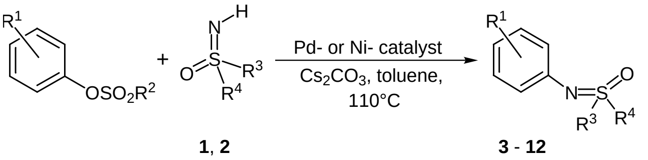
Herein, we report on the extension of this sulfoximine *N*-arylation method first, to palladium-catalyzed reactions of sulfoximines with aryl triflates and aryl nonaflates and second, to nickel-catalyzed couplings of sulfoximines and aryl tosylates.



Scheme 1

Reaction of aryl triflates with *S*-methyl-*S*-phenyl sulfoximine (**1**) and *S*-methyl-*S*-(*p*-tolyl) sulfoximine (**2**) under essentially identical reaction conditions as for couplings of aryl bromides, led to the formation of the corresponding products in good to high yields (Table, Entries 1-5). Interestingly, the substrate which is most susceptible toward hydrolysis – 4-nitrophenyl triflate – gave the highest yield of coupling product **7** at 86% indicating that triflate hydrolysis is no serious side reaction.

Aryl nonaflates[7,11] reacted also smoothly in the presence of a catalytic amount of Pd(OAc)$_2$/BINAP affording the corresponding *N*-aryl sulfoximines in good to high yields (Table, Entries 6-8). For example, *N*-(4-*tert*-butylphenyl) *S*-methyl-*S*-(*p*-tolyl) sulfoximine was obtained with a yield of 76%, which is remarkable taken into account that this compound is formed in only 67% yield from the corresponding aryl bromide. As in reactions with aryl triflates electron-deficient aryl nonaflates give the highest yields. Thus, coupling of [3,5-bis(methoxycarbonyl)phenyl] nonaflate with *S*-methyl-*S*-phenyl sulfoximine (**1**) gave the *N*-aryl sulfoximine in 87% yield. To our delight *N*-[4-(methoxycarbonyl)phenyl] *S*-methyl-*S*-phenyl sulfoximine (**8**) was obtained in an excellent yield (97%), which was again higher than that obtained in the coupling with the corresponding aryl bromide (90%).[9]



Scheme 2

Table Palladium- and Nickel-catalyzed *N*-Arylation of Sulfoximines **1** and **2** with Aryl Triflates, Aryl Nonaflates, and Aryl Tosylates.[a]

Entry	Aryl Group (Product)	-OSO$_2$R[b]	Sulfoximine	Yield [%][c]
1	phenyl (**3**)	Tf	**1**	51
2	1-naphthyl (**4**)	Tf	**1**	82
3	2-naphthyl (**5**)	Tf	**1**	76
4	4-tolyl (**6**)	Tf	**1**	63
5	4-nitrophenyl (**7**)	Tf	**2**	86
6	4-methoxycarbonylphenyl (**8**)	Nf	**1**	97
7	4-*tert*-butylphenyl (**9**)	Nf	**1**	76
8	3,5- bis(methoxy-carbonyl)phenyl (**10**)	Nf	**1**	87
9[d]	4-*tert*-butylphenyl (**11**)	Ts	**1**	41
10[e]	4-*tert*-butylphenyl (**11**)	Ts	**1**	69
11[e]	4-cyanophenyl (**12**)	Ts	**1**	35

[a] Conditions: 1 equiv of aryl sulfonate, 1.2 equiv of **1** or **2** as a 0.1 molar solution in toluene at 110 °C catalyzed by Pd(OAc)$_2$/BINAP (5 mol%/7.5 mol%) with 1.4 equiv Cs_2CO_3.

[b] Nf = -OSO$_2$C$_4$F$_9$; Tf = -OSO$_2$CF$_3$; Ts = -OSO$_2$(4-tolyl).

[c] Yields refer to isolated yields of pure material and are an average of at least two runs.

[d] Ni(COD)$_2$/BINAP (5 mol%/7.5 mol%) was used.

[e] Ni(COD)$_2$/BINAP (10 mol%/15 mol%) was used.

Finally, we were interested in the application of aryl tosylates for this process. Because very active palladium-catalysts for amination reactions of tosylates have been developed in recent years we assumed that those would also promote the reaction of sulfoximines with aryl tosylates. Disappointingly, none of the tested palladium-catalysts[12] provided any product in the reaction of **1** with 4-*tert*-butylphenyl tosylate. However, changing the metal source to a nickel-complex[13] increased the catalytic activity notably. Thus, using Ni(COD)$_2$/BINAP (5 mol%/7.5 mol%) afforded the desired *N*-aryl sulfoximine **11** in moderate yield (41%). Doubling of the catalyst amount even led to an increase in yield to satisfying 69%. Surprisingly, the coupling with 4-cyanophenyl tosylate gave the corresponding product **12** in only 35%, indicating that electronic factors, which are very pronounced in palladium-catalyzed couplings, do not influence the nickel-catalysis to such a great extent.

In summary, we have described the successful extension of our original protocol for the palladium-catalyzed *N*-arylation of sulfoximines onto aryl sulfonates. Here, aryl nonaflates were shown to be the coupling partners of choice giving *N*-aryl sulfoximines in good to excellent yield depending on the substitution pattern of the aryl fragment. Additionally, less reactive aryl tosylates can also be utilized when Ni(COD)$_2$/BINAP is used as catalyst. These transformations represent a rare example of palladium- or nickel-catalyzed arylation reactions with sp^2-hybridized nitrogen nucleophiles.[9,10,14]

For general experimental procedures of *N*-arylation reactions see reference 9. Aryl triflates were purchased from Aldrich Co. and used as received, aryl nonaflates were prepared from the corresponding phenols and nonafluorobutanesulfonylfluoride.[7, 15] NMR spectra were recorded on were recorded on a Varion VXR 300 and a Varion Gemini 300 (at 300 MHz for ^{1}H and 75 MHz for ^{13}C spectra) using $CDCl_3$ as solvent and TMS as internal standart. IR spectra were recorded on a Perkin-Elmer PE 1720 X and a Perkin Elmer PE 1760 FT.

N-(1-Naphthyl) *S*-Methyl-*S*-phenyl Sulfoximine (4)

^{1}H NMR: δ = 3.21 (s, 3H), 7.14–7.29 (m, 4H), 7.38–7.60 (m, 6H), 7.92 (m, 2H).

^{13}C NMR: δ = 46.14, 118.69, 123.83, 124.87, 125.96, 126.93, 127.52, 128.75, 128.79, 129.61, 129.67, 133.40, 134.51, 139.31, 142.92.

IR (KBr): 3055, 2928, 1572, 1504, 1459, 1395, 1337, 1285, 1247, 1220, 1177, 1087, 988, 848, 777 cm^{-1}.

MS (EI, 70 eV): *m/z* 281 (M$^+$, 100%)

Anal Calcd for $C_{17}H_{15}NOS$: C, 72.57; H, 5.37; N, 4.98. Found: C, 72.80; H, 5.64; N, 4.93.

N-(2-Naphthyl) *S*-Methyl-*S*-phenyl Sulfoximine (5)

^{1}H NMR: δ = 3.24 (s, 3H), 7.04–7.10 (m, 2H), 7.29–7.31 (m, 1H), 7.38–7.49 (m, 5H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.88–7.92 (m, 2H), 8.45 (d, *J* = 7.7 Hz, 1H).

^{13}C NMR: δ = 46.01, 116.61, 121.64, 124.09, 125.12, 126.00, 126.12, 127.85, 128.54, 129.63, 130.19, 133.36, 134.65, 139.44, 141.69.

MS (EI, 70 eV): *m/z* 281 (M$^+$, 100%).

IR (KBr): 3055, 2928, 1504, 1459, 1446, 1395, 1337, 1285, 1177, 1116, 1087, 988, 800 cm^{-1}.

HRMS: Calcd for $C_{17}H_{15}NOS$, 281.087437. Found 281.087479.

N-(4-Methylphenyl) *S*-Methyl-*S*-phenyl Sulfoximine (6)

^{1}H NMR: δ = 2.12 (s, 3H), 3.13 (s, 3H), 6.68 (s, 4H), 7.39–7.48 (m, 3H), 7.88 (m, 2H).

^{13}C NMR: δ = 20.74, 45.94, 123.29, 128.74, 129.56, 129.67, 131.11, 133.20, 139.69, 142.28.

MS (EI, 70 eV): *m/z* 245 (M$^+$, 100%).

IR (KBr): 2922, 1506, 1325, 1287, 1263, 1190, 1034, 748 cm^{-1}.

Anal Calcd for $C_{14}H_{15}NOS$: C, 68.54; H, 6.16; N, 5.71. Found: C, 68.78; H, 6.29; N, 5.79.

N-(4-Nitrophenyl) *S*-Methyl-*S*-(4-methylphenyl) Sulfoximine (7)

Mp: 122 °C.

^{1}H NMR: δ = 2.42 (s, 3H), 3.30 (s, 3H), 6.98–7.01 (d, *J* = 8.8 Hz, 2H), 7.33–7.36 (d, *J* = 8.0 Hz, 2H), 7.80–7.82 (d, *J* = 8.3 Hz, 2H), 7.96–7.98 (d, *J* = 8.8 Hz, 2H).

^{13}C NMR: δ = 21.58, 46.70, 122.35, 125.11, 128.38, 130.55, 135.01, 141.52, 145.12, 152.90.

MS (EI, 70 eV): *m/z* 290 (M$^+$, 52.16%), 59 (100%).

IR (cap. film): 3017, 2932, 1585, 1490, 1275 cm^{-1}.

Anal Calcd for $C_{14}H_{14}N_2O_3S$: C, 57.92; H, 4.86; N, 9.65. Found: C, 57.91; H, 4.80; N, 9.58.

N-[3,5-Bis(methoxycarbonyl)phenyl] *S*-Methyl-*S*-phenyl Sulfoximine (10)

^{1}H NMR: δ = 3.21 (s, 3H), 3.81 (s, 6H), 7.48–7.53 (m, 2H), 7.54–7.56 (m, 1H), 7.76–7.78 (m, 2H), 7.90–7.93 (m, 2H), 8.09–8.11 (m, 1H).

^{13}C NMR: δ = 46.32, 52.48, 123.95, 128.44, 128.66, 129.86, 131.31, 133.74, 138.82, 146.06, 166.30.

MS (EI, 70 eV): *m/z* 347 (M$^+$, 100%).

IR (KBr): 2954, 1723, 1437, 1333, 1206, 1058, 903, 750 cm^{-1}.

Anal Calcd for $C_{17}H_{17}NSO_5$: C, 58.78; H, 4.93; N, 4.03. Found: C, 58.44; H, 4.82; N, 3.91.

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