Synthesis of Diaryl Sulfides by Nickel(II)-Catalyzed Arylation of Arenethiolates

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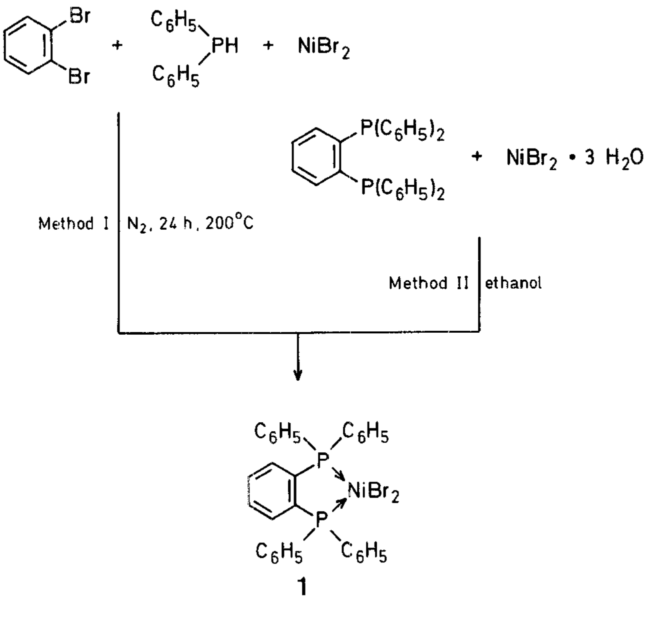
Practically useful methods for the synthesis of diaryl sulfides involve the use of (a) Grignard reagents[1], (b) organocuprates[2], (c) Friedel-Crafts reactions[3], (d) diazonium salts[4], (e) polar solvents[5,6], or (f) photochemical activation[7]. All of these methods have certain drawbacks such as the necessity to activate the reagents (a, b), lack of regioselectivity (c, d, f), unsatisfactory yields (e), or formation of side products (e).

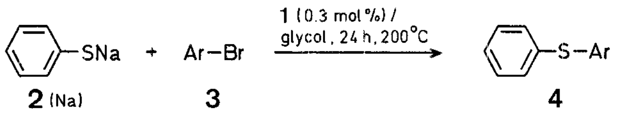
In a previous study[8], we have shown that phosphorus complexes of nickel(II) are able to catalyze the arylation of various tricoordinated phosphorus compounds. However, the catalytic activity of the complexes was reduced when they were used for the arylation of nucleophiles other than *P*-nucleophiles, for example, sulfides. The phosphorus ligand was indeed preferentially arylated, and eliminated as a phosphonium salt. We report here an approach in which the catalytic activity of the *o*-phenylene-bis[diphenylphosphino]-nickel(II) bromide complex (**1**) having a strong chelating phosphorus ligand is not destroyed.

Complex **1** may be prepared by two different methods: a one-pot synthesis starting with *o*-dibromobenzene and the easily available diphenylphosphine (Method I), and a synthesis starting with *o*-phenylene-bis-diphenylphosphine ("benzodiphos") which is commercially available or may be prepared according to Ref.[9] (Method II).

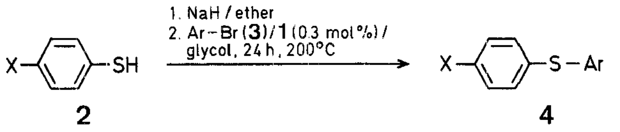


The diaryl sulfides **4** are prepared by reaction of sodium benzenethiolate [**2**(Na); Method A] or benzenethiols (**2**; Method B) with aryl bromides (**3**) in ethylene glycol (this solvent was chosen because of its high boiling point and its ability to solubilize sodium arenethiolates) in the presence of catalytic amounts of complex **1**.

Method A:



Method B:



It should be noted that the reaction is also catalyzed by anhydrous nickel bromide but the yields obtained in the temperature range of 160–200°C are much lower than those obtained using catalyst **1** and that the nickel bromide-catalyzed reaction shows a distinct decrease in yield at temperatures around 150°C.

When the reaction of sodium benzenethiolate with bromobenzene (Method A) is carried out in the absence of a catalyst the yield of diphenyl sulfide (**4a**) is only 3%; we could not, however, detect any coupling products with the solvent as reported in Ref.[6].

We used the syntheses of diphenyl sulfide (**4a**) and 4-methylphenyl phenyl sulfide (**4b**) as model reactions and found that Method A affords slightly higher yields than Method B. In contrast to the method using amide solvents[5,6], the efficiency of Methods A and B is not reduced by electron-releasing groups on the benzene nucleus of the aryl bromide **3** (cf. yields of products **4b, c, d, e, i** in Table 1), the reactivity of the aryl bromides **3b, c, d, e, i** being similar to that of aryl bromides **3g, h** which possess electron-withdrawing substituents. Steric hindrance does not seem to play a significant role since the yields of products **4c, f** obtained from 2-bromotoluene and 1-bromonaphthalene, respectively, are still high. With substrates having two halogen atoms on the benzene ring such as *o*-dibromobenzene, products of monosubstitution (**4j**) and disubstitution (**4j'**) are obtained when equimolar amounts of **2** and **3** are used. Similarly, from the reaction of 4-chlorobenzenethiol (**2**, X = Cl) with bromobenzene a monosubstitution product (**4k**) and a disubstitution product (**4k'**) are obtained.

The reaction is regioselective as can be seen from the exclusive formation of the three pure regioisomeric products **4b, c, d** from the corresponding *o*-, *m*-, and *p*-bromotoluenes.

Our method is also applicable to the synthesis of alkyl aryl sulfides as is shown by the preparation of phenyl propyl sulfide in 88% yield from bromobenzene and sodium propanethiolate. Although alkyl aryl sulfides can be easily prepared by the nucleophilic substitution of an alkyl halide by an arenethiolate[11] our method may be useful when the reverse type of substitution (i.e., aryl halide + alkanethiolate) is required.

Diphenylphosphine was prepared according to Ref.[10]. Anhydrous nickel(II) bromide was prepared from its trihydrate by dehydration over phosphorus pentoxide at 150°C/0.2 torr for 24 h and then at 200°C/2 torr for 48 h. Sodium benzenethiolate was prepared by swirling stoichiometric amounts of freshly drawn sodium wire and benzenethiol in anhydrous ether under nitrogen for 24 h. The aryl bromides were purchased from Aldrich and Fluka and were used without further purification except for the three isomeric bromotoluenes which were carefully purified by distillation on a spinning-band column in vacuo; the purity of the individual isomers was checked by I.R. spectrometry which shows the following strong absorptions: *o*-isomer, $\nu = 748$, 660 cm^{-1}; *m*-isomer, $\nu = 870$, 835, 770, 680 cm^{-1}; *p*-isomer, $\nu = 800$, 600 cm^{-1}. The ethylene glycol used as solvent was purified by distillation in vacuo.

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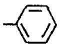
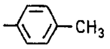
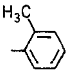
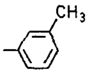
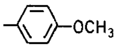
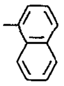
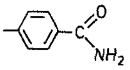
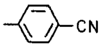
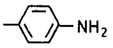
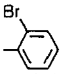
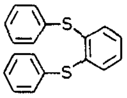
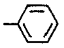
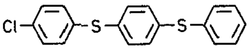
Table 1. Diaryl Sulfides (**4**)

4	X	Ar	Method	Yield[a] [%]	m.p.[b] or b.p./torr [°C]	n_D (°C)	Molecular formula[c] or Lit. data [°C]
a	H		A B	100[d] 95[d]	b.p. 110°/2	1.6330 (20)	b.p. 96°/0.1[12]
b	H		A B	94[e] 85[e]	b.p. 140°/2	1.6215 (20.1)	b.p. 136°/3[12]
c	H		A	90[e]	b.p. 140°/2	1.6250 (20.4)	b.p. 164°/12[2]
d	H		A	98[e]	b.p. 140°/2	1.6220 (20.4)	b.p. 167°/12[2]
e	H		A	80	b.p. 120°/2	1.6270 (20.2)	$C_{13}H_{12}OS$ (216.3)
f	H		A	90	m.p. 40° (hexane)		m.p. 39-40.5°[13]
g	H		A	80[f]	m.p. 152.5° (acetone/hexane)		$C_{13}H_{11}NSO$ (229.0)
h	H		A	80[g]	b.p. 120°/2	1.6481 (19)	$C_{13}H_9NS$ (211.3)
i	H		A	67	m.p. 95° (hexane)		$C_{12}H_{11}NS$ *(201.2)*
j	H	 + by-product :	A	69	b.p. 120°/2	1.6589 (22.4)	$C_{12}H_9BrS$ (265.2)
j'				15	b.p. 210°/2	1.6860 (22.4)	b.p. 187°/1[2]
k	Cl	 + by-product :	B	55	b.p. 120°/2	1.6357 (23.2)	$C_{12}H_9ClS$ (220.6)
k'				10	m.p. 73.5° (hexane)		$C_{18}H_{13}ClS_2$ (328.8)

[a] Yield of isolated product. Purity of liquid products: at least 99%, according to G.L.C. analysis.

[b] Melting points are uncorrected. They were measured using an automatic Mettler FP 5 melting-point apparatus at a heating rate of 2°C/min.

[c] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.27; H, ±0.30; N, ±0.12. Exception: **4j** (C, +0.98). The analytical samples required for the microanalyses were obtained by Kugelrohr distillation or by recrystallization.

[d] Identified by I.R. and G.L.C. comparison (co-injection) with an authentic sample.

[e] The three methylphenyl phenyl sulfides were isomerically pure. 2-Methylphenyl phenyl sulfide (**4c**) was shown to be different from 3-methylphenyl phenyl sulfide (**4d**) by G.L.C. comparison [injection and co-injection into a 6' × 0.125" stainless steel column packed with 10% SE 30 on PAW (80-100 mesh) using nitrogen (inlet pressure 14 psi) as carrier gas]. 4-Methylphenyl phenyl sulfide (**4b**) was shown to be different from **4c** by the signals of the methyl groups in the ^1H-N.M.R. spectra, and **4a** was shown to be different from **4d** by the presence in its I.R. spectrum of two strong absorptions at $\nu = 810$ and 518 cm^{-1} whereas for **4d** a strong absorption was found at $\nu = 778$ cm^{-1}.

[f] The component **3** used was 4-chlorobenzonitrile; the cyano group was hydrolyzed to the aminocarbonyl group by water present in the ethylene glycol.

[g] Obtained from 4-chlorobenzonitrile as component **3** using anhydrous diglyme as solvent.

o-Phenylene-bis[diphenylphosphino]-nickel(II) Bromide (1):

Method I: A mixture of diphenylphosphine[10] (2.1 g, 11.3 mmol), o-dibromobenzene (0.7 ml, 5.9 mmol), and anhydrous nickel(II) bromide (1.24 g, 5.7 mmol) is placed in a pressure tube under nitrogen and the sealed tube is heated at 200°C for 24 h. The contents of the tube are poured into ethanol to give **1** as a red-brown precipitate; yield: 1 g (27%).

$C_{30}H_{24}Br_2NiP_2$	calc.	C 54.18	H 3.64	P 9.32
(737.0)	found	53.90	3.45	9.35

^{31}P-N.M.R. (glycol/80% H_3PO_{4ext}): $\delta = 47.75$ ppm.

Method II: A solution of nickel(II) bromide trihydrate (0.35 g, 1.29 mmol) in ethanol (15 ml) is added dropwise to a stirred solution of o-phenylene-bis-diphenylphosphine (0.58 g, 1.29 mmol) in ethanol (30 ml), the mixture refluxed for 4 h, then allowed to cool, and kept at room temperature for 12 h. The resultant red-brown precipitate of **1** is isolated by suction and dried in vacuo; yield: 0.69 g (80%).

Diaryl Sulfides (4); General Procedures:

Method A: In a pressure tube are placed the aryl bromide **3** (4 mmol), sodium benzenethiolate [**2** (Na); 0.53 g, ~4 mmol), and a solution of complex **1** (8.8-9 mg, ~0.012 mmol) in ethylene glycol (2 ml). The tube is sealed and kept in a silicon oil bath at 200°C for 24 h. The resultant crude mixture is dissolved in dichloromethane (10 ml) and ether (100 ml) is added. The solution is washed with water (4 × 25 ml), dried with sodium sulfate, and concentrated in vacuo. The residual product is in general purified by short-column chromatography on silica gel (40 g); however, with starting materials which give rise to product mixtures (e.g., **4j** + **4j'**; **4k** + **4k'**), the products are isolated by chromatography on a usual-shape column of silica gel (70 g).

Table 2. Spectrometric Data of Diaryl Sulfides **(4)**

4	M.S.[a] m/e (relative intensity, %)	I.R.[b] ν [cm^{-1}]	^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$)[c] δ [ppm]
b	200 (M$^+$, 100); 185 (M$^+$ − CH$_3$, 29); 167 (M$^+$ − SH, 12); 152 (M$^+$ − CH$_3$SH, 7); 91 (C$_7$H$_7$, 24); 77 (C$_6$H$_5$, 14)	810, 738, 690, 518	7.45–6.9 (m, 9H$_{arom}$); 2.26 (s, 3H, CH$_3$)
c	200 (M$^+$, 100); 185 (M$^+$ − CH$_3$, 21); 167 (M$^+$ − SH, 11); 152 (M$^+$ − CH$_3$SH, 7); 115 (C$_7$H$_7$S, 30); 91 (C$_7$H$_7$, 22); 77 (C$_6$H$_5$, 12)	741, 690	7.5–7.0 (m, 9H$_{arom}$); 2.38 (s, 3H, CH$_3$)
d	200 (M$^+$, 100); 185 (M$^+$ − CH$_3$, 34); 167 (M$^+$ − SH, 7); 152 (M$^+$ − CH$_3$SH, 7); 91 (C$_7$H$_7$, 12); 77 (C$_6$H$_5$, 11)	778, 740, 690	7.5–6.9 (m, 9H$_{arom}$); 2.29 (s, 3H, CH$_3$)
e	216 (M$^+$, 100); 201 (M$^+$ − CH$_3$, 50); 185 (M$^+$ − OCH$_3$, 8); 77 (C$_6$H$_5$, 12)	690	AB system: δ_A = 7.39 (2H$_{ortho}$), δ_B = 6.84 (2H$_{meta}$), $^3J_{AB}$ = 9 Hz); 7.2–7.0 (m, 5H$_{arom}$, C$_6$H$_5$S); 3.75 (s, 3H, OCH$_3$)
f	236 (M$^+$, 100); 202 (M$^+$ − H$_2$S, 13); 115 (C$_7$H$_7$S, 24); 77 (C$_6$H$_5$, 10)	688	8.6–8.2 (m, 1H); 8.0–7.3 (m, 6H); 7.20 (s, 5H, C$_6$H$_5$S)
g	229 (M$^+$, 100); 213 (M$^+$ − NH$_2$, 35); 185 (M$^+$ − HCONH$_2$, 28); 77 (C$_6$H$_5$, 12)	3382, 3170 (NH); 1650 (C=O), 690	AB system: δ_A = 7.81 (2H$_{meta}$), δ_B = 7.31 (2H$_{ortho}$, J_{AB} = 8.1 Hz); 7.6–7.3 (m, 5H$_{arom}$, C$_6$H$_5$S); 2.96 (s, 2H, NH$_2$)
h	211 (M$^+$, 100); 77 (C$_6$H$_5$, 14)	2238 (C≡N); 690	AB system: δ_A = 7.50 (2H$_{meta}$), δ_B = 7.20 (2H$_{ortho}$, J_{AB} = 8.1 Hz); 7.50–7.40 (m, 5H, C$_6$H$_5$S)
i	201 (M$^+$, 100)	3470, 3375 (NH$_2$); 684	AB system: δ_A = 7.50 (2H$_{ortho}$), δ_B = 6.83 (2H$_{meta}$, J_{AB} = 8.65 Hz); 7.2 (s, 5H$_{arom}$, C$_6$H$_5$S); 3.70 (s, 2H, NH$_2$)
j	266 (M$^+$ ^{81}Br, 54); 264 (M$^+$ ^{79}Br, 54); 195 (100); 152 (22); 109 (C$_6$H$_5$S, 28)	690	7.65–6.70 (m)
j′	294 (M$^+$, 100); 184 (M$^+$ − C$_6$H$_5$SH, 30)	690	7.5–7.2 (m, 10H$_{arom}$); 7.12 (s, 4H$_{arom}$, C$_6$H$_4$S$_2$);
k	220 (M$^+$, 100); 184 (M$^+$ − HCl, 52)	690	7.60–7.10 (m)
k′	328 (M$^+$, 100); 219 (M$^+$ − C$_6$H$_5$S, 21); 184 (M$^+$ − ClC$_6$H$_4$SH, 29)	688	

[a] The mass spectra were recorded at 75 eV using a Jeol JMS D-100 spectrometer.

[b] The I.R. spectra were recorded using a Perkin-Elmer 377 spectrophotometer: compounds **4d, e, f, h, j, j′, k** in CCl$_4$; compounds **4a, b, c** as film; compounds **4g, i, k′** in KBr pellets. All absorptions were strong.

[c] The ^{1}H-N.M.R. spectra were recorded with a 60 MHz Varian EM 360 spectrometer. When *ortho*- and *meta*-positions are indicated, they refer to the phenylthio substituent.

Method B: Pure sodium hydride (obtained from commercial 50% dispersion in oil by washing with dry hexane; 96 mg, 4 mmol) is added portionwise to a solution of the arenethiol (**2**; 4 mmol) in dry ether (2 ml) in a Schlenk tube under nitrogen. After gas evolution has ceased, the ether is removed and the aryl bromide (**3**; 4 mmol), complex **1** (8.8–9 mg, 0.012 mmol), and ethylene glycol (2 ml) are added. The tube is sealed and from this point, Method A is followed.

Phenyl Propyl Sulfide:

Prepared according to Method B from ethanethiol (0.36 ml, 4 mmol), sodium hydride (96 mg, 4 mmol) and bromobenzene (0.31 ml, 4 mmol). Chromatography and distillation of the crude oil affords the phenyl propyl sulfide; yield: 535 mg (88%); b.p. 105 °C/2 torr; $n_D^{20.2}$: 1.6009.

I.R.: ν = 688 cm^{-1}.

^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$): δ = 1.00 (t, 3H); 1.2–2.0 (m, 2H); 2.83 (t, 2H, J = 7 Hz); 6.9–7.5 ppm (m, 5H).

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