Palladium-catalyzed amination of aromatic halides in water-containing solvent systems: a two-phase protocol

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The use of the six-fold sulfonated ligand BINAS-6 1 permits the Pd⁰-catalyzed amination of aromatic halides in water containing single- or two-phase systems.

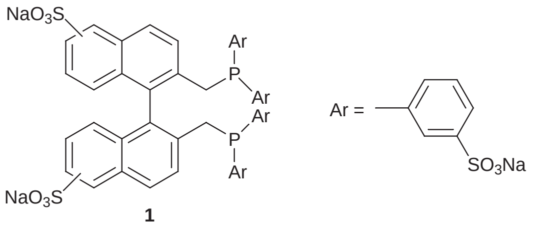
Following the initial investigations of Kosugi *et al.*,[1] both Buchwald[2] and Hartwig[3] and their co-workers have developed in recent years a new methodology for the amination of aromatic halides and triflates (ArX: X = Cl, Br, I, OSO_2CF_3) with amines RR^1NH to yield aromatic amines of the type $ArNRR^1$.[4] ArX and RR^1NH were reacted with (di)phosphine-complexed palladium [Pd^0L, 1–5 mol%] and sodium *tert*-butoxide (1.4 equiv.) in PhMe at 80–100°C under homogeneous reaction conditions [eqn. (1)].

$$\mathrm{ArX} + \mathrm{HNRR^1} \xrightarrow[\text{toluene, 80–100 °C}]{\mathrm{Pd^0L,\ NaOBu^t}} \mathrm{ArNRR^1} \qquad (1)$$

$$\mathrm{X = Cl, Br, I, OSO_2CF_3} \qquad \mathrm{R = H, alkyl, aryl} \qquad \mathrm{R^1 = aryl}$$

Under such conditions reapplication of the Pd⁰ catalyst would be difficult as is reuse of the relatively expensive (di)phosphine ligand L. In contrast, by using a two-phase protocol, the separation of products (and unreacted starting material) from the catalyst and subsequent reapplication of the catalyst in further reactions is made facile.[5] For this reason there is increasing interest in two-phase catalysis both in the laboratory[6,7] and for industrial applications.[8] Here we report on a two-phase protocol of the aforementioned Pd⁰-catalyzed amination reaction.

The ligand used here is the six-fold sulfonated 2,2′-bis(diphenylphosphinomethyl)-1,1′-binaphthyl **1** (BINAS-6) dissolved in water.[9]



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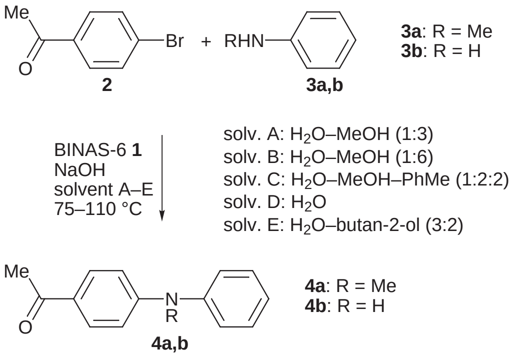
The reaction of 4-bromoacetophenone **2** with *N*-methylaniline **3a** in water–MeOH (1:3; solvent A) using NaOH as the base and the aforementioned catalyst Pd⁰–**1** afforded 1-[4-(*N*-methylanilino)phenyl]ethan-1-one **4a** in 88% yield [eqn. (2); Table 1, entry 1].

Reacting **2** with **3b** in the presence of Pd⁰–**1** and NaOH as the base in water–MeOH (1 : 6; solvent B) resulted in the formation of 1-(4-anilinophenyl)ethan-1-one **4b** in 91% yield [eqn. (2); Table 1, entry 2]. The Pd⁰–**1** catalyst, which is dissolved in the aqueous phase, can be reused after separation of the products. The reaction was repeated under similar conditions. The following yields were achieved: second reaction 85% **4b**, (5 h); third reaction 53% **4b**, (7 h); fourth reaction 36% **4b**, (7 h).



(2)

The use of a two-phase H_2O–MeOH–PhMe system (1 : 2 : 2; solvent C) in the reaction of **2** with **3a** afforded only low yields (36%) of **4a** [eqn. (2); Table 1, entry 3]. The use of emulsifying agents like tetradecyltrimethylammoniumbromide did not increase the yield of **4a**, but resulted in considerable problems during product recovery. With only water as the solvent (solvent D) **4a** was obtained in 36% yield [eqn. (2); Table 1, entry 4].

Butan-2-ol and water form a biphasic system with good miscibility of the two solvents. Thus in the reaction of **2** with **3b** in the presence of Pd⁰–**1** and water–butan-2-ol (3 : 2, solvent E) the product **4b** was obtained in 89% yield [eqn. (2); Table 1, entry 5]. NaOH was found to give the best results as compared to other group I hydroxides. The catalyst Pd⁰–**1** remains in the aqueous phase while the products can be collected conveniently by separation of the organic layer. Only small amounts of

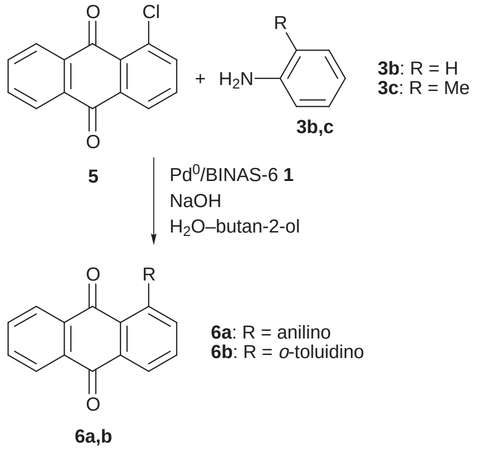
Table 1 Pd⁰–**1** catalysed aminations of ArX in water-containing solvent systems. All reactions were carried out under argon with degassed solvents and starting materials. **1** was applied in an aqueous solution (140 mmol l^{-1}). Physical and spectroscopic data of the products were consistent with those reported previously in the literature.

Entry[a]	Halide	Amine	Solvent	Reaction time/h	Product	Yield (%)
1	**2**	**3a**	A	2	**4a**	88
2	**2**	**3b**	B	3	**4b**	91
3	**2**	**3a**	C	32	**4a**	36
4	**2**	**3a**	D	25	**4a**	36
5	**2**	**3b**	E	6	**4b**	89
6	**5**	**3b**	E	6	**6a**	81
7	**5**	**3c**	E	8	**6b**	71

[a] Details of entries 1–7. 1: 160 µmol **1**, 20 µmol $Pd(OAc)_2$, 3 ml MeOH, 1 mmol ArX, 1.3 mmol amine, 1.3 mmol NaOH, 75 °C; products were extracted with Et_2O. 2: 70 µmol **1**, 9 µmol $Pd(OAc)_2$, 6 ml MeOH, 1 mmol ArX, 1.3 mmol amine, 1.4 mmol NaOH, 75 °C; products were extracted with Et_2O. 3: 840 µmol **1**, 100 µmol $Pd(OAc)_2$, 12 ml MeOH, 12 ml PhMe, 6 ml water, 2 mmol ArX, 2.4 mmol amine, 2.8 mmol NaOH, 70 °C; products were collected by separation of the organic layer. 4: 840 µmol **1**, 100 µmol $Pd(OAc)_2$, 12 ml water, 2 mmol ArX, 2.4 mmol amine, 2.8 mmol NaOH, 90 °C; products were extracted with Et_2O. 5–7: 80 µmol **1**, 11 µmol $Pd(OAc)_2$, 3 ml water, 2 ml butan-2-ol, 1 mmol ArX, 1.3 mmol amine, 1.3 mmol NaOH, 110 °C; products were collected by separation of the organic layer.

product (< 5%) remain in the aqueous phase. In this solvent system the catalyst can be reused as well.

Reacting 1-chloroanthraquinone **5** with aniline **3b** in the presence of Pd^0–**1** and NaOH in water–butan-2-ol (3 : 2) allowed amination of **5**, affording 1-anilinoanthraquinone **6a** in 81% yield [eqn. (3); Table 1, entry 6]. The use of *o*-toluidine **3c** under similar conditions gave 1-(*o*-toluidino)anthraquinone **6b** in 71% yield [eqn. (3); Table 1, entry 7].



(3)

In conclusion, it has been demonstrated that the Pd^0-catalyzed amination of aromatic halides with amines can be performed by means of a two-phase protocol with NaOH instead of the expensive $NaOBu^t$ as the base. Further advantages are the facile catalyst/product separation and the reusability of the water-soluble Pd^0/BINAS-6 catalyst. The catalyst system is also suitable for the preparation of substituted anthraquinones, which are important in dye stuff production.[10] Further work is being conducted to optimise the reaction conditions and to perform selective single amination reactions of dichloro-substituted anthraquinones.

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Notes and References

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1 M. Kosugi, M. Kameyama and T. Migita, *Chem. Lett.*, 1983, 927; M. Kosugi, M. Kameyama and T. Migita, *Nippon Kagaku Kaishi*, 1985, **3** 547.

2 A. S. Guram, R. A. Rennels and S. L. Buchwald, *Angew. Chem.*, 1995, **107**, 1456; *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1348; J. P. Wolfe, R. A. Rennels and S. L. Buchwald, *Tetrahedron*, 1996, **52**, 7525; J. P. Wolfe, S. Wagaw and S. L. Buchwald, *J. Am. Chem. Soc.*, 1996, **118**, 7215; S. Wagaw and S. L. Buchwald, *J. Org. Chem.*, 1996, **61**, 7240; palladium-catalyzed aminations of triflate-arenes J. P. Wolfe and S. L. Buchwald, *J. Org. Chem.*, 1996, **61**, 1133; J. P. Wolfe and S. L. Buchwald, *J. Org. Chem.*, 1997, **62**, 1264.

3 J. Louie and J. F. Hartwig, *Tetrahedron Lett.*, 1995, **36**, 3609; M. S. Driver and J. F. Hartwig, *J. Am. Chem. Soc.*, 1996, **118**, 7217; J. Louie, M. S. Driver and B. C. Hamann and J. F. Hartwig, *J. Org. Chem.*, 1997, **62**, 1268.

4 See also M. Beller, T. M. Riermeier, C.-P. Reisinger and W. A. Herrmann, *Tetrahedron Lett.*, 1997, **38**, 2073; N. P. Reddy and M. Tanaka, *Tetrahedron Lett.*, 1997, **38**, 4807.

5 B. Cornils, *Angew. Chem.*, 1995, **107**, 1709; *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1575.

6 W. A. Herrmann and C. W. Kohlpaintner, *Angew. Chem.*, 1993, **105**, 1588; *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 1524; P. Kalck and F. Monteil, *Adv. Org. Chem.*, 1992, **34**, 219.

7 T. Prinz, W. Keim and B. Drießen-Hölscher, *Angew. Chem.*, 1996, **108**, 1835; *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1708.

8 W. Keim, *Chem Ing. Tech.*, 1984, **56**, 850; G. Mercier and P. Chabardes, *Pure Appl. Chem.*, 1994, **66**, 1509; Y. Tokitoh, N. Yoshimura, T. Higashi, K. Mino and M. Murasawa, EP 436226, 1991; *Chem. Abstr.*, 1991, **115**, 158508z; A. Behr and W. Keim, *Arab. J. Sci. Eng.*, 1985, **10**, 377.

9 H. Bahrmann, K. Bergrath, H.-J. Kleiner, P. Lappe, C. Naumann, D. Peters and D. Regnat, *J. Organomet. Chem.*, 1996, **520**, 97.

10 H. S. Bien, J. Stawitz and K. Wunderlich, *Ullmann's Encyclopedia of Industrial Chemistry*, VCH, Weinheim, 1985, vol. A2, p. 355.

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