Pergamon

Tetrahedron Letters 40 (1999) 3877–3880

TETRAHEDRON
LETTERS

Preparation of *N,N'*-Aryl-disubstituted-1,2-diphenyl-1,2-diaminoethanes Using Palladium-Catalyzed Aromatic Amino Coupling.

Isabelle Cabanal-Duvillard and Pierre Mangeney*

Laboratoire de Chimie des Organo-Eléments URA 473 CNRS, 4 place Jussieu - Tour 44-45 -
Boîte 183 - 75252 PARIS Cédex 05 - France.
e.mail : mangeney@moka.jussieu.ccr.fr

Received 8 February 1999; accepted 19 March 1999

Abstract : A convenient and efficient method for the preparation of several *N,N'*-aryl-disubstituted-1,2-diphenyl-1,2-diaminoethanes is described using palladium-catalyzed amino coupling of arylbromides.

Keywords : diamine, palladium

Many *N,N'*-disubstituted ethanediamine derivatives bearing a C2 symmetry have been widely used in the literature and showed to be useful chiral tools in several reactions.[1] The most common approach was by reductive coupling of the corresponding imine, isomerization of the *meso* into the *dl* conformation,[2] and subsequent resolution of the racemate .

However, so far as we know, syntheses of *N,N'*-aryl-disubstituted 1,2-diphenyl-1,2-diaminoethanes have been scarcely developed.[1-3] As a matter of fact, while the racemate is easily available following the imine reductive coupling pathway, it appears very difficult to isolate it in its enantiomeric form. For instance, *N,N'*-1,2-tetraphenylethylene diamine has been already synthesized in its enantiomeric form, but this proved to be a fastidious, quite long and hazardous route. [4]

This prompted us to disclose in this paper our own results, and we wish to report a facile approach to enantiopure *N,N'*-diaryl-1,2-diphenyl-1,2-diaminoethane bearing a C2 symmetry .

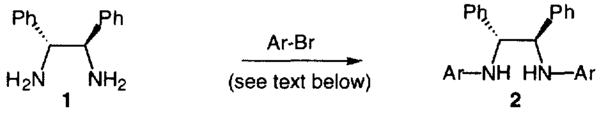
Catalytic carbon-heteroatom coupling reactions have emerged in the last few years and proved to offer considerable advantages over other classical methods, which required most of the time either activated molecules or severe conditions. Buchwald[5] and Hartwig[6] have independently developed palladium - or nickel - catalyzed aminopalladation which could be extended to various arylhalides or triflates and amines.[7]

Therefore, palladium catalyzed coupling of primary amines has been widely used, most examples dealing with secondary amines like piperidine or piperazine,[6,7a,8] or aniline derivatives.[7c,9] But only few efficient couplings of primary diamines have been described in the literature.[7a,10]

PII: S0040-4039(99)00612-7

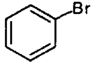
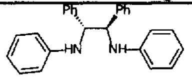
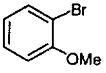
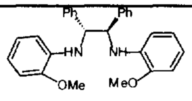
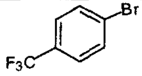
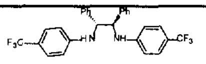
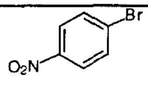
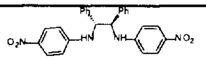
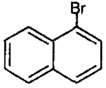
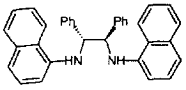
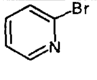
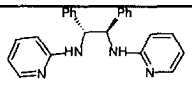
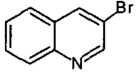
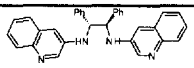
Since 1,2-diphenyl-1,2-diaminoethane **1** is easily available in its enantiomeric form,[11] it appeared of great interest to synthesize many different *N,N'*-aryl-disubstituted 1,2-diphenyl-1,2-diaminoethanes *via* palladium catalyzed amino coupling, offering yet a valuable alternative to the previous route.

Coupling of enantiopure (*S,S*)-1,2-diphenyl-1,2-diaminoethane **1** with several arylbromides was performed under typical conditions reported by Buchwald[6a] to give the corresponding diaryl-substituted amines **2** (Scheme and Table).



Scheme

It appears that, under these conditions, the majority of arylbromides reacts with diamine **1** to give the corresponding substituted diamine **2** in good yield. However, the presence of an electron-withdrawing function on the aromatic moiety makes the yield of reaction significantly decrease compared to the others (entries **3** and **4**, 33% and 0% respectively).

Entry	Ar-Br	time (h)	Diamine 2a-g	Yield (%)[12]	$[\alpha]_D$
1		2	 **2a**	89	-178[4] (c 0.7, benzene)
2		3	 **2b**	65	-97 (c 0.7, $CHCl_3$)
3		12	 **2c**	33	-101 (c 0.9, $CHCl_3$)
4		48	 **2d**	no reaction	//
5		4	 **2e**	76	-100 (c 0.7, $CHCl_3$)
6		1.5	 **2f**	97	-36 (c 0.9, $CHCl_3$)
7		5	 **2g**	96	-94 (c 0.7, $CHCl_3$)

Table

In a typical procedure :

All arylbromides were purchased from commercial sources and used without further purification. Toluene was used as a commercial grade. Dichloromethane was dried over $CaCl_2$.

A solution of Pd_2dba_3 (5% mmol) and (+/-)-BINAP[13] (10% mmol) was stirred under inert conditions for 1 hour in degassed toluene at room temperature. The aryl halide (1.8 eq) and freshly sublimed NaOtBu (2.8 eq) were then added and the mixture was stirred for 30 mn. Diamine **1** was added at last and the solution was vigourously stirred under reflux temperature.

The reaction was followed by TLC monitoring and reflux was maintained until completion of reaction. The mixture was quenched with H_2O, filtered over a plug of Celite, extracted with dichloromethane and dried over Na_2SO_4. After concentration under reduced pressure, the crude diamine was purified by flash chromatography over silica gel.

For each case, no *meso* compound was detected by ^1H NMR on the crude product.

Aknowledgments

The authors thank Firmenich for financial support.

References

1. For an excellent review, see : Lucet, D.; Le Gall, T.; Mioskowski, C., *Angew. Chem. Int. Ed.* **1998**, 37, 2580.
2. For recent papers, see : a) Alexakis, A.; Aujard, I.; Kanger, T.; Mangeney, P., *Org. Synth.* **1998,** 16 (in the press). b) Alexakis, A.; Aujard, T.; Mangeney, P., *Synlett* **1998**, 873. c) Alexakis, A.; Aujard, T.; Mangeney, P., *Synlett* **1998**, 875. d) Dutta, M. P.; Baruah, B.; Boruah, A.; Prajapati, D.; Sandhu, J. S., *Synlett* **1998**, 857.
3. a) Smith, J. G.; Doreen Veach, C., *Can. J. Chem.* **1966**, 44, 2497. b) Smith, J. G.; Ho, I., *J. Org. Chem.* **1972**, 37, 653. c) Betschart, C.; Seebach, D., *Helv. Chim. Acta* **1987**, 70, 2215. d) Imamoto, T.; Nishimura, S., *Chem. Lett.* **1990**, 1141. e) Neumann, W. P.; Werner, F., *Chem. Ber.* **1978**, 111, 3904. f) Talukdar, S.; Banerji, A., *J. Org. Chem.* **1998**, 63, 3468.
4. a) Kanemasa, S.; Hayashi, T.; Tanaka, J.; Yamamoto, H.; Sakurai, T., *J. Org. Chem.* **1991**, 56, 4473. b) Stuhmer, W.; Messwarb, G., *Arch. Pharm.* **1953**, 286, 221. $[\alpha]_D$lit. -204 (c 1.60, benzene).
5. Guram, A. S.; Rennels, R. A.; Buchwald, S. L., *Angew. Chem., Int. Ed. Engl.* **1995**, 34, 1348.
6. Louie, J.; Hartwig, J. F., *Tetrahedron Lett.* **1995**, 36, 3609.
7. a) Wagaw, S.; Buchwald, S. L., *J. Org. Chem.* **1996**, 61, 7240. b) Marcoux, J.-F.; Wagaw, S.; Buchwald, S. L., *J. Org. Chem.* **1997**, 62, 1568. c) Wolfe, J. P.; Ahman, J.; Sadighi, J. P.; Singer, R. A.; Buchwald, S. L., *Tetrahedron Lett.* **1997**, 38, 6367. d) Wolfe, J. P.; Buchwald, S. L., *J. Am. Chem. Soc.* **1997**, 119, 6054. e) For a recent review, see : Frost, C. G.; Mendonça, P., *J. Chem. Soc., Perkin Trans. 1* **1998**, 2615.
8. a) Zhao, S.-H.; Miller, A. K.; Berger, J.; Flippin, L. A., *Tetrahedron Lett.* **1996**, 37, 4463. b)

Kerrigan, F.; Martin, C.; Thomas, G. H. *Tetrahedron Lett.* **1998**, 39, 2219. c) Kamikawa, K.; Sugimoto, S.; Uemura, M., *J. Org. Chem.* **1998**, 63, 8407.

9. Sadighi, J. P.; Harris, M. C.; Buchwald, S. L., *Tetrahedron Lett.* **1998**, 39, 5327.

10. Hong, Y.; Senenayake, C. H.; Xiang, T.; Vandenbossche, C. P.; Tanoury, G. J.; Bakale, R. P.; Wald, S. A., *Tetrahedron Lett.* **1998**, 39, 3121.

11. For syntheses see : a) Pikul, S.; Corey, E. J., *Org. Synth.* **1993**, 71, 22. b) Corey, E. J.; Kühnle, F. N. M., *Tetrahedron Lett.* **1997**, 38, 8631.

12. Yields are calculated on the basis of arylhalide equivalent, after purification by column chromatography over silica gel.

13. a) Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J., *J. Org. Chem.* **1994**, 59, 7180. b) (+/-)-BINAP catalyst was used for the reaction as it is easily accessible from cheap and commercially available (+/-)-binaphtol. The (+/-)-Binaphtol ditriflate precursor was synthesized according to a modified procedure : (+/-)-binaphtol (17,45 mmoles) was dissolved in 100 ml CH_2Cl_2 in a 250 ml flask flushed with argon, and Et_3N (15 ml, 6 eq) was slowly added. After 10 mn stirring, Tf_2O (59,4 mmoles, 3.4 eq) was added over a period of 20 mn and stirring was maintained for 12 h at room temperature. The mixture was quenched with 50 ml of 1N HCl. The organic layer was decanted and washed with 50 ml of an aqueous saturated solution of $NaHCO_3$ and dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the crude ditriflate was purified by flash chromatography over silica gel (eluent cyclohexane/CH_2Cl_2 15/5) to give 6.7 g of pure (+/-)-binaphtol ditriflate (69%).