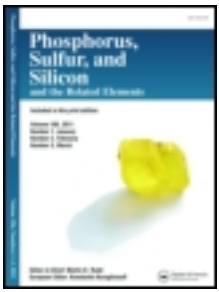


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

Chiral 2-(2-Diphenylphosphinophenyl)-oxazolines: Synthesis and Use in Pd-Catalyzed Asymmetric Allylic Alkylation

Benjamin Ganchegui [a], Carole Chevrin [a], Sandrine Bouquillon [a], Jean Le Bras [a], Françoise Hénin [a] & Jacques Muzart [a]

[a] Unité Mixte de Recherche "Réactions Sélectives et Applications," CNRS Université de Reims Champagne-Ardenne, France

Published online: 01 Feb 2007.

To cite this article: Benjamin Ganchegui , Carole Chevrin , Sandrine Bouquillon , Jean Le Bras , Franoise Hnin & Jacques Muzart (2006) Chiral 2-(2-Diphenylphosphinophenyl)-oxazolines: Synthesis and Use in Pd-Catalyzed Asymmetric Allylic Alkylation, Phosphorus, Sulfur, and Silicon and the Related Elements, 181:11, 2635-2639, DOI: 10.1080/10426500600781367

To link to this article: http://dx.doi.org/10.1080/10426500600781367

Phosphorus, Sulfur, and Silicon, 181:2635–2639, 2006

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500600781367

Chiral 2-(2-Diphenylphosphinophenyl)-oxazolines: Synthesis and Use in Pd-Catalyzed Asymmetric Allylic Alkylation

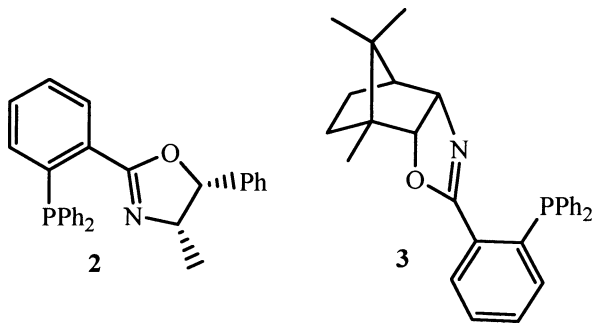
Benjamin Ganchegui
Carole Chevrin
Sandrine Bouquillon
Jean Le Bras
Françoise Hénin
Jacques Muzart
Unité Mixte de Recherche "Réactions Sélectives et Applications," CNRS
Université de Reims Champagne–Ardenne, France

The synthesis of 2-(2-diphenylphosphinophenyl)-oxazolines from o-fluorobenzonitrile and (−)-norephedrine or (+)-endo-2-hydroxy-endo-3-aminobornane is described. The Pa-catalyzed alkylation of (E)-1,3-diphenylallyl acetate with the sodium salt of dimethylmalonate using these chiral ligands occurs with an 82–87% yield and 88–93% ee.

Keywords η^3-allylpalladium; allylic alkylation; asymmetry; catalysis; oxazolines

Over the last 20 years, we have been strongly involved in the enantioselective protonation of prochiral enolic species produced either photochemically[1] or from Pd catalysis.[2] The chiral protic sources were ephedrine-type compounds, (+)-*endo*-2-hydroxy-*endo*-3-aminobornane (**1**),[3] and its *N*-alkylated derivatives. Being also interested in Tsuji–Trost reactions,[4] we have prepared oxazolines **2** and **3** from (−)-norephedrine and **1**, respectively, (Scheme 1) to test them for the Pd-catalyzed asymmetric alkylation of (*E*)-1,3-diphenylallyl acetate (**4**). Indeed, homochiral phosphinoaryloxazolines are a class of ligands commonly used in metal-catalyzed enantioselective reactions, in particular

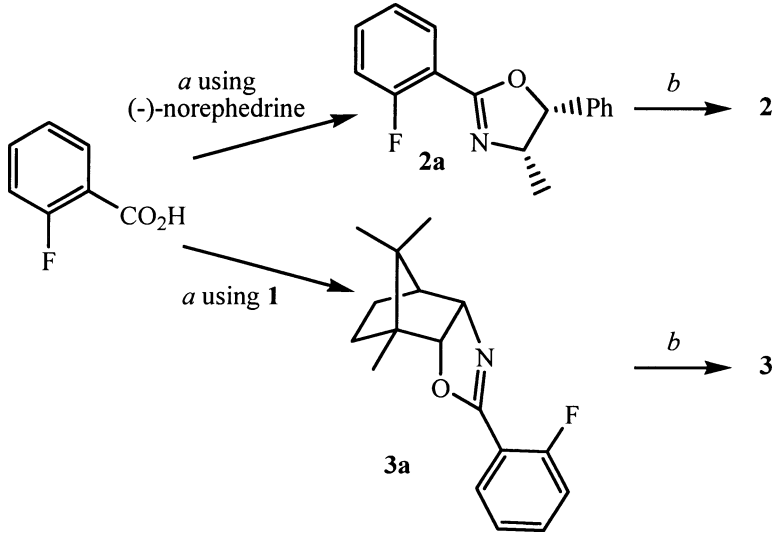
Received February 9, 2006; accepted April 22, 2006.
We are grateful to "Ministère de la Recherche et de la Technologie" and "Région Champagne-Ardenne" for PhD studentships to Benjamin Ganchegui and Carole Chevrin, respectively.
Address correspondence to Jacques Muzart, Unité Mixte de Recherche "Réactions Sélectives et Applications," UMR 1039, CNRS–Université de Reims, Champagne–Ardenne, B.P. 1039, Reims, cedex 2, 51687 France. E-mail: jacques.muzart@univ-reims.fr



SCHEME 1

in the Pd-catalyzed allylic alkylation of **4**.[5–7] Oxazoline **2** already has been used with **4** to synthesize the corresponding η^3-allylpalladium complex,[8] but its synthesis, analytical properties[9] and use in catalysis have not been disclosed. Our results are here reported.

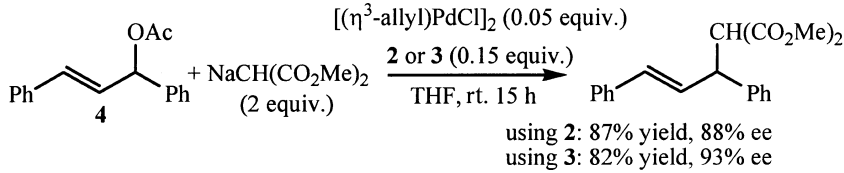
The synthesis of **2** and **3** was attempted via the synthesis of the corresponding 2-(2-fluorophenyl)-4,5-dihydrooxazoles **2a** and **3a**. Refluxing a mixture of o-fluorobenzonitrile, (−)-norephedrine and $ZnCl_2$ in chlorobenzene[6,10] yielded 30% of **2a**. The yield was improved to 76% using *o*-fluorobenzoic acid[10] under conditions depicted in Scheme 2. These experimental conditions using 1 instead of (−)-norephedrine



SCHEME 2 (a) 1: PPh_3 (1 equiv.), CCl_4/MeCN (4:1), 0°C, 2.5 h; 2: (−)-norephedrine or **1** (1 equiv.), NEt_3 (3.25 equiv.), r.t., 1 h; 3: 0°C, PPh_3 (0.37 equiv.); 4: r.t., 1 h (b) Ph_2PK (1.1 equiv.), THF, 0°C, 20–30 min.

afforded **3a** in a 94% yield. The treatment of **2a** and **3a** with potassium diphenylphosphide[6] led to **2** and **3** in 86% and 71% yields, respectively.

The reaction of **4** with the sodium salt of dimethylmalonate in THF at r.t. using $[(\eta^3\text{-allyl})PdCl]_2$/**2**(or **3**) as the catalytic system led to dimethyl 2-((*E*)-1,3-diphenylallyl)malonate in an 82–87% yield with 88–93% ee (Eq.(1)).



(1)

In conclusion, we have synthesized two phosphorus-containing oxazolines that have been used for the first time as chiral ligands for efficient Pd-catalyzed Tsuji–Trost reactions.

EXPERIMENTAL

All reactions were carried out under an argon atmosphere using dry solvents. The Pd-catalyzed reactions were carried out according to a published procedure;[6] the enantiomeric excesses were determined by HPLC using a Daicel Chiracel OD column and hexane/*i*-PrOH (99:1) as an eluent (254 nm, 0.5 mL/min). IR analyses were recorded on a Spectrafile IR-TF plus Midac. NMR spectra were recorded on Bruker spectrometers (^{1}H, 250 or 500 MHz; ^{13}C, 62.9 or 125.8 MHz, ^{19}F, 235.4 MHz, ^{31}P, 120.2 MHz) and referenced to TMS, $CFCl_3$ and 85% H_3PO_4, respectively. MS analyses were performed on a Q-TOF micro (Micromass) with an electrospray source.

The Synthesis of 2a

MeCN (8 mL) and CCl_4 (2 mL) were added to a round-bottom flask containing o-fluorobenzoic acid (560 mg, 4 mmol) and PPh_3 (1050 mg, 4 mmol) cooled at 0°C. After stirring for 2.5 h, a solution of (−)-norephedrine (605 mg, 4 mmol) and NEt_3 (1315 mg, 13 mmol) in MeCN (2 mL) was added. After stirring at r.t. for 1 h, the reaction was cooled at 0°C, and a supplementary portion of PPh_3 (393 mg, 1.5 mmol) was added. The mixture was stirred at r.t. for 1 h. The residue obtained after evaporation of the solvents under reduced pressure was dissolved in CH_2Cl_2 (20 mL). This was washed with 2M of aqueous NaOH,

evaporated, and then subjected to column chromatography to afford **2a** (775 mg, 76%).

IR (KBr, cm^{-1}): 699, 745, 766, 1455, 1497, 1584, 1613, 1649. ^1H NMR ($CDCl_3$, δ ppm): 1.55 (d, 6.7 Hz, 3H), 4.22 (quint, 6.8 Hz, 1H), 5.08 (d, 7.9 Hz, 1H), 7.16 (m, 1H), 7.29 (m, 1H), 7.35 (m, 5H), 7.40 (m, 1H), 7.94 (dt, 1.7 and 7.4 Hz). ^{13}C NMR ($CDCl_3$, δ ppm): 21.2, 71.0, 87.4, 115.9 (d, $J_{CF} = 10.3$ Hz), 116.6 (d, $J_{CF} = 21.9$ Hz), 123.8 (d, $J_{CF} = 3.8$ Hz), 125.4, 128.4, 128.6, 131.0 (d, $J_{CF} = 1.3$ Hz), 132.8 (d, $J_{CF} = 8.7$ Hz), 140.1, 159.2 (d, $J_{CF} = 5.7$ Hz), 161.1 (d, $J_{CF} = 258.5$ Hz). ^{19}F NMR ($CDCl_3$, δ ppm): −108.9.

The Synthesis of 2

A 0.5-M Ph_2PK solution in THF (11 mL, 5.5 mmol) was added dropwise to a solution of **2a** (1275 mg, 5 mmol) in THF (10 mL) at 0°C. The mixture was stirred at 0°C until the color changed from red to yellow (20–30 min). After the addition of water (15 mL) and extraction of the aqueous phase with CH_2Cl_2 (3 × 10 mL), the organic phases were washed with brine and dried over $MgSO_4$. Evaporation of the solvent followed by column chromatography led to **2** (1810 mg, 86%).

$[\alpha]_D^{20} = +73.2$ (c = 0.7, CH_2Cl_2). ^1H NMR ($CDCl_3$, δ ppm): 1.26 (d, 6.6 Hz, 3H), 4.02 (quint., 7.7 Hz, 1H), 4.71 (d, 8.3 Hz, 1H), 6.88 (m, 1H), 7.13 (d, 5.9 Hz, 2H), 7.34 (m, 15H), 7.98 (m, 1H). ^{13}C NMR ($CDCl_3$, δ ppm): 20.6, 70.8, 87.8, 125.8, 127.9, 128.0, 128.3 (d, $J_{CP} = 6.8$ Hz), 128.4 (d, $J_{CP} = 8$ Hz), 128.5, 128.7, 130.0 (d, $J_{CP} = 2.5$ Hz), 133.5 (d, $J_{CP} = 2.4$ Hz), 133.9 (d, $J_{CP} = 20.9$ Hz), 134.4 (d, $J_{CP} = 21.2$ Hz), 138.0 (d, $J_{CP} = 10.8$ Hz), 138.1 (d, $J_{CP} = 12.2$ Hz), 139.4 (d, $J_{CP} = 25.9$ Hz), 140.0, 162.3 (d, $J_{CP} = 3.5$ Hz). ^{31}P NMR ($CDCl_3$, δ ppm): −4.4. M. S. (E. S.): 422(M + 1).

The same procedures were used for the synthesis of **3a** and **3**.

3a (770 mg, 94%) from o-fluorobenzoic acid (420 mg, 3 mmol). IR (KBr, cm^{-1}): 764, 1457, 1497, 1612, 1643. ^1H NMR ($CDCl_3$, δ ppm): 0.92 (s, 3H), 0.96 (s, 6H), 1.20 (m, 2H), 1.49 (m, 2H), 2.14 (wide s, 1H), 4.58 (d, 9.8 Hz, 1H), 4.72 (dd, 9.8 and 5.0 Hz, 1H), 7.14 (m, 2H), 7.37 (m, 1H), 7.83 (t, 7.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, δ ppm): 15.0, 18.4, 19.9, 20.6, 27.1, 49.1, 49.3, 49.5, 71.8, 88.6, 116.6 (d, $J_{CF} = 22$ Hz), 123.9 (d, $J_{CF} = 3.9$ Hz), 131.0, 132.5, 132.6, 160.2 (d, $J_{CF} = 6.0$ Hz), 161.2 (d, $J_{CF} = 273.8$ Hz). ^{19}F NMR ($CDCl_3$, δ ppm): −109.7.

3 (312 mg, 71%) from **3a** (723 mg, 2.65 mmol). $[\alpha]_D^{20} = +77.4$ (c = 0.7, CH_2Cl_2). ^1H NMR ($CDCl_3$, δ ppm): 0.74 (s, 3H), 0.79 (s, 6H), 1.10 (m, 4H), 1.90 (t, 1.2 Hz, 1H), 4.28 (d, 9.9 Hz, 1H), 4.41 (dd, 4.9 and 9.9 Hz, 1H), 6.81 (m, 1H), 7.23 (m, 12H), 7.92 (m, 1H). ^{13}C NMR ($CDCl_3$,

δ ppm): 14.8, 18.3, 198.8, 20.3, 27.0, 49.1, 49.2, 49.2, 71.8, 88.6, 128.0, 128.2 (d, $J_{CP} = 7.3$ Hz), 128.3 (d, $J_{CP} = 4.6$ Hz), 129.9 (d, $J_{CP} = 2.9$ Hz), 130.2, 132.3 (d, $J_{CP} = 19.9$ Hz), 133.9, 134.0, 134.1, 138.1 (d, $J_{CP} = 37.9$ Hz), 138.4 (d, $J_{CP} = 39.2$ Hz), 138.8 (d, $J_{CP} = 25.6$ Hz), 163.4 (d, $J_{CP} = 2.5$ Hz). ^{31}P NMR ($CDCl_3$, δ ppm): -5.7. M. S. (E. S.): 440 (M + 1).

REFERENCES AND NOTES

[1] (a) F. Hénin, R. Mortezaei, J. Muzart, and J.-P. Pète, *Tetrahedron Lett.*, **26,** 4945 (1985); (b) O. Piva, R. Morteza, F. Hénin, J. Muzart, and J.-P. Péte, *J. Am. Chem. Soc.*, **112,** 9263 (1990); (c) J. Muzart, F. Hénin, J.-P. Péte, and A. M'Boungou-M'Passi, *Tetrahedron: Asymmetry*, **4,** 2531 (1993); (d) F. Hénin, J. Muzart, J.-P. Péte, A. M'Boungou-M'Passi, and H. Rau, *Angew. Chem., Int. Ed. Engl.*, **30,** 416 (1991); (e) F. Hénin, S. Létinois, and J. Muzart, *Tetrahedron: Asymmetry*, **11,** 2037 (2000).

[2] (a) F. Hénin and J. Muzart, *Tetrahedron: Asymmetry*, **3,** 1161 (1992); (b) J. Muzart, F. Hénin, and S. Jamal Aboulhoda, *Tetrahedron: Asymmetry*, **8,** 381 (1997); (c) O. Roy, A. Riahi, F. Hénin, and J. Muzart, *Eur. J. Org. Chem.*, 3986 (2002); (d) C. Thorey, S. Bouquillon, A. Helimi, F. Hénin, and J. Muzart, *Eur. J. Org. Chem.*, 2151 (2002); (e) M. A. Baur, A. Riahi, F. Hénin, and J. Muzart, *Tetrahedron: Asymmetry*, **14,** 2755 (2003); (f) O. Roy, F. Loiseau, A. Riahi, F. Hénin, and J. Muzart, *Tetrahedron*, **59,** 9641 (2003); (g) J.-F. Detalle, A. Riahi, V. Steinmetz, F. Hénin, and J. Muzart, *J. Org. Chem.*, **69,** 6528 (2004).

[3] A. M'Boungou-M'Passi, F. Hénin, J. Muzart, and J.-P. Péte, *Bull. Soc. Chim. Fr.*, **130,** 214 (1993).

[4] (a) D. Ferroud, J. P. Genêt, and J. Muzart, *Tetrahedron Lett.*, **25,** 4379 (1984); (b) C. Chevrin, J. Le Bras, F. Hénin, J. Muzart, A. Pla-Quintana, A. Roglans, and R. Pleixats, *Organometallics*, **23,** 4796 (2004).

[5] (a) P. von Matt and A. Pfaltz, *Angew. Chem., Int. Ed. Engl.*, **32,** 566 (1993); (b) J. Sprinz and G. Helmchen, *Tetrahedron Lett.*, **34,** 1769 (1993).

[6] G. J. Dawson, C. G. Frost, J. M. J. Williams, and S. J. Coste, *Tetrahedron Lett.*, **34,** 3149 (1993).

[7] For reviews, see (a) J. M. J. Williams, *Synlett*., 705 (1996); (b) A. Pfaltz, *Synlett.*, 835 (1999); (c) G. Helmchen and A. Pfaltz, *Ace. Chem. Res.*, **33,** 336 (2000); (d) A. Pfaltz, *Chimia*, **55,** 708 (2001).

[8] S. Liu, J. F. K. Müller, M. Neuburger, S. Schaffner, and M. Zehnder, *J. Organomet. Chem.*, **549,** 283 (1997).

[9] Zehnder's team[8] has used a synthetic method (G. Koch, G. C. Lloyd-Jones, O. Loiseleur, A. Pfaltz, A. Prétôt, S. Schaffner, P. Schnider, and P. von Matt, *Recl. Trav. Chim. Pays-Bas*, **114,** 206 (1995)) different from the one reported here.

[10] M. Peer, J. C. de Jong, M. Kiefer, T. Langer, H. Rieck, H. Schell, P. Sennhenn, J. Sprinz, H. Steinhagen, B. Wiese, and G. Helmchen, *Tetrahedron*, **52,** 7547 (1996).