Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 8461–8465

TETRAHEDRON LETTERS

Studies in the preparation of novel *P*-chirogenic binaphthyl monophosphanes (MOPs)

Nessan J. Kerrigan,[a] Eoin C. Dunne,[a] Desmond Cunningham,[b] Patrick McArdle,[b] Karen Gilligan[b] and Declan G. Gilheany[a,*]

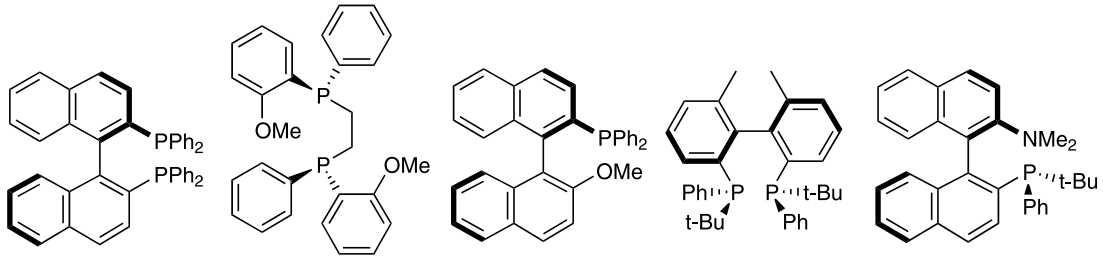
[a]*Chemistry Department, The Centre for Synthesis and Chemical Biology, Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Belfield, Dublin 4, Ireland*
[b]*Chemistry Department, National University of Ireland, Galway, Ireland*

Received 21 July 2003; revised 29 August 2003; accepted 12 September 2003

Abstract—Several routes to *P*-chirogenic binaphthyl monophosphanes (MOPs) and their derivatives were investigated. Palladium catalysed coupling gave access to a new class of P-chirogenic phosphane oxides from which the phosphane can be obtained by reduction. Substituents on phosphorus strongly influence the efficiency of the P–C coupling reaction, which is only slightly stereoselective.

Chiral biaryls[1] are valuable sources of chiral information in a wide range of efficient asymmetric reactions. Chiral phosphanes are similarly prized.[2] The C_2-symmetric diphosphanes, BINAP (**1**)[3] and diPAMP (**2**)[4] are leading representatives of two classes of chiral phosphane: those possessing axial chirality (BINAP) and those possessing chirogenic phosphorus centres (diPAMP). Both of these phosphanes are known as highly efficient ligands for transition-metal catalysed asymmetric transformations which led to the Nobel Prize being awarded to their respective developers.[5] BINAP and other chiral phosphanes have also been used as organocatalysts with mixed results in a number of reactions.[6] Recently monophosphanes such as Hayashi's binaphthyl-substituted monophosphane ligand (MOP) (**3**)[7] and Morrison's NMDPP[8] have shown increased utility in a variety of asymmetric transformations. Hayashi has employed MOP as a ligand in asymmetric C–C and C–Si bond formation reactions.[7] In 1996, Cereghetti and co-workers reported the first phosphane possessing both chiral phosphorus atoms and an axially chiral biphenyl moiety (**4**),[9] while in 2002 Buchwald and co-workers reported the synthesis and use of a *P*-chirogenic dimethylamino analogue of MOP (MAP, **5**).[10,11] At the time of that report we were also working on the synthesis of a monophosphane possessing both axial chirality and a stereogenic phosphorus centre. Herein we report on our preliminary studies including, to our knowledge, the synthesis of the first example of a *P*-chirogenic MOP.

Our first attempts were with the Merck Company procedure[12] involving the nickel catalysed coupling of secondary phosphine to resolved[13] binaphthyl ditriflate (**6**), in an attempt to synthesise 2-(*tert*-butylphenylphos-



(*R*)-**1** (*S,S*)-**2** (*R*)-**3** (*S,R,R*)-**4** (*R,R*)-**5**

* Corresponding author. Tel.: +353-1-7162308; fax: +353-1-7162127; e-mail: declan.gilheany@ucd.ie

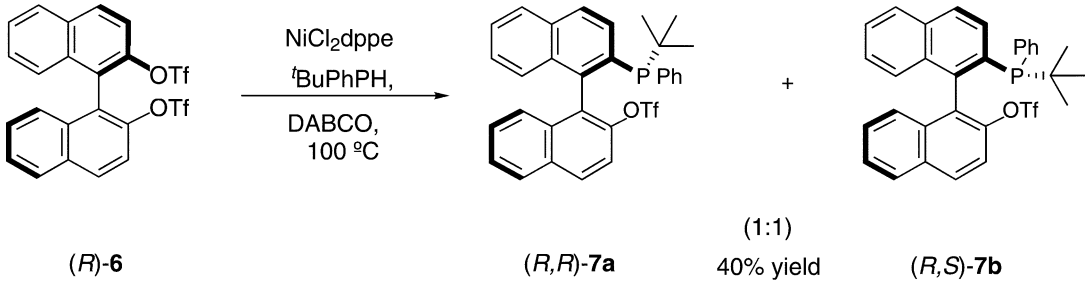
0040-4039/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2003.09.109

pino)-2′-(triflate)-1,1′-binaphthyl (**7**) (Scheme 1). We envisaged that the steric bulk of the *t*-butylphenyl phosphane group might prevent the second cross coupling from occurring leading to the desired *P*-chirogenic monophosphane products. Another point of interest was whether any asymmetric induction or kinetic resolution[14] due to the asymmetry of the binaphthyl backbone would be observed. A complex mixture of monophosphane products (53% conversion) with the desired diastereomeric products (55:45) as major components was obtained. However the diastereomers (**7a** and **7b**) could not be separated by chromatography and, considering the moderate conversion, this route was not further pursued for these types of compound.

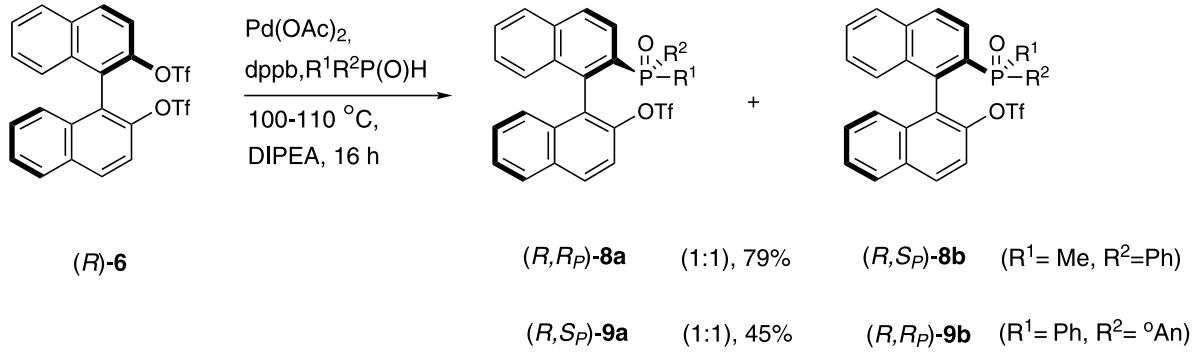
The Morgans/Hayashi palladium-catalysed cross coupling of secondary phosphane oxides with triflate (**6**) was then explored.[15] (Scheme 2). Using methylphenylphosphine oxide,[16] the desired diastereomeric products (**8a** and **8b**) were formed in a 1:1 ratio and could be separated and isolated from side products by chromatography on silica in a combined yield of 79%.[17,18] As a further indication of the utility of this method, triflate (**6**) could also be coupled with the bulkier anisylphenyl phosphine oxide and the desired diastereomeric products (**9a** and **9b**) were again obtained in a ratio of 1:1, albeit with a lower combined yield of 45% (Scheme 2).[19] The absolute configuration of **9a** was determined to be R,S_P by X-ray analysis (Fig. 1).[20]

Both **8a** and **8b** were hydrolysed to **10a** and **10b** in excellent yield (92 and 86%, respectively)[21] which were in turn alkylated with methyl iodide to afford **11a** and **11b** in very good yields (76 and 81%, respectively) (Scheme 3).[22] The absolute configuration of **10b** was determined to be (R,S_p) by X-ray analysis[20] (Fig. 2).

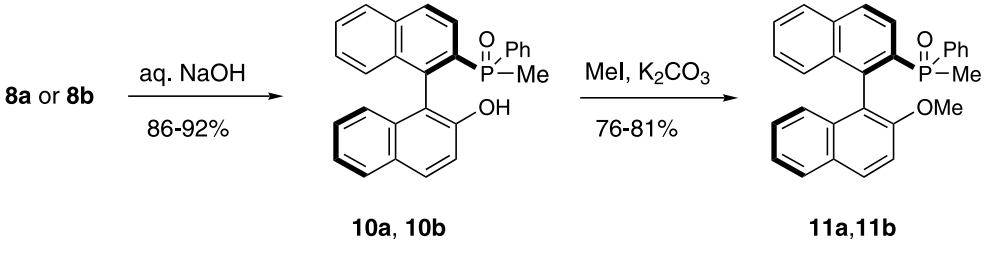
In preliminary studies, a number of literature methods[23–25] were examined for the stereospecific reduction of **11a** and **11b** and the results are shown in Table 1. Of all these methods only hexachlorodisilane afforded diastereomerically pure *P*-chirogenic MOP (**12a**).[26] The configuration at phosphorus is assumed to be *S* as this procedure is known to give inversion of



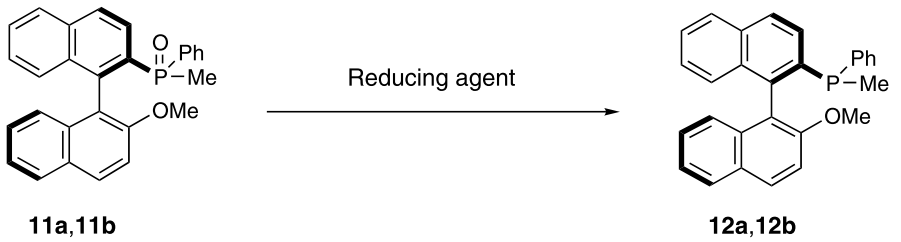
Scheme 1. Merck route to *P*-chirogenic MOPs.



Scheme 2. Morgans/Hayashi route to *P*-chirogenic MOP oxide triflates.



Scheme 3. Hayashi route to *P*-chirogenic MOP oxides.



11a,11b **12a,12b**

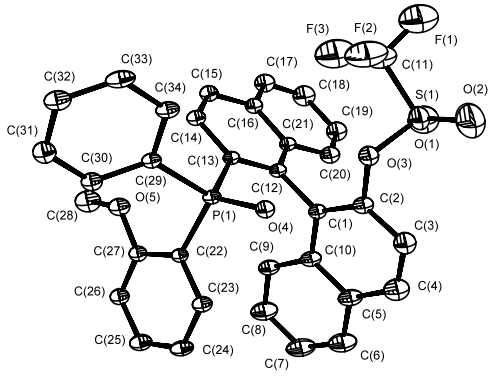


Figure 1. ORTEP diagram of **9a**.

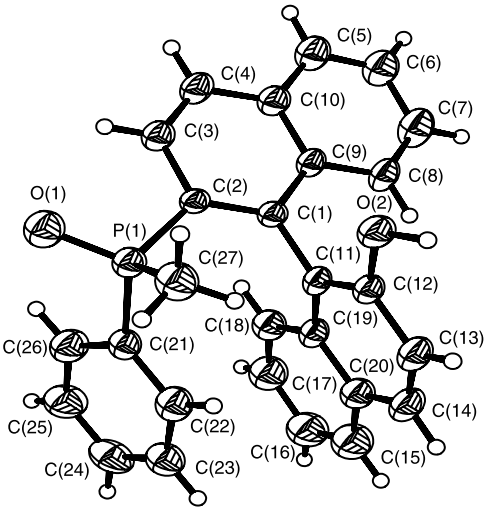


Figure 2. ORTEP diagram of **10b**.

configuration of acyclic substrates.[23,25] All other procedures allowed complete or partial epimerisation at phosphorus to occur. As can be seen from Table 1 no route to diastereomerically pure **12b** was found, with the highest de in favour of **12b** being 72%. Clearly **12b** is more prone to epimerisation at phosphorus under all conditions tested.

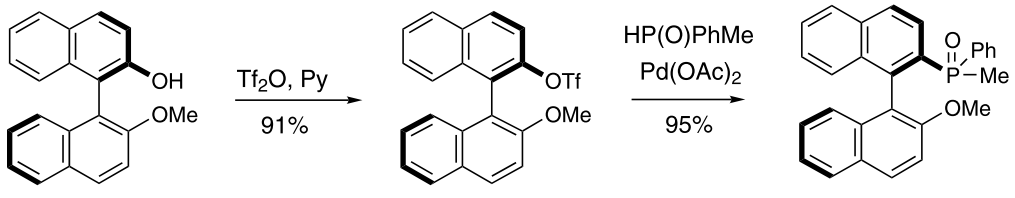
Table 1. Reduction of *P*-chirogenic MOP-oxides (**11a**, **11b**) to *P*-chirogenic MOPs

ArP(O)MePh	Reducing agent	Yield (%)	% **12a**[c]	% **12b**
11a	$HSiCl_3/Et_3N$	65	50	50
11a	$LiAlH_4$/MeOTf	83	92	8
11a	Si_2Cl_6[a]	60	100	0
11b	Si_2Cl_6[a]	70	30	70
11b	Si_2Cl_6[b]	36	14	86
11b	$LiAlH_4$/MeOTf	70	14	86

[a] Time = 30 min.
[b] Time = 10 min.
[c] Determined by ^1H NMR integration of CH_3 signals.

An alternative route (Scheme 4) to **11a**/**11b** was also investigated.[27] The desired MOP oxide diastereomers (ratio approx. 1:1) were obtained in excellent yield (95%) but, to our chagrin, they could not be separated by silica gel chromatography under any conditions.

In summary, we have developed a route to the first *P*-chirogenic MOP. During the work, it was apparent that there is little, if any, selectivity in the coupling reactions of BINOL triflate with phosphorus sources. This has both the disadvantage that separation of diastereomers is necessary and the advantage that both are available. It was also clear that the separation itself may not be possible, that substituents on phosphorus strongly influence the efficiency of the coupling reaction and that reduction of the precursor diastereomeric MOP oxides cannot be assumed to be straightforward. We are currently developing routes to other *P*-chirogenic MOPs, and to *P*-chirogenic BINAPs and examining the use of these compounds as ligands and organocatalysts in asymmetric synthesis.



11a,11b (1:1)

Scheme 4. Huang route to *P*-chirogenic MOP oxide.

Acknowledgements

We thank Enterprise Ireland (Basic Research Grant SC/96/435 and Studentship for E.C.D.), and University College Dublin (Demonstratorships for N.J.K. and E.C.D).

References

1. (a) *Catalytic Asymmetric Synthesis*, 2nd Ed.; Ojima, I., Ed.; Wiley-VCH; New York, 2000; (b) *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer-Verlag: Berlin, 1999; Vols. 1–3.
2. (a) Brunner, H.; Zettlmeier, W. *Handbook of Enantioselective Catalysis with Transition Metal Compounds Vol. I, Products and Catalysts*, VCH: Weinheim, 1993; (b) Pietrusiewicz, K. M.; Zablocka, M. *Chem. Rev.* **1994**, *94*, 1375–1411; (c) Komarov, I. V.; Börner, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 1197–1200.
3. (a) Miyashita, A.; Yasda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932; (b) Noyori, R.; Tomino, I.; Tanimoto, Y.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709.
4. Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J.; Bachman, G. L.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 5946.
5. (a) Noyori, R. *Angew. Chem., Int. Ed. Engl.* **2002**, *41*, 2008–2022; (b) Knowles, W. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 1998–2007.
6. (a) Dalko, P. I.; Moisan, L. *Angew. Chem., Int. Ed.* **2001**, *40*, 3726 and references cited therein; (b) Vedejs, E.; Daugulis, O.; MacKay, J. A.; Rozners, E. *Synlett* **2001**, *10*, 1499–1505.
7. Hayashi, T. *Acc. Chem. Res.* **2000**, *33*, 354 and references cited therein.
8. (a) Morrison, J. D.; Burnett, R. E.; Aguiar, A. M.; Morrow, C. J.; Philips, C. *J. Am. Chem. Soc.* **1971**, *93*, 1301–1303; (b) Miller, K. M.; Huang, W.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2003**, *125*, 3442.
9. Cereghetti, M.; Arnold, W.; Broger, E. A.; Rageot, A. *Tetrahedron Lett.* **1996**, *37*, 5347.
10. Hamda, T.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 999.
11. However both diastereomers were afforded in a moderate combined yield of 39%.
12. Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1994**, *59*, 7180.
13. We have recently improved substantially the resolution of the precursor binaphthol: Schanz, H.-J.; Linseis, M. A.; Gilheany, D. G. *Tetrahedron: Asymmetry* **2003**, *14*, 2763.
14. Moncarz, J. R.; Laritcheva, N. F.; Glueck, D. S. *J. Am. Chem. Soc.* **2002**, *124*, 13356.
15. (a) Kurz, L.; Lee, G.; Morgans, D., Jr.; Waldyke, M. J.; Ward, T. *Tetrahedron Lett.* **1990**, *31*, 6321–6324; (b) Uozumi, Y.; Tanahashi, A.; Lee, S.-Y.; Hayashi, T. *J. Org. Chem.* **1993**, *58*, 1945.
16. Prepared according to: Horner, L.; Hoffmann, H.; Beck, P. *Chem. Ber.* **1958**, *91*, 1583.
17. The side products included those of hydrolysis **10a** (5%) and **10b** (5%) and their hydrogenolysed analogues lacking hydroxyl groups (10%). The crude mixture was purified by flash column chromatography (hexane/EtOAc, 4:1) to give pure **8a** but with **8b** slightly contaminated with **10b**. The absolute configurations were established by an X-ray determination on **10b** after complete hydrolysis (vide infra).
18. (R,R_p)-**8a** (40%), $R_f=0.26$; ^{1}H (300 MHz, $CDCl_3$) δ 8.19–8.13 (m, 3H, ArH), 8.03 (d, $J=9.0$ Hz, 1H, ArH), 7.96 (d, $J=8.0$ Hz, 1H, ArH), 7.94 (d, $J=8.0$ Hz, 1H, ArH), 7.58–7.47 (m, 3H, ArH), 7.37–7.17 (m, 6H, ArH), 7.12 (d, $J=9.0$ Hz, 1H, ArH), 7.02 (d, $J=9.0$ Hz, 1H, ArH), 1.55 (d, 3H, $^2J_{HP}=13.0$ Hz, CH_3); ^{13}C (75 MHz, $CDCl_3$) δ 145.7 (s, ArC or CF_3), 135.2–119.5 (multiple ^{31}P coupled signals, ArC), 16.9, 16.0 (q, apt d, P-CH_3); ^{31}P (121 MHz, $CDCl_3$) δ 30.74; m/z: 540 (M^+, 0.1), 409 (0.7), 408 (3.7), 407 (4.60), 393 (3.6), 392 (25), 391 (98), 268 (36), 195 (19), 139 (100); IR (KBr, cm^{-1}) 3033, 2895, 2815, 1401, 1194, 1160, 1060, 660. Anal. calcd for $C_{28}H_{20}F_3O_4PS$: C, 62.22; H, 3.73; F, 10.55; P, 5.73; S, 5.93. Found: C, 62.15; H, 3.71; F, 10.46; P, 5.77; S, 5.91. (R,S_p)-**8b** (39%), $R_f=0.20$; ^{1}H (300 MHz, $CDCl_3$) δ 8.20–8.12 (m, 3H, ArH), 7.97 (d, $J=9.0$ Hz, 1H, ArH), 7.95 (d, $J=8$Hz, 1H, ArH), 7.84 (d, $J=8.5$ Hz, 1H, ArH), 7.55 (apt t, $J=8.5$ Hz, 1H, ArH), 7.43 (apt t, $J=8.5$ Hz, 1H, ArH), 7.38 (d, $J=9.0$ Hz, 1H, ArH), 7.31–7.14 (m, 4H, ArH), 7.08–7.03 (m, 3H, ArH), 6.91 (d, $J=9.0$ Hz, 1H, ArH), 1.83 (d, 3H, $^2J_{HP}=13.0$ Hz, CH_3); ^{13}C (75 MHz, $CDCl_3$) δ 145.3 (s, ArC or CF_3), 134.9–119.0 (multiple ^{31}P coupled signals, ArC), 17.2, 16.2 (q, apt d, P-CH_3); ^{31}P (121 MHz, $CDCl_3$) δ 30.79.
19. Another 15% was accounted for by hydrolysed and hydrogenolysed products. Product **9a** crystallised from the mixture while **9b** was isolated (somewhat impure) by chromatography. Selected analytical data: (R,S_P)-**9a**: ^{1}H (300 MHz, $CDCl_3$) δ 7.97–6.65 (m, 21H, ArH), 3.51 (s, 3H, OCH_3); ^{31}P (121 MHz, $CDCl_3$) δ 27.0. Anal. calcd for $C_{34}H_{24}O_5F_3SP$: C, 64.56; H, 3.82. Found: C, 64.59; H, 3.57; m/z: 500 (M^+, 1.6), 499 (3.7), 485 (3), 484 (17), 483 (60), 467 (3), 268 (13), 252 (3); $[\alpha]_D=+57.5$ (c 0.386, $CHCl_3$). (R,R_P)-**9b**: ^{1}H (300 MHz, $CDCl_3$) δ 7.96–6.67 (m, ArH), 3.55 (s, 3H, OCH_3); ^{31}P (121 MHz, $CDCl_3$) δ 27.5.
20. Crystallographic data: **9a**: $C_{34}H_{24}F_3O_5PS$, $M=632.56$, orthorhombic, $P2_12_12_1$, $a=11.2625(18)$, $b=13.953(2)$, $c=19.020(3)$ Å, $V=2989.0(8)$ Å^3, $Z=4$, $D_{calcd}=1.406$ Mg/m^3; **10b**: $C_{27}H_{21}O_2P$, $M=408.41$, orthorhombic, $P2_12_12_1$, $a=9.02(9)$ Å, $b=13.15(9)$ Å, $c=17.67(9)$ Å, $V=2096(28)$ Ags^3, $Z=4$, $D_{calcd}=1.294$ Mg/m^3. Crystallographic data (excluding structure factors) for the structures in this paper, have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 219883 (**9a**) and 219882 (**10b**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).
21. (R,R_p)-**10a**: ^{1}H (300 MHz, $CDCl_3$) δ 8.37 (br s, 1H, OH), 8.12–7.91 (m, 3H, ArH), 7.71 (d, $J=9.0$ Hz, 1H, ArH), 7.50 (m, 2H, ArH), 7.35 (d, $J=9.0$ Hz, 1H, ArH), 7.18 (m, 1H, ArH), 7.07–6.93 (m, 4H, ArH), 6.82–6.65 (m, 4H, ArH), 6.17 (d, $J=9.0$ Hz, 1H, ArH), 2.04 (d, 3H, $^2J_{HP}=13.0$ Hz, CH_3); ^{13}C (75 MHz, $CDCl_3$) δ 153.6, 140.1, (s, ArC), 133.7–123.0 (multiple ^{31}P coupled signals, ArC), 18.6, 18.0 (q, apt d, P-CH_3); ^{31}P (121 MHz,

$CDCl_3$) δ 35.11. Anal. calcd for $C_{27}H_{21}O_2P$: C, 79.40; H, 5.18; P, 7.58. Found: C, 79.35; H, 5.20; P, 7.52. (R,S_p)-**10b**: ^1H (300 MHz, $CDCl_3$) δ 8.28 (br s, 1H, OH), 7.95 (d, $J=8.5$ Hz, 1H, ArH), 7.85 (m, 2H, ArH), 7.67 (m, 2H, ArH), 7.57–7.42 (m, 5H, ArH), 7.38–7.21 (m, 4H, ArH), 7.11 (m, 2H, ArH), 6.71 (d, $J=8.5$ Hz, 1H, ArH), 1.27 (d, $^2J_{HP}=13.0$ Hz, 3H, CH_3); ^{13}C (75 MHz, $CDCl_3$) δ 153.6, 140.1 (s, ArC), 133.7–123.0 (multiple ^{31}P coupled signals, ArC), 18.6, 18.0 (q, apt d, P-CH_3); ^{31}P (121 MHz, $CDCl_3$) δ 36.89; m/z 410 (M^+, 0.1), 408, (10.3), 268 (68.7), 239 (14.5), 125 (3.6), 77 (93.1), 44 (11.46), 32 (35.48), 28 (100); IR (KBr, cm^{-1}) 3055, 2913, 2834, 1602, 1511, 1312, 1225, 1150, 800, 750.

22. (R,R_p)-**11a**: mp 186–187°C; ^1H (300 MHz, MeOD) δ 8.43 (dd, $J=8$ Hz and 11 Hz, 1H, ArH), 8.09 (d, $J=10.5$ Hz, 1H, ArH), 7.94 (d, $J=8$ Hz, 1H, ArH), 7.92 (d, $J=9$ Hz, 1H, ArH), 7.82 (d, $J=9$ Hz, 1H, ArH), 7.51 (apt t, $J=9$ Hz, 1H, ArH), 7.34–7.09 (m, 9H, ArH), 7.05 (d, $J=9$ Hz, 1H, ArH), 6.86 (d, $J=8.5$, 1H, ArH), 3.27 (s, 3H, OMe), 1.24 (d, 3H, $^2J_{HP}=13.5$ Hz, CH_3); ^{13}C (75 MHz, MeOD) δ 154.9 (s, ArC) 135.2–123.9 (multiple P-coupled signals, ArC), 112.6 (s, ArC), 55.4 (s, OCH_3), 16.3 (d, CH_3); ^{31}P (121 MHz, MeOD) δ 31.84; IR_A (KBr, cm^{-1}) 3054, 2923, 2838, 1690, 1670, 1509, 1258, 1208, 998, 743; $[\alpha]_D^{20}=+38.1$ (c 0.21, MeOH). Anal. for $C_{28}H_{23}O_2P$ requires C, 79.61; H, 5.49; O, 7.57; P, 7.33%. Found C, 79.56; H, 5.51; P, 7.35%. (R,S_p)-**11b**: mp 206–207°C; ^1H (300 MHz, MeOD) δ 8.43 (apt t, $J=9.5$ Hz, 1H, ArH), 8.07 (d, $J=8$ Hz, 1H, ArH), 7.92 (d, $J=9$ Hz, 1H, ArH), 7.91 (d, $J=8$, 1H, ArH), 7.67 (d, $J=8$ Hz, 1H, ArH), 7.48 (apt t, $J=7$ Hz, 1H, ArH), 7.32 (d, $J=9$ Hz, 1H, ArH), 7.27–6.86 (m, 6H, ArH), 6.80 (apt t, $J=8$ Hz, 1H ArH), 6.38 (d, $J=8.5$ Hz, 1H, ArH), 3.69 (s, 3H, OCH_3), 1.61 (d, $^2J_{HP}=13.5$ Hz, 3H, CH_3) ^{13}C (75 MHz, $CDCl_3$) δ 153.7 (s, ArC) 137.5–119.0 (multiple P-coupled signals, ArC), 111.4 (s, ArC), 54.8 (s, OCH_3), 14.4, (d, CH_3); ^{31}P (121 MHz, $CDCl_3$) δ 31.66; $[\alpha]_D^{20}=-18.8$ (c 0.25, $CHCl_3$); IR_B (KBr, cm^{-1}) 3054, 2923, 2838, 1690, 1670, 1509, 1258, 1208, 998, 743. Anal. for $C_{28}H_{23}O_2P$ requires C, 79.61; H, 5.49; O, 7.57; P, 7.33%. Found C, 79.30; H, 5.73%.

23. (a) Naumann, K.; Zon, G.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 7012; (b) Zon, G.; Mislow, K. *Fortschr. Chem. Forsch.* **1971**, *19*, 61.
24. Imamoto, T.; Kikuchi, S.-I.; Miura, T.; Wada, Y. *Org. Lett.* **2001**, *1*, 87.
25. (a) DeBruin, K. E.; Naumann, K.; Zon, G.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 7027; (b) Calas, R.; Dunogues, J.; Deleris, G.; Duffaut, N. *J. Organomet. Chem.* **1982**, *225*, 117.
26. (R,S_p)-**12a**: ^1H (300 MHz, $CDCl_3$) δ 8.00–6.97 (m, 17H, ArH), 3.58 (s, 3H, OCH_3), 1.37 (d, 3H, $^2J_{HP}=4.5$ Hz, CH_3); ^{31}P (121 MHz, $CDCl_3$) δ −33.51; (R,R_p)-**12b**: ^1H (300 MHz, $CDCl_3$) δ 8.01–6.98 (m, 17H, ArH), 3.82 (s, 3H, OCH_3), 1.51 (d, 3H, $^2J_{HP}=5$ Hz, CH_3); ^{31}P (121 MHz, $CDCl_3$) δ −33.90.
27. Huang, L. F.; Zhang, J.; Ma, W. P. *Abstr. Pap. Am. Chem. Soc.* **1998**, *216*: 156-ORGN.