Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters 49 (2008) 3120–3123
Tetrahedron Letters

A *P**-chiral bisdiamidophosphite ligand with a 1,4:3,6-dianhydro-D-mannite backbone and its application in asymmetric catalysis

Konstantin N. Gavrilov [a,*], Sergey V. Zheglov [a], Pavel A. Vologzhanin [a], Marina G. Maksimova [a], Anton S. Safronov [b], Sergey E. Lyubimov [b], Vadim A. Davankov [b], Benjamin Schäffner [c], Armin Börner [c]

[a] *Department of Chemistry, Ryazan State University, 46 Svoboda Street, 390000 Ryazan, Russia*
[b] *Institute of Organoelement Compounds, Russian Academy of Sciences, 28 Vavilov Street, 119991 Moscow, Russia*
[c] *Leibniz-Institut für Katalyse an der Universität Rostock e.V., A.-Einstein-Str. 29a, 18059 Rostock, Germany*

Received 19 December 2007; revised 21 February 2008; accepted 7 March 2008
Available online 18 March 2008

Abstract

A novel readily available *P*,*P*-bidentate diamidophosphite ligand with *P**-stereocentres is prepared from an inexpensive C_2-symmetric 1,4:3,6-dianhydro-D-mannite. By using this efficient ligand, up to 98% ee is achieved in Pd-catalysed asymmetric allylic alkylation, up to 92% ee in Pd-catalysed asymmetric allylic amination and up to 87% ee in Rh-catalysed asymmetric hydrogenation. The influence of the precatalyst, substrate and solvent on the enantioselectivity is discussed.

Keywords: Asymmetric reactions; Phosphorus ligands; Rhodium; Hydrogenation; Palladium; Amination

Asymmetric metal complex catalysis is a powerful synthetic method for producing valuable chiral compounds.[1] To achieve the highest levels of reactivity and selectivity in enantioselective catalytic reactions, different reaction parameters must be explored and adjusted. In this optimisation process, a careful selection and design of the chiral ligand is perhaps the most crucial step, since the choice of the best ligand strongly depends on each particular reaction.[2] Therefore, the design of new ligands for efficient asymmetric catalysis remains a challenge of high importance. Diphosphines have played a dominant role amongst the phosphorus-containing ligands, but recently a group of less electron-rich organophosphorus compounds, phosphite ligands, have received much attention. These ligands are extremely attractive for catalysis because they are easy to prepare from the readily available starting materials and are also less sensitive to air than to phosphines. Hence, this makes it possible to develop protocols for the whole process including the ligand synthesis that do not necessitate the use of a glove box. In addition, phosphites are characterised by pronounced π-acidity and low cost.[3] At the same time, there are only a few examples of very promising *P*,*P*-bidentate phosphite-type ligands with stereogenic phosphorus atoms in the literature.[4]

Chiral diol-based phosphite ligands are readily available and are highly functionalised with several stereogenic centres.[2,3] A series of *P*,*P*-bidentate chiral phosphites with a 1,4:3,6-dianhydro-D-mannitol backbone and biphenyl or binaphthyl moieties was synthesised and screened in the search for high activities and selectivities in asymmetric hydrogenation and allylic substitution (some examples are shown in Fig. 1).[5]

On the other hand, we have recently reported the synthesis of *P**-mono- and *P**,*N*-bidentate diamidophosphites and demonstrated that they can serve as a new class of very efficient ligands for Pd-catalysed allylation.[6] Encouraged

* Corresponding author. Tel.: +7 4912 280580; fax +7 4912 281435.
E-mail address: k.gavrilov@rsu.edu.ru (K. N. Gavrilov).

0040-4039/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.03.042

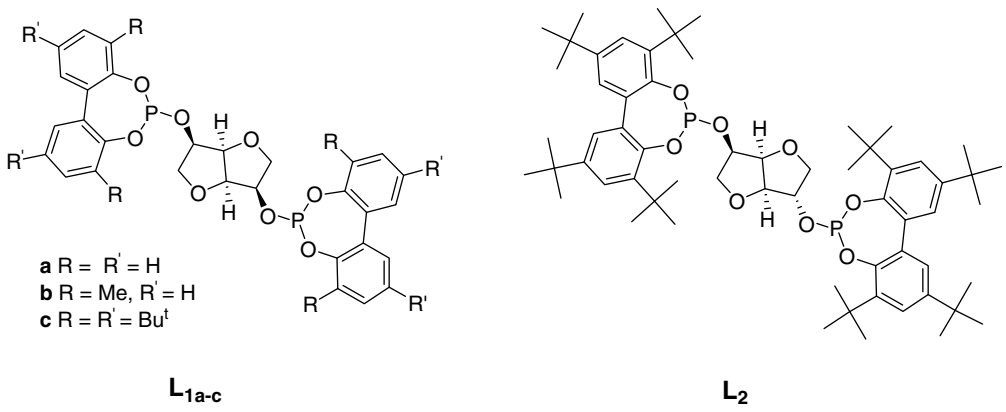


Fig. 1. Examples of *P*,*P*-bidentate phosphite ligands.

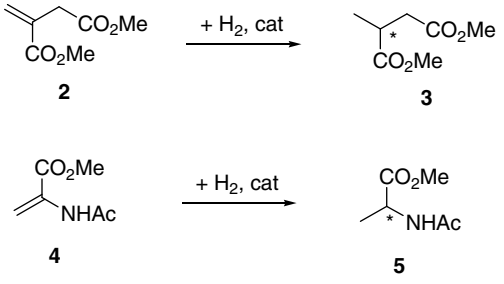
by these observations and motivated by our continuing efforts in the design and application of novel P^*-chiral ligands for use in asymmetric catalysis,[7] we have prepared P^*,P^*-bidentate bisdiamidophosphite compound **1** as a ligand for an application in asymmetric catalysis.

As stated above, the development of asymmetric catalysis requires access to the novel classes of structurally diverse phosphorus-containing ligands. Such diversity is quite difficult with phosphine ligands, whose syntheses can often require multiple steps.[8] Phosphite-type compounds, however, can be assembled in a much easier way by reacting alcohols or amines with phosphorus halides. In particular, bisphosphites can be readily prepared by the reaction between different phosphorochloridites and diols. The diol moiety bridges the two phosphite moieties and controls the bite angle of the resulting ligand. By using this strategy, we have synthesised very efficiently bisdiamidophosphite **1** in one step from the inexpensive 1,4:3,6-dianhydro-D-mannitol and (2*R*,5*S*)-2-chloro-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane (Scheme 1). The reaction was performed in the presence of Et_3N (~1.1 equiv/OH) in THF.

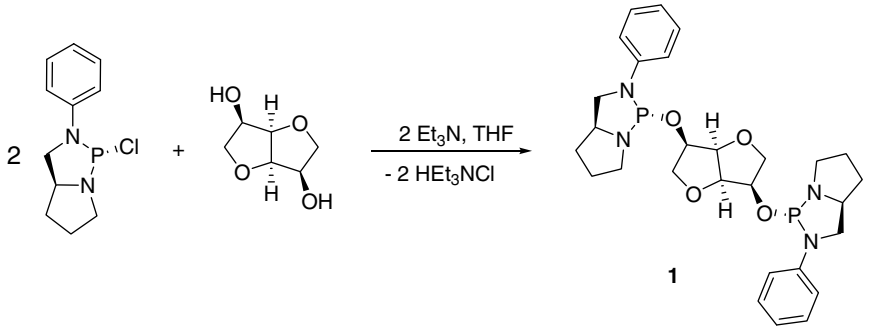
Compound **1** was obtained as a white powder after filtration, evaporation of THF from the filtrate and trituration of the resulting solid with hexane.[9] The new P^*,P^*-bidentate ligand **1** is stable on prolonged storage. Since the phosphorylating reagent is easily prepared from the readily accessible (*S*)-(2-anilinomethyl)pyrrolidine,[6a] **1** can be obtained on gram scale. As follows from the characteristic ^2J(C(8′),*P*) value (37.9 Hz) in the ^{13}C NMR spectrum,[9] the phosphorylation of 1,4:3,6-dianhydro-D-mannitol results in the exclusive formation of stereospecific bisdiamidophosphite **1** with the (*R*) configuration at the P^*-stereocentres (see Ref. 10 and references cited therein).

Asymmetric hydrogenation is a highly attractive strategy for the synthesis of optically active organic molecules of academic and/or industrial interest.[1] In this connection, we describe our results on the Rh-catalysed hydrogenation of dimethyl itaconate **2** and methyl 2-acetamidoacrylate **4** with ligand **1** (Scheme 2).

These benchmark substrates have been investigated with a wide variety of ligands carrying various donor groups.



Scheme 2. Rh-catalysed hydrogenation.



Scheme 1. Synthesis of P^*-chiral ligands.

Table 1
Rh-catalysed hydrogenation of α-dehydrocarboxylic acid esters ([Rh(COD)$_2$]BF$_4$/**1**, 1 bar H$_2$, 20 °C)[a]

Entry	Substrate	Solvent	Time (min)	ee[d,e] (%)
1	**2**	PC[b]	35	80 (*S*)
2	**2**	CH_2Cl_2	25	86 (*S*)
3[c]	**2**	CH_2Cl_2	120	81 (*S*)
4	**4**	PC	5	13 (*S*)
5	**4**	CH_2Cl_2	120	87 (*R*)

[a] 100% conversion in all cases.
[b] Propylene carbonate.
[c] [Rh(COD)$_2$]SbF$_6$ added as precatalyst.
[d] The conversion of substrate **2** and enantiomeric excess of **3** were determined by GC (Lipodex E, 25 m × 0.25 mm, 80 °C, 1 mL/min) or HPLC (Daicel Chiralcel OD-H, C_6H_{14}/*i*-PrOH = 98/2, 0.8 mL/min, 220 nm, $t(R) = 9.1$ min, $t(s) = 16.1$ min).
[e] The conversion of substrate **4** and enantiomeric excess of **5** were determined by GC (XE-valin(*tert*-butylamide) 4 × 0.25 mm, 85 °C, 1 mL/min).

We can therefore compare directly the efficacy of different ligand systems. The reactions were performed in propylene carbonate (PC) or CH_2Cl_2 at room temperature (with [Rh(COD)$_2$]BF$_4$ or [Rh(COD)$_2$]SbF$_6$, L/Rh = 1) according to the published procedures.[7a,11] In the transformation of **2** to succinate **3**, ligand **1** showed good enantioselectivity (81–86% ee), irrespective of the solvent and precatalyst (Table 1, entries 1–3). It is important to note that propylene carbonate as a reaction medium makes it possible to recycle the chiral catalyst successfully.[12]A good enantioselectivity (87%, Table 1, entry 5) was also obtained in the Rh-catalysed hydrogenation of substrate **4**, but only in CH_2Cl_2. In propylene carbonate, product **5** was formed with low optical purity and with the opposite (*S*) configuration (Table 1, entry 4).

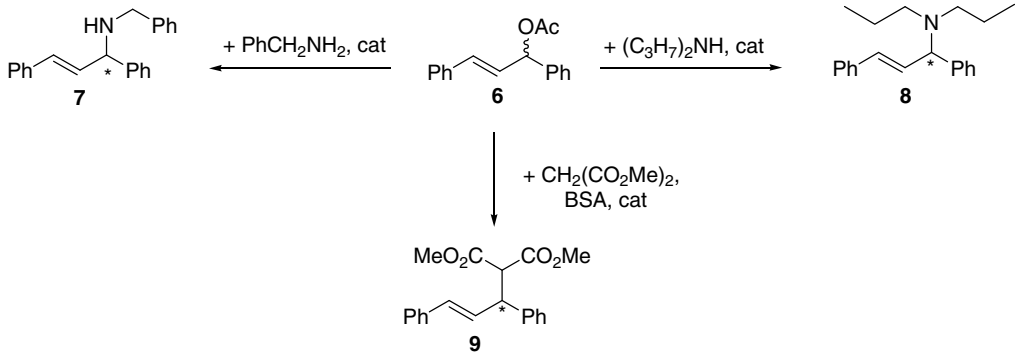
Allylic substitution is a versatile, widely used process in organic synthesis that can result in the enantioselective formation of carbon–carbon and carbon–heteroatom bonds.[13] To study further the potential of bisdiamidophosphite **1**, we tested it in the Pd-catalysed allylic substitution of (*E*)-1,3-diphenylallyl acetate **6** (which is widely used as a model substrate) with C- and N-containing nucleophiles (Scheme 3).

The reactions were performed in THF, propylene carbonate or CH_2Cl_2 at room temperature (with [Pd(allyl)Cl]$_2$ or Pd(CF$_3$CO$_2$)$_2$, L/Pd = 1 or 2) according to the published procedures.[6a,14,15] In the allylic amination of **6** with benzylamine and dipropylamine, the use of ligand **1** resulted in moderate to very good conversions and enantioselectivities in all the cases (Table 2). The best enantioselectivities of products **7** and **8** (92% and 90%, respectively) were obtained in CH_2Cl_2 at a molar ratio L/Pd = 1 (Table 2, entries 2 and 3). In the allylic alkylation of **6** with dimethyl malonate, bisdiamidophosphite **1** showed excellent enantioselectivity, up to 98% for (*S*)-**9** was obtained, CH_2Cl_2 being the solvent of choice (Table 2, entry 9). Interestingly,

Table 2
Pd-catalysed allylic amination of **6** with benzylamine and dipropylamine (20 °C) and allylic alkylation of **6** with dimethyl malonate (BSA, KOAc, 20 °C)

Entry	Precatalyst	L/Pd	Solvent	Time (h)	Conv. (%)	ee (%)
Allylic amination with benzylamine[a]						
1	[Pd(allyl)Cl]$_2$	1/1	PC	12	98	72 (*R*)
2	[Pd(allyl)Cl]$_2$	1/1	CH_2Cl_2	12	40	92 (*R*)
Allylic amination with dipropylamine[b]						
3	[Pd(allyl)Cl]$_2$	1/1	CH_2Cl_2	48	100	90 (+)
4	[Pd(allyl)Cl]$_2$	2/1	CH_2Cl_2	48	100	77 (+)
5	[Pd(allyl)Cl]$_2$	1/1	THF	48	57	76 (+)
6	[Pd(allyl)Cl]$_2$	2/1	THF	48	100	70 (+)
Allylic alkylation with dimethyl malonate[c]						
7	Pd(CF$_3$CO$_2$)$_2$	1/1	PC	14	78	67 (*S*)
8	Pd(CF$_3$CO$_2$)$_2$	1/1	CH_2Cl_2	14	91	86 (*S*)
9	[Pd(allyl)Cl]$_2$	1/1	CH_2Cl_2	48	72	98 (*S*)
10	[Pd(allyl)Cl]$_2$	2/1	CH_2Cl_2	48	80	95 (*S*)

[a] The conversion of substrate **6** and enantiomeric excess of **7** were determined by HPLC (Daicel Chiralcel OJ, C_6H_{14}/*i*-PrOH = 80/20, 0,5 mL/min, 254 nm).
[b] Enantiomeric excess of **8** determined by HPLC (Daicel Chiralcel OD-H, 1000/1/1 hexane/*i*-PrOH/HN(Et)$_2$, 0.4 mL/min, 254 nm, $t(+) = 8.2$ min, $t(-) = 9.1$ min). The conversion of **6** was determined according to ^{1}H NMR.
[c] The conversion of substrate **6** and enantiomeric excess of **9** were determined by HPLC (Daicel Chiralcel OD-H, C_6H_{14}/*i*-PrOH = 99/1, 0.6 mL/min, 254 nm).



Scheme 3. Pd-catalysed allylation.

the precatalyst $Pd(CF_3CO_2)_2$ provided higher conversion but reduced asymmetrising ability in comparison with $[Pd(allyl)Cl]_2$ (Table 2, entries 8 and 9).

In conclusion, bisdiamidophosphite **1** is an efficient ligand in asymmetric catalysis. In the Rh-catalysed hydrogenation of dimethyl itaconate **2**, ligand **1** was slightly inferior to $\mathbf{L_{1a–c}}$ (up to 86% and 98% ee, respectively), but in the Rh-catalysed hydrogenation of methyl 2-acetamidoacrylate **4** the enantioselectivities of the product **5** were almost equal (up to 87% and 89%).[5a] At the same time, in the Pd-catalysed allylic substitution of (*E*)-1,3-diphenylallyl acetate **6** with benzylamine and dimethyl malonate, ligands $\mathbf{L_{1c}}$ and $\mathbf{L_2}$ only gave up to 36% and 49% ee, respectively,[5b] being significantly lower than the enantioselectivities achieved with **1** (92% and 98%). Further testing of bisdiamidophosphite **1** in other benchmark asymmetric reactions is in progress in our laboratories.

Acknowledgements

This work was supported by the INTAS Open Call 2005–2006 Grant (INTAS Ref. No. 05-1000008-8064) RFBR Grant No. 08-03-00416-9 and the Graduate School 1213 of DFG. M.G.M. thanks the DAAD Foundation and Professor Manfred T. Reetz (Max-Planck-Institut für Kohlenforschung, Germany) for a research fellowship.

References and notes

1. (a) Brown, J. M. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. I, pp 121–182; (b) Ohkuma, T.; Kitamura, M.; Noyori, R. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH: New York, 2000; pp 1–110; (c) Blaser, H.-U.; Schmidt, E. *Asymmetric Catalysis on Industrial Scale*; Wiley-VCH: Weinheim, 2004.
2. Dieguez, M.; Ruiz, A.; Claver, C. *Dalton Trans.* **2003**, 2957–2963.
3. (a) Ansel, J.; Wills, M. *Chem. Soc. Rev.* **2002**, *31*, 259–268; (b) Alexakis, A.; Benhaim, C. *Eur. J. Org. Chem.* **2002**, *19*, 3221–3236; (c) Molt, O.; Shrader, T. *Synthesis* **2002**, 2633–2670; (d) Fache, F.; Schultz, E.; Tommasino, M. L.; Lemaire, M. *Chem. Rev.* **2000**, *100*, 2159–2232; (e) Gavrilov, K. N.; Bondarev, O. G.; Polosukhin, A. I. *Russ. Chem. Rev.* **2004**, *73*, 671–699; (f) Reetz, M. T.; Mehler, G.; Meiswinkel, A.; Sell, T. *Tetrahedron Lett.* **2002**, *43*, 7941–7943.
4. (a) Pastor, S. D.; Rodebaugh, R. K.; Odorisio, P. A.; Pugin, B.; Rihs, G.; Togni, A. *Helv. Chim. Acta* **1991**, *74*, 1175–1193; (b) Dros, A. C.; Meetsma, A.; Kellogg, R. M. *Tetrahedron* **1999**, *55*, 3071–3090; (c) Reetz, M. T.; Mehler, G.; Bondarev, O. *Chem. Commun.* **2006**, 2292–2294.
5. (a) Reetz, M. T.; Neugebauer, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 179–181; (b) Dieguez, M.; Pamies, O.; Claver, C. *J. Org. Chem.* **2004**, *104*, 3189–3216.
6. (a) Tsarev, V. N.; Lyubimov, S. E.; Shiryaev, A. A.; Zheglov, S. V.; Bondarev, O. G.; Davankov, V. A.; Kabro, A. A.; Moiseev, S. K.; Kalinin, V. N.; Gavrilov, K. N. *Eur. J. Org. Chem.* **2004**, 2214–2222; (b) Gavrilov, K. N.; Tsarev, V. N.; Shiryaev, A. A.; Bondarev, O. G.; Lyubimov, S. E.; Benetsky, E. B.; Korlyukov, A. A.; Antipin, M. Yu.; Davankov, V. A.; Gais, H.-J. *Eur. J. Inorg. Chem.* **2004**, 629–634; (c) Tsarev, V. N.; Lyubimov, S. E.; Bondarev, O. G.; Korlyukov, A. A.; Antipin, M. Yu.; Petrovskii, P. V.; Davankov, V. A.; Shiryaev, A. A.; Benetsky, E. B.; Vologzhanin, P. A.; Gavrilov, K. N. *Eur. J. Org. Chem.* **2005**, 2097–2105.
7. (a) Gavrilov, K. N.; Lyubimov, S. E.; Bondarev, O. G.; Maksimova, M. G.; Zheglov, S. V.; Petrovskii, P. V.; Davankov, V. A.; Reetz, M. T. *Adv. Synth. Catal.* **2007**, *349*, 609–616; (b) Gavrilov, K. N.; Lyubimov, S. E.; Zheglov, S. V.; Benetsky, E. B.; Petrovskii, P. V.; Rastorguev, E. A.; Grishina, T. B.; Davankov, V. A. *Adv. Synth. Catal.* **2007**, *349*, 1085–1094; (c) Benetsky, E. B.; Zheglov, S. V.; Grishina, T. B.; Macaev, F. Z.; Bet, L. P.; Davankov, V. A.; Gavrilov, K. N. *Tetrahedron Lett.* **2007**, *48*, 8326–8330.
8. Cobley, C. J.; Gardner, K.; Klosin, J.; Praquin, C.; Hill, C.; Whiteker, G. T.; Zanotti-Gerosa, A. *J. Org. Chem.* **2004**, *69*, 4031–4040.
9. *Procedure for the preparation of 3,6-bis[(2′R,5′S)-3′-phenyl-1′,3′-diaza-2′-phosphabicyclo[3.3.0]octyloxy]-(3R,3aS,6R,6aS)-hexahydrofuro[3,2-b]furan* (**1**): A solution of 1,4:3,6-dianhydro-D-mannitol (0.73 g, 5 mmol) in THF (15 ml) was added dropwise at 20 °C over 20 min to a vigorously stirred solution of (2*R*,5*S*)-2-chloro-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane (2.41 g, 10 mmol) and Et_3N (1.45 ml, 10.4 mmol) in THF (25 ml). The mixture was then heated to the boiling point, stirred for 1.5 h and cooled to 20 °C. Solid $Et_3N{\cdot}HCl$ was filtered off, and the filtrate concentrated in vacuo (40 Torr). The residue was washed with hexane and dried for 45 min in vacuo (1 Torr) to give the desired product. Yield: 2.02 g (73%). White solid, mp 69–70 °C. Spectral data of **1**: ^{31}P NMR (100.6 MHz, $CDCl_3$): 123.1. ^{13}C NMR (100.6 MHz, $CDCl_3$): 26.3 (d, $^3J = 3.7$ Hz, C(7′)), 31.9 (s, C(6′)), 48.3 (d, $^2J = 37.9$ Hz, C(8′)), 54.7 (d, $^2J = 6.9$ Hz, C(4′)), 62.5 (d, $^2J = 8.4$ Hz, C(5′)), 71.3 (s, C(2) and C(5)), 72.7 (d, $^2J = 5.5$ Hz, C(3) and C(6)), 80.8 (d, $^3J = 1.8$ Hz, C(3a) and C(6a)), 115.0 (d, $^3J = 11.7$ Hz, CH_{Ar}), 119.2 (s, CH_{Ar}), 129.0 (s, CH_{Ar}), 145.5 (d, $^2J = 16.4$ Hz, C_{Ar}). MS (EI), *m*/*z* (*I*, %): 554 (8) $[M]^+$. Anal. Calcd for $C_{28}H_{36}N_4O_4P_2$: C, 60.64; H, 6.54; N, 10.10. Found: C, 60.89; H, 6.63; N, 9.89.
10. Gavrilov, K. N.; Benetsky, E. B.; Grishina, T. B.; Zheglov, S. V.; Rastorguev, E. A.; Petrovskii, P. V.; Macaev, F. Z.; Davankov, V. A. *Tetrahedron: Asymmetry* **2007**, *18*, 2557–2564.
11. Vallianatou, K. A.; Kostas, I. D.; Holz, J.; Börner, A. *Tetrahedron Lett.* **2006**, *47*, 7947–7950.
12. Bayardon, J.; Holz, J.; Schäffner, B.; Andrushko, V.; Verevkin, S.; Preetz, A.; Börner, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 5971–5974.
13. (a) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921–2943; (b) Graening, T.; Schmalz, H.-G. *Angew. Chem., Int. Ed.* **2003**, *42*, 2580–2584.
14. Lyubimov, S. E.; Davankov, V. A.; Gavrilov, K. N. *Tetrahedron Lett.* **2006**, *47*, 2721–2723.
15. Birkholz, M.-N.; Dubrovina, N. V.; Shuklov, I. A.; Holz, J.; Paciello, R.; Waloch, C.; Breit, B.; Börner, A. *Tetrahedron: Asymmetry* **2007**, *18*, 2055–2060.