Asymmetric Catalysis with a Phosphoramidite Derived from (−)-(a*R*)-[1,1′-Binaphthalene]-8,8′-diol

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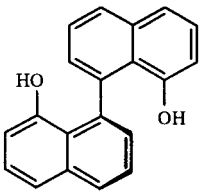
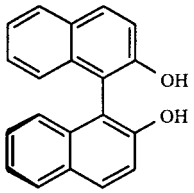
Treatment of (a*R*)-[1,1′binaphthalene]-8,8′-diol ((−)-**1**) with hexamethylphosphorous triamide afforded the *N,N*-dimethylphosphoramidite (−)-**3** (*Scheme 1*). The synthesis of the analogous *N,N*-diisopropylphosphoramidite **4** failed, however, and afforded the acyclic phosphonamidate (−)-**5**. The application of the cyclic phosphoramidite (−)-**3** towards asymmetric catalysis was investigated. The borane reduction of acetophenone (**6**) to (*R*)-1-phenylethanol (**7**) in the presence of (−)-**3** proceeded with 96% ee (*Scheme 2*). The use of (−)-**3** as ligand in several Cu-catalyzed addition and substitution reactions resulted in enantioselectivities ranging from 0 to 50% (*Schemes 3* and *4*).

Introduction. – Racemic [1,1′-binaphthalene]-8,8′-diol (8,8′-BINOL; **1**) has been synthesized by *Cram* and co-workers in 1985 [1]. Enantiomer separation of **1** has been achieved *via* the bis(menthyl carbonate) [2], the diester of *O*-acetylmandelic acid [3] and the monoester of (*R*)-2-phenylpropionic acid [4]. Binaphthalenes having sp^2-hybridized substituents such as CHO or COOH in 8,8′-positions were found extremely prone to racemization, but when the substituents were sp^3-hybridized, the 8,8′-binaphthalenes were significantly more resistant to racemization [5][6]. The 2,2′-disubstituted 1,1′-binaphthalenes (BINAP), including BINOL ([1,1′-binaphthalene]-2,2′-diol; **2**) have found numerous successful applications in asymmetric synthesis [7][8] and molecular recognition [3][9], but the isomeric 8,8′-BINOL (**1**) has so far rarely been used. Derivatives of enantiomerically pure **1** have served as chiral proton sources [3], as derivatizing reagents for the NMR determination of absolute configurations of carboxylic acids [4], and as chiral auxiliaries for asymmetric 1,2- and 1,4-additions of organocuprates [10] and for *Diels-Alder* reactions [11]. An 8,8′-disubstituted binaphthalene produced remarkable enantioselectivities when applied as a ligand to the Pd-catalyzed reduction of allylic carbonates with formic acid [12]. We now report the application of **1** *via* a cyclic phosphor amidite **3** as catalyst in asymmetric borane reductions and as ligand in Cu-catalyzed substitution and addition reactions.



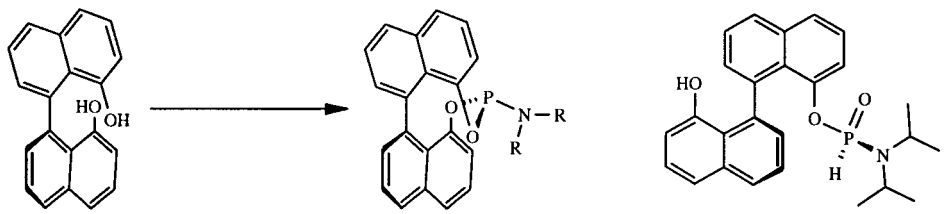
(−)-**1** (a*R*)



(a*R*)-**2**

Results and Discussion. – *Synthesis of Dimethylphosphoramidite (−)-**3** from 1,1′-Binaphthalene-8,8′-diol* ((−)-**1**). Racemic 8,8′-BINOL (**1**) was synthesized as described by *Cram* and co-workers [1], and enantiomer separation was effected *via* the bis(menthyl carbonate) according to *Fabbri et al.* [2]. The diastereoisomeric purity of the carbonate was >98% (by HPLC, *OD-H* column; hexane/i-PrOH 9:1). The isolated enantiomer of **1** had $[\alpha]_D^{25} = -25.2$ ($c = 1.05$, $CHCl_3$) and $[\alpha]_D^{23} = -331$ ($c = 1.14$, THF). Its enantiomeric purity was >98% (HPLC, *AD* column; hexane/i-PrOH 9:1). Literature values for the optical rotation of **1** are confusing: *Fabbri et al.* [2] reported $[\alpha]_D^{25} = 16.5$ ($c = 1.0$, $CHCl_3$) for a sample of unknown abs. configuration, while *Fuji et al.* [3] gave $[\alpha]_D^{20} = -336.5$ ($c = 1.1$, THF) for the (a*R*)-isomer. The absolute configuration of the isolated (−)-**1** was assigned to be (a*R*) on the grounds of the X-ray structure of **3** (see below). Reaction of (−)-**1**, with hexamethylphosphorous triamide (HMPT), under the conditions used by *Feringa* and co-workers for the synthesis of the isomeric 1,1′-BINOL derivative (refluxing $CHCl_3$, in the presence of NH_4Cl) [13] afforded the phosphoramidite (−)-**3** in 81% (*Scheme 1*).

Scheme 1



(−)-**1** (a*R*) (−)-**3** (a*R*) R = Me; **4** (a*R*) R = i-Pr (−)-**5** (a*R*,*R*)

The structure and the absolute (a*R*) configuration of (−)-**3** follow from the X-ray crystal-structure analysis (*Fig. 1*). The nine-membered ring adopts a *twist-boat-boat* (*TBB*) [14] conformation with a quasi ideal C_2 axis passing through the P-atom and the middle of the C(1)−C(11) bond (arbitrary numbering according to *Fig. 1*) ($\Delta C_2(P) = 0.032(1)$ [15]). The whole structure is severely strained as evidenced by the distortion of both naphthalene rings (dihedral angles: C(7)−C(8)−C(2)−C(3) = 7.80(5)°; C(17)−C(18)−C(12)−C(13) = 6.66(5)°) and the out-of-plane deviations of the naphthalene linkages: O(1) and C(11) are located at −0.37 and +0.48 Å, respectively, out of the C(1) to C(10) naphthalene mean plane, and O(2) and C(9) are located at 0.32 and −0.46 Å, respectively of the C(11) to C(20) naphthalene mean plane (*Fig. 2*).

Attempts to synthesize the *N*,*N*-diisopropylphosphoramidite analogue **4** of (−)-**3** failed, however. Reaction of (−)-**1** with diisopropylphosphoramidous dichloride [16][17] afforded only the acyclic compound (−)-**5**. A single resonance line was found in the ^{31}P-NMR, indicating the presence of only one diastereoisomer. Attempts to cyclize (−)-**5** with dicyclohexylcarbodiimide (DCC) or $POCl_3$ to **4** were unsuccessful. This failure may be ascribed to steric interactions owing to the presence of the ^{i}Pr groups. Inspection of the X-ray structure of (−)-**3** shows that the dimethylamino moiety is situated almost within contact distance of one of the naphthalene rings; thus, the

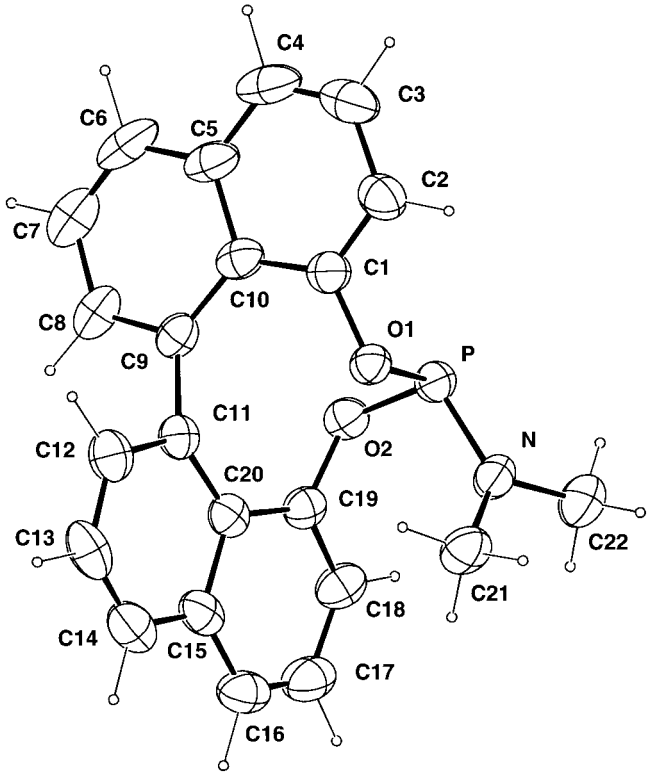


Fig. 1. *Perspective view of the crystal structure of (−)-***3** *with atom numbering* (arbitrary). Ellipsoids are represented with 40% probability.

skeleton of (−)-**3** has insufficient space to accommodate the bulkier i-Pr groups. The structure of (−)-**5** (*Fig. 3*) is also distorted, although only slightly. The methine H-atom (H(24)) of one of the i-Pr groups is located at 2.47 Å from the mean plane of one of the naphthalene rings (*Fig. 4*), and this leads to small deformations of the naphthalene rings at the ring junctions. Selected structural parameters of **3** and **5** are given in *Table 1*.

*Exploratory Experiments in Asymmetric Catalysis with Phosphoramidite (−)-***3** *of (−)-(a*R*)-8,8′-BINOL* ((−)-**1**). Exploratory experiments were carried out to test the activity and selectivity of (−)-**3** in asymmetric catalysis (*Scheme 2*). Addition of $BH_3 \cdot$ THF [18] to a solution of acetophenone (**6**) and (−)-**3** (5%) afforded (*R*)-1-phenylethanol (**7**) in excellent yield and with 96% ee. Under the same conditions, imine **8** was reduced to (*S*)-amine **9**, but with a low enantioselectivity of only 11%.

In a second series of experiments, (−)-**3** was used as ligand for Cu-catalyzed substitution and addition reactions. Cyclohexene oxide (**10**) was converted at $-10°$ with MeMgBr in the presence of $[Cu(OTf)_2]$ and (−)-**3** (12%) to the (1*S*,2*S*)-alcohol **11** (45% yield and 15% ee), while the corresponding ring opening of the *meso*-aziridine **12** with MeMgBr [19] proceeded in 64% yield with 42% ee to the sulfonamide **13** (*Scheme 3*). Conjugate addition of Et_2Zn to cyclohex-2-en-1-one (**14**) [20][21] and 1,3-

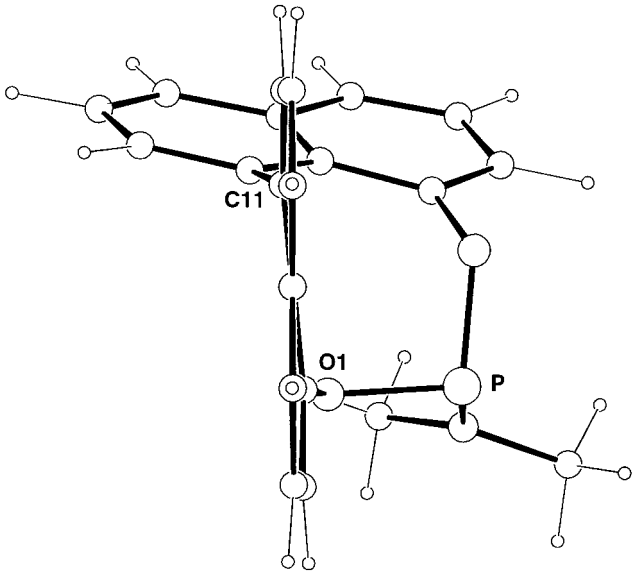
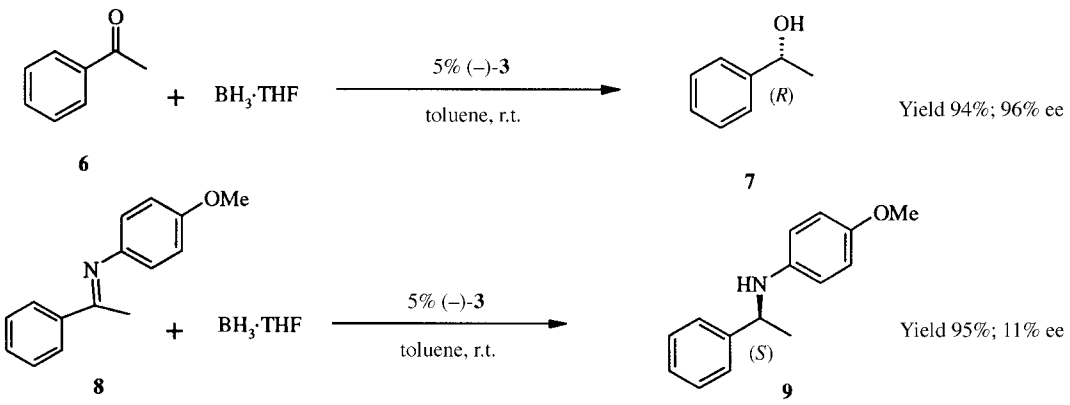


Fig. 2. *Perspective view of the crystal structure of (−)-***3** *showing the C(1) to C(10) naphthalene plane deformation and the out-of-plane deviations of the atoms O(1) and C(11)*

diphenylprop-2-en-1-one (**16**) [20] with [$Cu(OTf)_2$] (3%) and (−)-**3** (6%) furnished the ketones **15** and **17** with ee values of 50 and 31%, respectively.

In contrast, results for the Cu-catalyzed transfer of carbenes and nitrenes in the presence of (−)-**3** were disappointing. The Cu-catalyzed cyclopropanation of styrene (**18**) with ethyl diazoacetate (EDA) [22] afforded 3:2 mixture of *cis*- and *trans*-cyclopropanecarboxylates **19** without asymmetric induction (*Scheme 4*). Cu-Catalyzed nitrene transfer [23] from TsN=IPh to styrene (**18**), in turn, yielded the aziridine derivative **20** in high yield (96%), but with only marginal enantioselectivity (11%).

Scheme 2



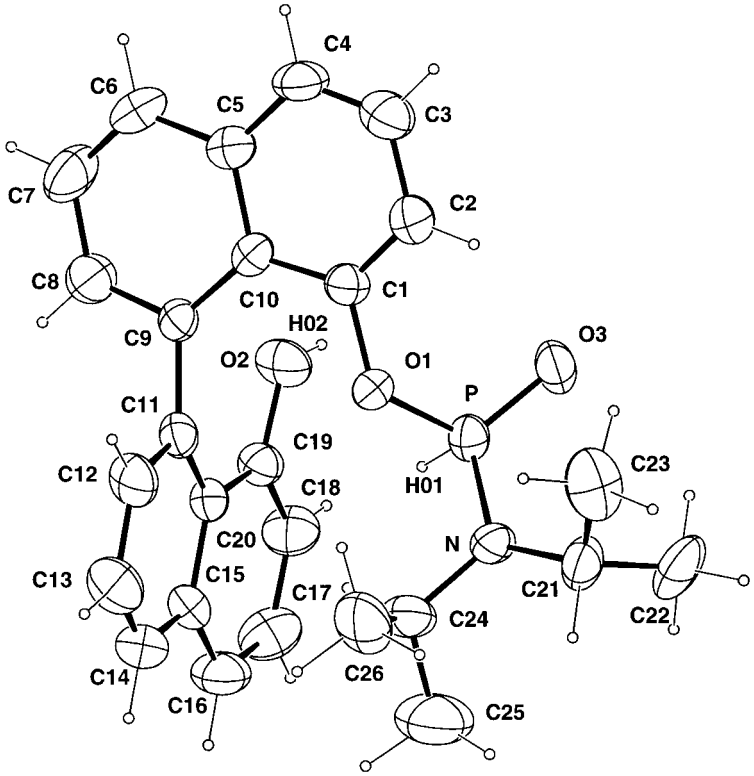


Fig. 3. *Perspective view of the crystal structure of (−)-***5** *with atom numbering* (arbitrary). Ellipsoids are represented wtih 40% probability.

Conclusion. – The phosphoramidite (−)-**3** is sufficiently stable with respect to structure and configuration to be used as chiral catalyst in its own right or as ligand for asymmetric Cu-catalyzed reactions. The Cu-catalyst derived from (−)-**3** exhibits satisfactory reactivity in cuprate additions and substitutions, but is ill-suited for the enantioselective transfer of carbenes and nitrenes. Enantioselectivity varies greatly according to the reactions and must be optimized. However, the possibilities for optimization of the ligand appear somewhat problematic owing to the steric hindrance of the 8,8′-BINOL skeleton.

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Experimental Part

General. See [24]. FC = flash chromatography.

1. (−)-(*a*R)-*[1,1′-Binaphthalene]-8,8′-diyl Dimethylphosphoramidite* (=*(−)-(a*R)-N,N-*Dimethyl-8*H-*dinaphtho[1,8*-de:*1′,8′*-gh*][1,3,2]dioxaphosphorin-8-amine*; ((−)-**3**). Racemic 8,8′-BINOL (**1**) was synthesized according to [1], and enantiomer separation was effected *via* the menthyl carbonate [2]: (−)-**1** (a*R*). $[\alpha]_D^{20} = -25.2$ ($c = 1.05$, $CHCl_3$) ([2]: $[\alpha]_D^{25} = +16.5$ ($c = 1.0$, $CHCl_3$; abs. configuration not determined); [3]: $[\alpha]_D^{20} = -336.5$ ($c = 1.1$, THF; for (a*R*)-enantiomer).

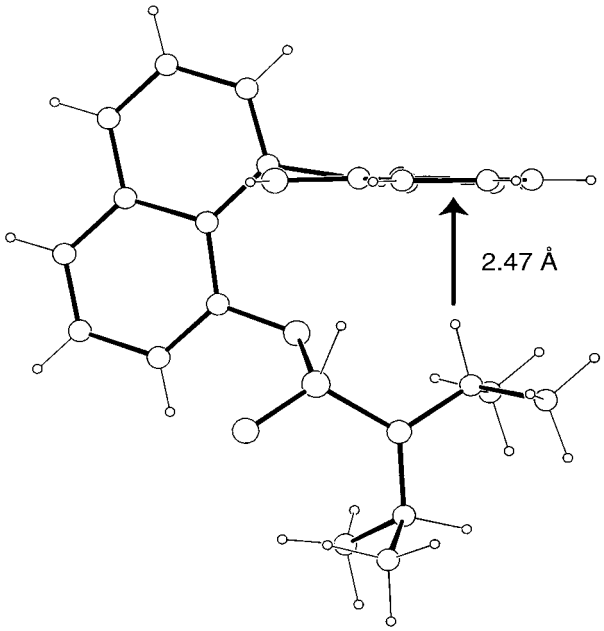


Fig. 4. *Perspective view of the crystal structure of (−)-***5** *showing the short contact between H(24) and the C(11)–C(20) naphthalene ring*

Scheme 3

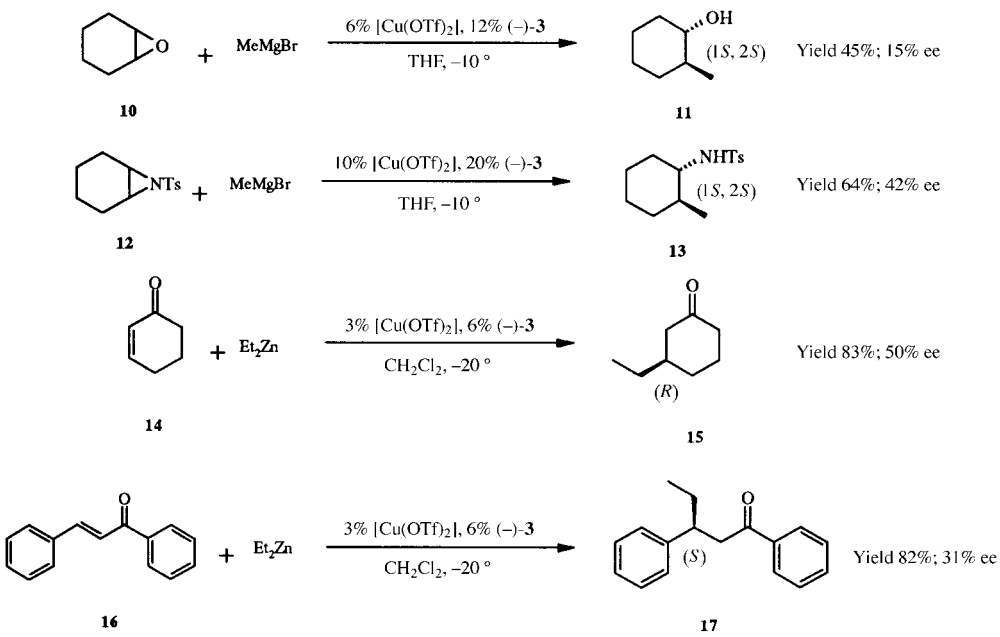
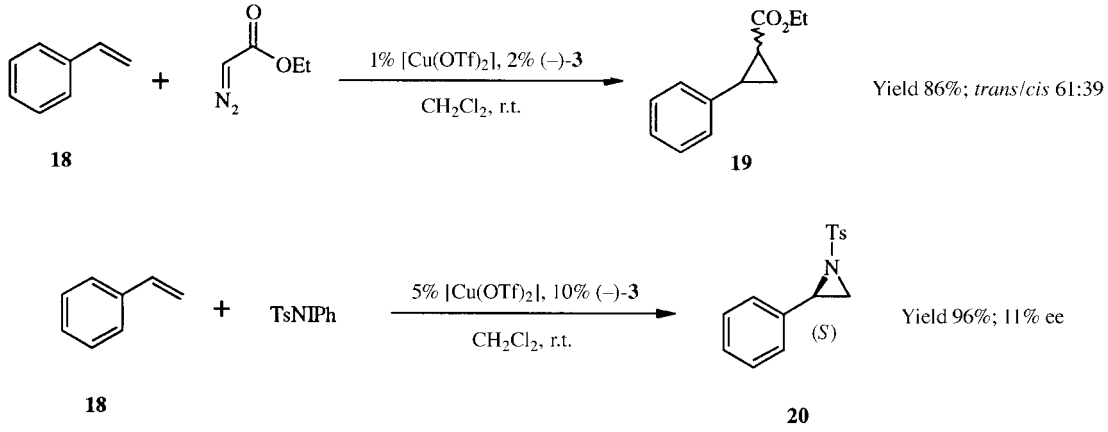


Table 1. *Selected Bond Lengths* [Å], *Bond Angles* [°], *and Torsional Angles* [°] *for* **3** *and* **5**

	3	**5**
P–H(01)	–	1.34(6)
P–N	1.646(4)	1.613(6)
P–O(1)	1.668(3)	1.601(5)
P–O(3)	–	1.471(5)
P–O(2)	1.667(3)	–
O(1)–C(1)	1.402(6)	1.410(8)
O(2)–C(19)	1.387(5)	1.357(9)
C(1)–C(10)	1.412(7)	1.42(1)
C(9)–C(10)	1.435(7)	1.41(1)
C(9)–C(11)	1.498(6)	1.502(9)
C(11)–C(20)	1.415(7)	1.44(1)
C(19)–C(20)	1.424(7)	1.42(1)
O(1)–P–O(3)	–	114.5(3)
O(3)–P–N	–	115.8(3)
O(1)–P–N	97.1(2)	105.3(3)
N–P–O(2)	108.6(2)	–
O(1)–P–O(2)	98.2(2)	–
P–O(1)–C(1)	109.8(3)	125.2(4)
O(1)–C(1)–C(10)	119.5(4)	118.4(6)
C(1)–C(10)–C(9)	124.7(4)	126.4(6)
C(10)–C(9)–C(11)	125.8(4)	126.2(6)
C(9)–C(11)–C(20)	126.8(4)	124.8(6)
C(11)–C(20)–C(19)	125.1(4)	124.0(6)
O(2)–C(19)–C(20)	119.4(4)	117.9(7)
P–O(2)–C(19)	118.6(3)	–
O(3)–P–O(1)–C(1)	–	27.7(6)
O(2)–P–O(1)–C(1)	−84.5(3)	–
P–O(1)–C(1)–C(10)	85.6(4)	117.9(6)
O(1)–C(1)–C(10)–C(9)	13.3(7)	0(1)
C(11)–C(9)–C(10)–C(1)	18.8(8)	9(1)
C(10)–C(9)–C(11)–C(20)	−93.9(6)	−102.1(9)
C(9)–C(11)–C(20)–C(19)	16.6(8)	12(1)
O(2)–C(19)–C(20)–C(11)	12.1(7)	1(1)
P–O(2)–C(19)–C(20)	85.0(4)	–
O(1)–P–O(2)–C(19)	−69.5(3)	–
Angle between naphthalene mean planes	76.5(1)	89.8(1)

(−)-(a*R*)-8,8′-BINOL (**1**; 100 mg, 0.35 mmol) in $CHCl_3$ (10 ml) was heated to reflux in the presence of NH_4Cl (10 mg) and hexamethylphosphorous triamide (HMPT) for 30 min [25]. After usual workup, the crude product was purified by FC (petroleum ether/AcOEt 7:3): 102 mg (81%) of (−)-**3**. Colorless solid. M.p. 196–198°. $[\alpha]_D^{20} = -653$ ($c = 0.42$, $CHCl_3$). UV (CH_2Cl_2): 308 (3.51). CD: (CH_2Cl_2, 445 μM): 305.5 (−110.72). IR ($CHCl_3$): 3011*s*, 2978*s*, 2928*w*, 2875*m*, 1568*w*, 1453*w*, 1383*w*, 1362*w*, 1234*s*, 1110*s*, 1072*w*, 979*s*, 826*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.00 (*s*, 3 H); 2.02 (*s*, 3 H); 6.78 (*dd*, $J = 7.1$, 1.0, 1 H); 6.87 (*dd*, $J = 6.3$, 0.7, 1 H); 6.91 (*dd*, $J = 7.3$, 0.7, 1 H); 7.22–7.26 (*m*, 1 H); 7.36 (*dd*, $J = 8.08$, 7.06, 1 H); 7.40 (*dd*, $J = 8.08$, 7.04, 1 H); 7.46 (*dd*, $J =$ 7.6, 7.6, 1 H); 7.51 (*dd*, $J = 7.8$, 7.8, 1 H); 7.70–7.79 (*m*, 3 H); 7.85 (*dd*, $J = 8$, 0.7, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 34.87 (*q*); 35.06 (*q*); 119.3 (*dd*, J(C,P) = 1.6); 120.1 (*dd*, J(C,P) = 7.4); 124.25 (*d*); 124.95 (*d*); 125.0 (*dd*, J(C,P) = 3.3); 125.2 (*d*); 126.2 (*dd*, J(C,P) = 2.5); 126.3 (*d*); 126.5 (*d*); 127.05 (*d*); 128.4 (*ds*, J(C,P) = 4.9); 129.3 (*ds*, J(C,P) = 1.6); 129.85 (*d*); 130.2 (*d*); 135.1 (*s*); 135.5 (*s*); 139.9 (*s*); 140.3 (*s*); 149.05 (*ds*, J(C,P) = 7.4); 150.8 (*ds*, J(C,P) = 7.6). ^{31}P-NMR (162 MHz, $CDCl_3$): 139.38. MS: 360 (9), 359 ($M^{+\cdot}$, 36), 316 (21), 315 (68), 284 (4), 268 (6), 255 (4), 253 (5), 252 (19), 250 (6), 240 (8), 239 (35), 237 (9), 226 (5), 174 (11), 173 (100), 170 (7),

Scheme 4



75 (4), 60 (12). HR-MS: 359.1030 ($C_{22}H_{18}NO_2P^{+\cdot}$; calc. 359.1075). Anal. calc. for $C_{22}H_{18}NO_2P$: C 73.53, H 5.05, N 3.90; found: C 73.45, H 5.27, N 3.76.

*(–)-[a*R,P(R)*]-8′-Hydroxy-[1,1′-binaphthalen]-8-yl* N,N-*Diisopropylphosphonamidate* ((–)-**5**). Diisopropylphosphoxamidous dichloride [16] (0.283 g, 1.396 mmol) was added at –60° to (–)-**1** (400 mg, 1.396 mmol) and Et_3N (0.40 ml, 2.8 mmol) in dry toluene (20 ml). The mixture was stirred for 21 h at r.t. The solvent was evaporated at 25° and the crude product purified by FC (petroleum ether/AcOEt 7:3): 248 mg (43%) of **5**. Colorless solid. M.p. 193° (dec.). $[\alpha]_D^{23} = -238.2$ ($c = 0.41$, $CHCl_3$). UV (CH_2Cl_2): 303 (3.05), 245 (3.61). CD (5075 μM, CH_2Cl_2): 259.5 (–190.0). IR ($CHCl_3$): 3512*w*, 3027*s*, 1577*w*, 1455*w*, 1370*w*, 1267*w*, 1228*s*, 1213*s*, 1188*w*, 1097*w*, 990*m*, 909*m*, 822*w*, 733*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.93 (*d*, $J = 7.3$, 3 H); 0.96 (*d*, $J = 7.3$, 3 H); 2.8–3.1 (*m*, 2 H); 6.83 (*dd*, $J = 7.5$, 1.25, 1 H); 5.52 (*d*, $J = 681$, 1 H); 7.10 (*dd*, $J = 7.1$, 1.25, 1 H); 7.30–7.56 (*m*, 8 H); 7.65–7.74 (*m*, 1 H); 7.79 (*dd*, $J = 8.2$, 1.1, 1 H); 7.91 (*dd*, $J = 8.1$, 1.2, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 18.9 (*dq*, J(C,P) = 3.4); 22.4 (*q*); 22.8 (*dq*, J(C,P) = 2.3); 44.9 (*dd*, J(C,P) = 5.7); 47.1 (*d*); 112.2 (*d*); 117.5 (*dd*, J(C,P) = 5.7); 120.5 (*d*); 123.6 (*s*); 124.4 (*d*); 124.9 (*d*); 125.3 (*d*); 125.9 (*d*); 126.8 (*d*); 127.5 (*d*); 127.7 (*d*); 128.6 (*d*); 130.0 (*d*); 135.1 (*s*); 135.7 (*s*); 137.7 (*s*); 138.9 (*s*); 146.9 (*ds*, J(C,P) = 9.1); 153.5 (*s*). ^{31}P-NMR (162 MHz, $CDCl_3$): 8.6. MS: 433 (3, $M^{+\cdot}$), 415 (1), 372 (3), 333 (21), 332 (80), 315 (3), 288 (7), 287 (53), 286 (100), 285 (23), 284 (18), 269 (15), 268 (18), 267 (5), 258 (6), 257 (9), 256 (7), 255 (10), 253 (7), 241 (5), 240 (11), 239 (41), 237 (7), 226 (11), 190 (7), 189 (58), 173 (7), 155 (5), 147 (5), 143 (11), 134 (11), 132 (8), 128 (5), 121 (5), 120 (29), 119 (15), 113 (9), 107 (6), 101 (27), 90 (19), 88 (5), 87 (12), 86 (91), 70 (5), 58 (34), 45 (9). HR-MS: 433.1778 ($C_{26}H_{28}NO_3P^{+\cdot}$; calc. 433.1807).

2. *Asymmetric Catalysis with Phosphoramidite (–)-***3**. *(+)-(*R*)-1-Phenylethanol* (**7**). To acetophenone (**6**; 100 mg, 0.84 mmol) and (–)-**3** (15.2 mg, 0.042 mmol) in dry toluene (2.0 ml), $BH_3 \cdot THF$ (1.0 mmol; 1M in THF) was added. The mixture was stirred at r.t. for 1.0 h, whereupon 2M HCl (2.0 ml) was added. The org. phase was dried (Na_2SO_4) and evaporated, and the crude product purified by FC (SiO_2, pentane/AcOEt 4:1): **7** (96 mg, 94%). $[\alpha]_D^{23} = +43.1$ ($c = 1.0$, MeOH) ([26][27]: $[\alpha]_D^{25} = -45.3$ ($c = 3.0$, MeOH) for (*S*)-enantiomer). HPLC (*Chiracel OD-H*, hexane/^{i}PrOH 99:1, flow 0.5 ml/min; t_R 28.0 ((*R*)) and 32.1 min ((*S*))): 96% ee. IR ($CHCl_3$): 3060*s*, 3438*s*, 3008*s*, 1452*s*, 1376*m*, 1255*m*, 1075*s*, 1007*m*, 896*m*, 697*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.47 (*d*, $J = 5$, 3 H); 2.11 (*s*, 1 H); 4.86 (*q*, $J = 5$, 1 H); 7.24–7.28 (*m*, 1 H); 7.32–7.37 (*m*, 4 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 25.1 (*q*); 70.3 (*d*); 125.1 (*d*); 127.4 (*d*); 128.7 (*d*); 145.8 (*s*).

*(–)-(*S*)-4-Methoxy-*N*-(1-phenylethyl)benzenamine* (**9**). As described for **7**, with 4-methoxy-N-(1-phenylethylidene)benzenamine (**8**; 189 mg, 0.84 mmol): 178 mg (93%) of **9**. Colorless solid. M.p. 62–64° ([28]: 61–62°). HPLC (*Chiracel OD-H*, hexane/^{i}PrOH 99:1, flow 0.5 ml/min; t_R 30.7 ((*S*)) and 34.8 min ((*R*))): 11% ee ([28]: *Chiracel AD*, hexane/EtOH 99.2: 0.8, flow 0.5 ml/min; t_R 17.45 ((*R*)) and 19.79 min ((*S*))). ($CHCl_3$): 3683*w*, 3619*m*, 3459*w*, 3020*s*, 2399*s*, 1512*s*, 1222*s*, 778*s*, 675*m*, 627*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.48 (*d*, $J = 5.3$, 3 H); 3.68 (*s*, 3 H); 4.65 (br. *s*, 1 H); 6.46 (*d*, $J = 7$, 2 H); 6.68 (*d*, $J = 7$, 2 H); 7.20–7.25 (*m*, 1 H); 7.28–7.37 (*m*, 4 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 25.1 (*q*); 54.2 (*d*); 55.5 (*q*); 114.5 (*d*); 114.75 (*d*); 125.9 (*d*); 126.8 (*d*); 128.6 (*d*); 141.6 (*s*); 145.45 (*s*); 151.9 (*s*).

(+)-(1S,2S)-2-Methylcyclohexan-1-ol (**11**). A soln. of $[Cu(OTf)_2]$ (3.6 mg, 0.011 mmol) and (−)-**3** (7.6 mg, 0.021 mmol) in THF (2.0 ml) was stirred at r.t. for 1 h under N_2, then cooled to −78°, and treated with cyclohexene oxide (= 7-oxabicyclo[4.1.0]heptane; **10**; 33 µl, 0.33 mmol). After dropwise addition of 3M MeMgBr in THF (0.12 ml, 0.36 mmol), the mixture was allowed to reach r.t. slowly and was then hydrolyzed with sat. NH_4Cl soln. (10 ml) and extracted with Et_2O (3 × 10 ml). The org. layer was dried ($MgSO_4$) and evaporated and the crude product purified by FC (SiO_2, pentane/AcOEt 4:1): 17 mg of **11** (45%) [29]. Colorless liquid. $[\alpha]_D^{23} = +5.2$ ($c = 1.1$, MeOH). GLC (*Lipodex E* at 60°; t_R 29.2 ((1*R*,2*R*)) and 31.2 min ((1*S*,2*S*))): 15% ee ([30]: $[\alpha]_D^{25} = +42.9$ ($c = 1.0$, MeOH for (1*S*,2*S*)-enantiomer **11**)). IR ($CHCl_3$): 3683*m*, 3618*s*, 3482*w*, 3014*s*, 2400*s*, 1522*s*, 1420*w*, 1272*w*, 1207*s*, 1046*s*, 928*m*, 878*w*, 764*s*, 676*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 1.01 (*d*, *J* = 6.3, 3 H); 1.1–1.4 (*m*, 5 H); 1.45–1.8 (*m*, 4 H); 1.85–2 (*m*, 1 H); 3.0–3.21 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 18.5 (*q*); 25.2 (*t*); 25.7 (*t*); 33.6 (*t*); 35.4 (*t*); 40.2 (*d*); 76.5 (*d*).

*4-Methyl-*N*-[(1S,2S)-2-methylcyclohexyl]benzenesulfonamide* (**13**). A mixture of (−)-**3** (47.8 mg, 0.133 mmol) and $[Cu(OTf)_2]$ (23.7 mg, 0.066 mmol) in THF (2.0 ml) was stirred under N_2 during 1 h at r.t. The aziridine **12** (100 mg, 0.40 mmol) was added and the soln. cooled to 0°. Then, 3M MeMgBr in Et_2O (0.15 ml, 0.45 mmol) was added dropwise, and the mixture was stirred at 0° for 1 h. After addition of sat. NH_4Cl soln. (15 ml), the aq. phase was extracted with Et_2O (3 × 15 ml). The org. phase was concentrated, washed with sat. NaCl soln. (15 ml), dried ($MgSO_4$), and evaporated. FC (SiO_2, hexane/AcOEt 4:1) of the crude product afforded **13** (68 mg, 64%). Colorless crystals. M.p. 98–100°. HPLC (*Chiracel OD-H*, hexane/^{i}PrOH 9:1; t_R 13.4 ((1*S*,2*S*)) and 14.5 min ((1*R*,2*R*))): 42% ee. Abs. configuration: see [21]. IR ($CHCl_3$): 2929*s*, 2857*s*, 1448*w*, 1415*w*, 1328*s*, 1157*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.81 (*d*, *J* = 6.8, 3 H); 1.08–1.25 (*m*, 5 H); 1.57–1.58 (*m*, 2 H); 1.70–1.72 (*m*, 2 H); 2.41 (*s*, 3 H); 2.64–2.65 (*m*, 1 H); 4.70–4.80 (*m*, 1 H); 7.27 (*d*, *J* = 8, 2 H); 7.76 (*d*, *J* = 8, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 19.1 (*q*); 21.5 (*q*); 25.3 (*t*); 34.5 (*t*); 38.3 (*d*); 59.1 (*d*); 126.9 (*d*); 129.5 (*d*); 138.7 (*s*); 142.9 (*s*). MS: 267 (66, M^+), 225 (5), 224 (38), 212 (7), 210 (100), 184 (9), 172 (8), 157 (6), 156 (8), 155 (94), 133 (5), 112 (61), 96 (20), 95 (18), 91 (95), 70 (5), 69 (7), 67 (5), 65 (20), 56 (11), 55 (13). HR-MS: 267.1280 ($C_{14}H_{21}NO_2S^+$; calc. 267.1293). Anal. calc. for $C_{14}H_{21}NO_2S$: C 62.87, H 7.92, N 5.27; found: C 62.70, H 7.86, N 5.27.

*(+)-(*R*)-3-Ethylcyclohexan-1-one* (**15**). A soln. of $[Cu(OTf)_2]$ (3.6 mg, 0.011 mmol) and (−)-**3** (7.6 mg, 0.021 mmol) in CH_2Cl_2 (2.0 ml) was stirred at r.t. for 1 h under N_2. After cooling to −20°, cyclohex-2-en-1-one (**14**; 32 µl, 0.33 mmol) followed by 1M Et_2Zn in toluene (0.50 ml, 0.50 mmol) was added. The mixture was stirred for 3 h at −20°, then decomposed with 1M HCl (3.0 ml), and extracted with AcOEt (2 × 10 ml). The combined org. phase was washed with sat. NaCl soln. (10 ml), dried ($MgSO_4$), and evaporated. The crude product was purified by FC (SiO_2, pentane/AcOEt 4:1): 34.6 mg (83%) of **15** [31]. Colorless liquid. $[\alpha]_D^{23} = +6.1$ ($c = 3.0$, $CHCl_3$) ([21b]: $[\alpha]_D > 0$). GLC (*Lipodex E* at 60°; t_R 25.6 ((*S*)) and 30.6 min ((*R*))): 50% ee. IR ($CHCl_3$): 2979*m*, 2934*w*, 2143*s*, 1728*s*, 1370*s*, 1326*s*, 1240*s*, 1159*m*, 1089*s*, 1032*m*, 950*w*, 850*w*, 753*m*, 701*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.83 (*t*, *J* = 5.9, 3 H); 1.17–1.37 (*m*, 3 H); 1.53–1.66 (*m*, 2 H); 1.81–1.87 (*m*, 1 H); 1.90–2.02 (*m*, 2 H); 2.18 (*dddd*, *J* = 11, 10, 5, 1, 1 H); 2.25–2.31 (*m*, 1 H); 2.33–2.28 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.2 (*q*), 25.3 (*t*); 29.3 (*t*); 30.9 (*t*); 40.8 (*d*); 41.5 (*t*); 47.85 (*t*); 212.2 (*s*).

*(+)-(*S*)-1,3-Diphenylpentan-1-one* (**17**). As described for **15**, with 1,3-diphenylprop-1-en-3-one (**16**; 69 mg, 0.33 mmol): **17** (65 mg, 82%). Colorless solid. M.p. 62–64° ([32]: 59–60°). $[\alpha]_D^{23} = +2.54$ ($c = 0.77$, EtOH). HPLC (*Chiracel OD-H*, hexane/^{i}PrOH 99:1, flow 0.5 ml/min; t_R 15.9 ((*S*)) and 16.7 min ((*R*))): 31% ee ([21a]: *Chiralcel OD-H*, hexane/^{i}PrOH 99.5:0.5, flow 0.5 ml/min; t_R 14.6 ((*S*)) and 15.5 min ((*R*))). IR ($CHCl_3$): 3080*m*, 3050*m*, 3015*m*, 2970*s*, 2920*s*, 2850*s*, 1680*s*, 1579*m*, 1450*s*, 1375*m*, 1320*w*, 1260*m*, 1245*w*, 1190*w*, 1180*m*, 1160*w*, 1060*w*, 1002*w*, 950*w*, 845*w*, 690*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.84 (*t*, *J* = 5.8, 3 H); 1.63–1.72 (*m*, 1 H); 1.79–1.87 (*m*, 1 H); 3.24–3.35 (*m*, 3 H); 7.19–7.34 (*m*, 5 H); 7.44–7.48 (*m*, 2 H); 7.55–7.60 (*m*, 1 H); 7.92–7.95 (*m*, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.95 (*q*); 29.05 (*t*); 42.9 (*d*); 45.6 (*t*); 126.2 (*d*); 127.6 (*d*); 128.05 (*d*); 128.4 (*d*); 128.5 (*d*); 132.9 (*d*); 137.2 (*s*); 144.6 (*s*); 199.2 (*s*).

Ethyl 2-Phenylcyclopropanecarboxylate (**19**). The catalyst was prepared by stirring $[CuOTf_2]$ with 2.0 equiv. of **3** in CH_2Cl_2 for 1 h under N_2. The addition of ethyl diazoacetate (EDA) to (**18**) was carried out with 5% of catalyst as described previously [22][24].

*(*S*)-1-[(4-Methylphenyl)sulfonyl]-2-phenylaziridine* (**20**): $[Cu(OTf)_2]$ (3.6 mg, 0.011 mmol) and (−)-**3** (7.6 mg, 0.021 mmol) in CH_2Cl_2 (2.0 ml) were stirred for 1 h at r.t. under N_2. After addition of styrene (**18**; 21.0 mg, 0.2 mmol), TsN=IPh [33] (112 mg, 0.3 mmol) was added. The suspension was stirred for 2.0 h and then filtered through silica gel, which was eluted with AcOEt (200 ml). The crude product was purified by FC (SiO_2, pentane/AcOEt 4:1): **22** (52 mg, 95%). Colorless crystals. M.p. 87–89° ([30]: 88–89°). $[\alpha]_D^{23} = +7.9$ ($c = 2.0$, $CHCl_3$). HPLC (*Chiracel OJ*, hexane/^{i}PrOH 9:1, flow 1 ml/min, t_R 22.4 ((*R*)) and 27.2 min ((*S*))): 11% ee. ([34]: $[\alpha]_D^{25} = -97.9$ ($c = 1.0$, CH_2Cl_2) for (*R*)-enantiomer of **22**). IR ($CHCl_3$): 3016*m*, 1598*w*, 1460*w*, 1325*s*, 1101*s*,

1094*s*, 915*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 2.39 (*d*, *J* = 4.5, 1 H); 2.42 (*s*, 3 H); 2.98 (*d*, *J* = 7.2, 1 H); 7.78 (*dd*, *J* = 7.2, 4.5, 1 H); 7.22 (*m*, 7 H); 7.87 (*d*, *J* = 8.3, 2 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 21.7 (*q*); 35.9 (*t*); 41.0 (*d*); 126.6 (*d*); 127.9 (*d*); 128.3 (*d*); 128.6 (*d*); 129.8 (*d*); 134.9 (*s*); 135.1 (*s*); 144.7 (*s*).

3. *Crystal Structure Determination of (−)-***3** *and (−)-***5**[1]) (*Table 2*). Cell dimensions and intensities were measured at r.t. on a *Stoe-STADI4* diffractometer with graphite-monochromated MoK_α radiation (λ 1.481 Å); ω-2θ scans; two reference reflections measured every 45 min showed no variation. Data were corrected for *Lorentz* and polarization effects and for absorption [35]. The structures were solved by direct methods with MULTAN 87 [36], all other calculations were performed with XTAL [37] programs. For both structures, the *Flack* parameter *x* [38] was refined and the absolute configuration determined.

Table 2. *Summary of Crystal Data, Intensity Measurement, and Structure Refinement for* **3** *and* **5**

	(−)-**3**	(−)-**5**
Formula	$C_{22}H_{18}NO_2P$	$C_{26}H_{28}NO_3P$
M_r	359.4	433.5
Crystal size	0.25 × 0.28 × 0.32	0.075 × 0.039 × 0.045
Crystal system	orthorhombic	orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
a [Å]	8.5404(6)	9.8350(6)
b [Å]	12.5204(7)	10.3635(7)
c [Å]	16.795(1)	22.540(1)
V [Å^3]	1795.9(2)	2297.4(2)
Z	4	4
F(000)	752	920
D_c [g·cm^{-3}]	1.329	1.253
μ(MoK_α) mm^{-1}	1.481	1.275
*A** min., max.	1.356, 1.496	1.104, 1.501
$(\sin\theta/\lambda)_{max}$ [Å^{-1}]	0.53	0.53
Temperature [*K*]	293	293
No. measured reflections	3269	3358
No. observed reflections	2024	2256
Criterion for observed	$\|F_o\| > 4\sigma(F_o)$	$\|F_o\| > 4\sigma(F_o)$
Refinement (on *F*)	Full-matrix	Full-matrix
No. parameters	237	324
Weighting scheme	$\omega = 1/[\sigma^2(F_o) + 0.0005\ (F_o^2)]$	$\omega = 1/[\sigma^2(F_o) + 0.0002\ (F_o^2)]$
Max. and average Δ/σ	$0.32 \cdot 10^{-3}$, $0.17 \cdot 10^{-4}$	$0.21 \cdot 10^{-2}$, $0.23 \cdot 10^{-3}$
Max. and min. $\Delta\rho$ (eÅ^{-3})	0.14, −0.17	0.23, −0.29
Flack parameter *x*	0.01(4)	−0.05(5)
S	1.98(5)	2.15(5)
R, ωR	0.038, 0.046	0.050, 0.047

H-Atoms were placed in calculated positions and, for the Me groups, refined with restraints on bond lengths and bond angles and blocked in the last cycles. In (−)-**5**, the H-atoms of the hydroxy (H(02)) and phosphonate (H(01)) group were observed and refined with a fixed value of their isotropic displacement parameters (U = 0.05 Å^2). The molecular packing of (−)-**5** shows H-bond interactions involving the OH group and the O-atom of the phosphonate (O(1)−H(02) = 1.69(6) Å, O(2)···O(3^i) = 2.688(7) Å, O(2)−H···O(3^i) = 175(6)°, i = 1/2 + x, 3/2 − y, 1 − z).

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[1]) Crystallographic data (excluding structure factors) have been deposited with the *Cambridge Crystallographic Data Base* (deposition Nos. CCDC-138369 and 138370 for (−)-**3** and (−)-**5**, resp.). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ,UK (fax: +44 (1223) 336-033; e-mail: deposit@ccdc.cam.ac.uk).

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