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SYNTHESIS AND CATALYTIC PROPERTIES OF AN ACYCLIC ANALOGUE OF HYDROXY NORPHOS

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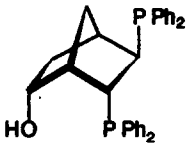
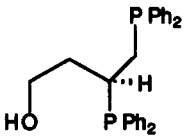
Abstract. The synthesis of (S)-1,2-bis(diphenylphosphino)butane-4-ol **1** an acyclic analogue of hydroxy norphos is described, starting from L-ascorbic acid. Problems which arose during the cleavage of OH-protective groups in the presence of phosphino groups are discussed. The hydrogenation properties of the catalyst derived from the new ligand are compared with those obtained with hydroxy norphos.[1]

Introduction

Recently we described the synthesis of hydroxy norphos[2] with the aim of using the hydroxyl group for the introduction of a Lewis acid while the diphosphine system is bonded to a soft metal such as rhodium.[3,4]



hydroxy norphos



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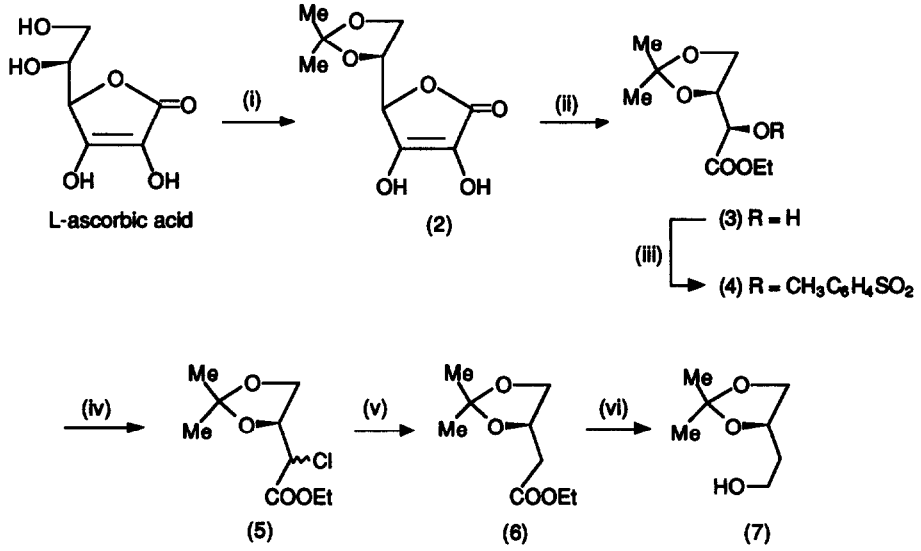
Our intention is to prepare dual chiral ligands for achieving asymmetric catalysis with substrate specificity and increased enantioselectivity, due to a secondary interaction between chiral ligands

and substrates.[5] In our first approach we embarked on a program aimed at the synthesis of hydroxy phosphines and their utilization as ligands in asymmetric hydrogenation.[7] It was satisfying to see that the neutral catalyst derived from hydroxy norphos was much more efficient than the catalyst which was prepared from norphos.[2] This prompted us to investigate the influence of the hydroxyl group, specifically regarding its spatial disposition, on the course of the metal catalyzed asymmetric reduction. On this basis, hydroxy phosphine **1** was chosen as a model compound.

Results and Discussion

Synthesis of the hydroxy phosphine. The protected chiral butane-1,2,4-triol **7** was revealed as a key intermediate for the synthesis of the desired hydroxy phosphine. A number of synthetic routes to this compound, which start from malic acid have been developed.[8] However, some of these were accompanied by the formation of regioisomeric acetonides.[9] In order to circumvent these difficulties, we selected the approach which starts from L-ascorbic acid as proposed by Abushanab and co-workers (Scheme 1).[10]



reagents:

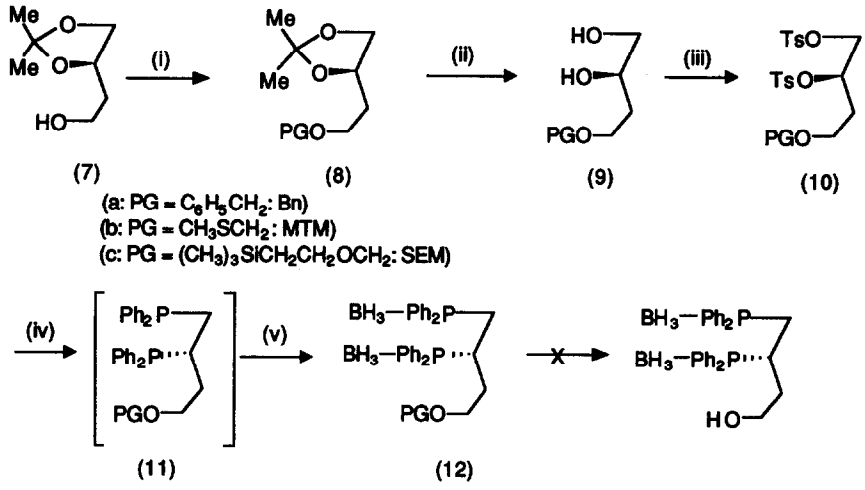
(i) acetone, cat. AcCl (85%) (ii) 30% H_2O_2, K_2CO_3 then EtI, CH_3CN, reflux (85%)
(iii) TsCl, Py (90%) (iv) LiCl, DMF, 24h (85%) (v) Pd/C, H_2, NEt_3 (90%) (vi) $LiAlH_4$, THF (68%).

Scheme 1

In the first step L-ascorbic acid was converted into the acetonide **2** by a known method.[11] Cleavage of the double bond with aqueous hydrogen peroxide followed by esterification with ethyl iodide in acetonitrile afforded ethyl L-threonate **3**. Tosylation of the free hydroxyl group and subsequent substitution of the tosyl group gave a mixture of the epimeric chloro compounds **5**. Without separation, **5** was subjected to reductive dehalogenation. The product **6** was isolated and purified by distillation. Reduction of the ester with $LiAlH_4$ gave the protected triol **7**.

The key step in the subsequent synthesis of the diphosphine was the protection of the hydroxyl group in compound **7**. Desired was a protective group which is stable under the conditions of the cleavage of the isopropylidene group. Furthermore it must allow the introduction of the two phosphine groups. A third very important criterion is, that it should easily be cleaved in the presence of the phosphine. Most of the known O-protective groups[12] suffer serious drawbacks, due either to their being attacked by phosphide ions, or to their problematic deprotection in the presence of incorporated phosphine groups. In the first attempt we chose the tert-butyl ether as proposed by Stille.[13] However under the conditions of the acid-catalyzed addition of isobutylene to the alcohol, the isopropylidene group was also affected. Therefore the reaction afforded poor yields of the 4-O-tert-butyl ether.[14] Superior results were obtained in the alkylation reaction with benzyl bromide, MTM-Cl[16] and SEM-Cl[17] which gave rise to the formation of ethers **8a**, **8b** and **8c**, respectively (Scheme 2). The O-protective groups applied are reputed to be stable under acidic conditions. In fact, the three chosen protective groups allowed the cleavage of the dioxolane to give the diols **9a-c** in high yields. Esterification of the free hydroxyl groups with tosyl chloride gave rise to the ditosylates **10a-c**. Displacement of the tosylate with lithium diphenylphosphide furnished the crude diphosphines **11a-c**. However, the purification procedures of the phosphines gave rise to considerable amounts of oxidation products. To avoid the inefficient and toxic purification of diphosphines by nickel complexes reported in the literature[13], the phosphines were converted after the substitution reaction without being isolated into the phosphine boranes **12a-c** by treatment with BH_3 in THF. The products obtained could be purified by flash chromatography that took place without decomposition of the borane complexes. The phosphine boranes proved to be stable in air for some time.

However, all attempts to cleave the O-protective groups using standard conditions failed. No reaction occurred when debenzylation of **12a** was tried with catalytic or stoichiometric amounts of palladium on charcoal. Under more drastic conditions, such as the heating of the benzyl ether in THF with $LiAlH_4$, the borane group was lost and we obtained a complex mixture of oxidized phosphines that we did not characterize further. Similarly, all attempts to cleave the MTM or SEM ether in the phosphine boranes **12b** and **12c** by methyl iodide[18] or fluoride[17], respectively, gave poor yields of the unprotected alcohol.

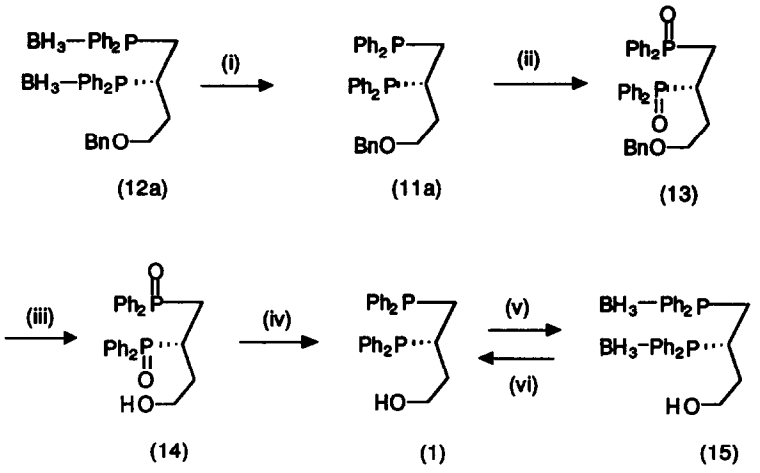


reagents

(i) (a) NaH, BnBr, $(n\text{-}Bu)_4NI$, THF (78%); (b) NaH, CH_3SCH_2Cl, $(n\text{-}Bu)_4NI$, THF (82%)
(c) NaH,$(CH_3)_3SiCH_2CH_2OCH_2Cl$, $(n\text{-}Bu)_4NI$, THF (73%) (ii) CH_3COOH, CH_3OH, H_2O (quant.)
(iii) TsCl, Py: (a) 76%, (b) 75%, (c) 79% (iv) $LiPPh_2$, THF (v) 1M BH_3-THF: (a) 60%, (b) 46%, (c) 53%.

Scheme 2

In view of these findings, an alternative protective group for the phosphine had to be visualized. "Oxygen" was revealed to be a more reliable protection of the phosphine than borane. As a model compound for this approach the benzyl ether **11a** was chosen (Scheme 3). It could be obtained by the reaction of the borane adduct **12a** with an excess of diethylamine.[19] Subsequent oxidation of the phosphine groups was achieved by treatment with aqueous hydrogen peroxide in acetone to give the phosphine oxide **13**. Then O-deprotection proceeded without any difficulties. The debenzylation could be carried out with catalytic palladium on charcoal.[20] Also the electrolytic deprotection[22] afforded the alcohol **14**. The phosphine oxide was in turn subjected to reduction. Thus treatment of the diphosphine oxide **14** with trichlorosilane in the presence of triethylamine, in order to avoid displacement of the hydroxyl group by chloride, afforded the desired crude hydroxy phosphine **1**. Without isolation the product was converted into the BH_3 adduct. Purification by flash chromatography and decomposition of the phosphine borane by treatment with diethylamine gave the highly air sensitive hydroxy phosphine **1**.



reagents

(i) Et_2NH excess (80%) (ii) 30% H_2O_2, CH_3OH, acetone (80%) (iii) 10% Pd/C, H_2 (95%) or electrolysis, 50 mA, $(n\text{-}Bu)_4NBF_4$, THF (90%) (iv) Cl_3SiH, Et_3N, toluene, 80°C (80%) (v) 1M BH_3-THF (quant) (vi) Et_2NH excess (83%).

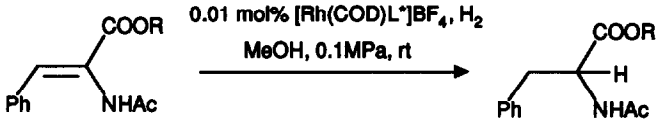
Scheme 3

Asymmetric Hydrogenations. To check the catalytic properties of the synthesized hydroxy phosphine the corresponding cationic rhodium complexes of the phosphines **1** and **11a** were prepared by reaction with $[Rh(COD)_2]BF_4$ in THF. While the benzyl diphosphine **11a**, just as hydroxy norphos, gave a unique complex [^{31}P NMR ($CDCl_3$): δ 60.2 (dd, $^2J_{PP}$=31.4Hz, $^1J_{RhP}$=148.8Hz), 43.8 (dd, $^1J_{RhP}$=146.5Hz)], the hydroxy phosphine **1** formed different complexes. They were characterized in the ^{31}P NMR by groups of signals in the region of δ 62 and 46, respectively. Unfortunately, all attempts to separate these complexes failed. Some of them probably arise from association of the hydroxyl group with the metal, which may cause the formation of different geometrical species.[23]

As a test for selectivity and activity, reductions of N-acetyl dehydrophenylalanine (AH) and its methyl ester (AMe) were chosen. The results of the hydrogenation are indicated in Table 1, which also includes for comparison data obtained with the corresponding cationic hydroxy norphos complex. It is interesting to note, that a remarkable difference of the catalytic properties of the complex which derived from hydroxy norphos can be found in comparison to the catalyst which is formed with the more flexible hydroxy phosphine **1**. The latter is especially characterized by a significant loss of activity. The enantiomeric excess obtained in these hydrogenations was similar to that of the complex derived from **11a** or those reported using other 1,2-diphosphines such as prophos[13,25]. A special stereodifferentiating effect, which can be attributed to the

hydroxyl group could not be detected. It is noteworthy that the reduction rate is appreciably enhanced by replacement of the hydroxyl by the benzyloxy group as shown by the results obtained with the complex formed with **11a**.

Table 1. Asymmetric hydrogenation of N-acetyl dehydrophenylalanine (AH) and its methyl ester (AMe).



R = H : AH
R = Me: AMe

ligand	substrate[a]	t/2 (min)	ee%[b]	configuration
(R,R,R)-hydroxy norphos	AMe	100	80.1	(S)
	AH	75	88.4	(S)
(S)-1	AMe	265	75.4	(R)
	AH	285	75.0	(R)
(S)-11a	AMe	115	74.4	(R)
	AH	165	77.6	(R)

[a] 1 mmol substrate in 15 ml MeOH; [b] Measured on the crude product: gc with chiral columns for N-acetyl phenylalanine after esterification with diazomethane and for methyl ester of N-acetyl phenylalanine with XE 60-L-valine tert-butylamide, 150 °C.

Conclusion

In summary, we have developed a general and straightforward procedure for the synthesis of enantiomerically pure (S)-1,2-bis(diphenylphosphino)butane-4-ol starting from L-ascorbic acid. The cationic complex obtained from hydroxy phosphine 1 gave only a moderately active catalyst in comparison to the more rigid catalyst derived from hydroxy norphos. This result is consistent with reported sporadic observations, wherein the presence of a hydroxyl group in the catalyst gave rise to diminished reaction rates during the hydrogenation.[13,26] However, our results with hydroxy norphos revealed that this negative effect can be expected only when coordination of the hydroxyl group to the metal is sterically possible.[27] Other investigations of chiral hydroxy phosphines, like the study of their complexation behaviour are currently being explored in our respective groups.

Experimental

General procedures.

All reactions with phosphines were performed under argon using conventional Schlenk technique owing to the sensitivity of compounds to oxygen. Solvents were purified and dried by standard techniques. Electrolysis was carried out on a platinum-tip electrode with a farradayic current of 50 mA. Preparative thin-layer chromatography was performed on pre-coated TLC plates (silica gel 60 F_{254}, layer thickness 2 mm, Merck). Flash chromatography was carried out with silica gel 60 (particle size 0.040-0.063 mm, Merck). ^1H, ^{31}P and ^{13}C NMR were recorded on a Bruker AM 250 instrument operating at 250, 101 and 63 MHz, respectively. Chemical shifts are reported in ppm downfield from internal TMS (^1H and ^{13}C) and external 85% H_3PO_4 (^{31}P). Mass spectra were recorded on an AMD 402 (Firma Intectra) at 70 eV. Optical rotations were measured on a "gyromat-HP" (Firma Dr. Kernchen). GC analysis of chiral products were performed on a HP 5890 Series II gas chromatograph. IR spectra were recorded on a Perkin Elmer 88 instrument. Rhodium complexes were prepared in THF by classic methods.[28]

(R)-4-O-Benzyl-1,2-O-isopropylidene-butane-1,2,4-triol (8a).

NaH (0.24 g, 10 mmol) was added to a solution of (R)-1,2-O-isopropylidene-butane-1,2,4-triol[10] **7** (0.365 g, 2.5 mmol) in THF (5 ml) and the resulting mixture was stirred at ambient temperature for 1 h. Benzyl bromide (0.59 ml, 5 mmol) and n-Bu_4NI (0.2 g) were added and stirring continued. After 4 h the mixture was carefully dropped into MeOH (20 ml) to decompose the excess of NaH. Then the solvents were removed under reduced pressure. The resulting sirup was extracted with CH_2Cl_2 (3x25 ml). The combined organic extract was washed with water (2x25 ml) and then dried (Na_2SO_4). The residue was subjected to column chromatography on silica gel (n-hexane:ethyl acetate=9:1) to give **8a** as a colourless oil (78 %). $[\alpha]_D^{23}$ = 0.6 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.27 (5H, aromat), 4.49 (2H, s), 4.23 (1H, m), 4.07 (1H, dd, J=8.0Hz, 5.9Hz), 3.58 (3H, m), 1.90 (2H, m), 1.42 (3H, s), 1.38 (3H, s); ^{13}C NMR ($CDCl_3$) δ 138.3-127.6 (aromat), 108.5 (C), 73.9 (CH), 73.1, 69.7, 67.1, 33.9 (CH_2), 26.9, 25.8 (CH_3); IR (cm^{-1}, neat) 2984, 2936, 2904, 2864, 1496, 1454, 1380, 1376, 1368, 1216, 1160, 1096, 1072, 1060, 860, 738, 698; Found C 71.27, H 8.37, $C_{14}H_{20}O_3$ (236.313): requires C 71.16, H 8.53.

(R)-1,2-O-Isopropylidene-4-O-(methylthiomethyl)butane-1,2,4-triol (8b).

NaH (0.24 g, 10 mmol) was added to a solution of (R)-1,2-O-isopropylidene-butane-1,2,4-triol[10] **7** (0.365 g, 2.5 mmol) in THF (5 ml) and the resulting mixture stirred for 1 h at room temperature. Chlorothiomethyl ether (MTM-Cl) (0.385 ml, 5 mmol) and n-Bu_4NI (0.2 g, 0.5 mmol) were added and stirring continued. After 4 h the mixture was worked up as described for **8a** to give **8b** as a colourless oil (82 %). $[\alpha]_D^{23}$ = -8.3 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 4.48 (2H, s), 4.08 (1H, m), 3.90 (1H, dd, J=7.9Hz, 5.9Hz), 3.46 (3H, m), 1.98 (3H, s), 1.72 (2H, m, J=7.6Hz, 1.4Hz), 1.35 (3H, s), 1.25 (3H, s); ^{13}C NMR ($CDCl_3$) δ 108.4 (C), 75.3 (CH_2), 73.7 (CH), 69.4, 63.2, 33.4 (CH_2), 26.9, 25.7, 13.7 (CH_3); IR (cm^{-1}, neat) 2984, 2924, 1370, 1246, 1080, 860; MS *m/e* (Ion, rel. Int.) 191 (M^+-CH_3, 2.8), 159 (M^+-SCH_3, 5), 149 (3), 107 (30), 101, (36), 89 (48), 71 (75), 61 (87), 43 (100); Found C 52.20, H 8.87, $C_9H_{18}O_3S$ (206.305): requires C 52.40, H 8.79.

(R)-1,2-O-Isopropylidene-4-O-[2'-(trimethylsilyl)eth-1'-oxymethyl]butane-1,2,4-triol (8c).

NaH (0.264 g, 11 mmol) was added to to a solution of (R)-1,2-O-isopropylidene-butane-1,2,4-triol[10] **7** (0.365 g, 2.5 mmol) in THF (5 ml) and the resulting mixture was stirred for 1h at room temperature. Trimethylsilylethoxymethyl chloride (SEM-Cl) (0.5 ml, 2.7 mmol) and n-Bu_4NI (0.2 g) were added and stirring continued. After 4 h the mixture was worked up as described for

8a to give **8c** as a colourless oil (73 %); $[\alpha]_D^{24}$ = -7.5 (*c* 1.26, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 4.62 (2H, s), 4.05 (1H, dd, J=8.0Hz, 6.0Hz), 3.58 (6H, m), 1.82 (2H, m), 1.40 (3H, s), 1.30 (3H, s), 0.92 (2H, t, J=8.4Hz), 0.03 (9H, s); ^{13}C NMR ($CDCl_3$) δ 108.5 (C), 94.7 (CH_2), 73.6 (CH), 69.5, 65.0, 64.3, 33.7 (CH_2), 26.9, 25.7 (CH_3), 18.0 (CH_2), -1.48 (CH_3); IR (cm^{-1}, neat) 2954, 2876, 1379, 1248, 1159, 1106, 1060, 859, 835; Found C 56.52, H 10.28, $C_{13}H_{28}O_4Si$ (276.452): requires C 56.48, H 10.21.

***General procedure for the hydrolysis of the isopropylidene group in compounds* 8a-c:**

A solution of the acetonide (5 mmol) in glacial acetic acid (15 ml), H_2O (5 ml) and THF (5 ml) was heated 4 h at 40 °C. Then a mixture of toluene/EtOH (1:1) was codistilled several times. The residue was dried *in vacuo* to give the corresponding diols as colourless oils in quantitative yields.

(R)-4-O-Benzyl-butane-1,2,4-triol (9a).

$[\alpha]_D^{24}$ = -4.2 (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.38-7.27 (5H, aromat), 4.52 (2H, s), 3.88 (1H, m), 3.62 (3H, m), 3.48 (1H, dd, J=11.3Hz, 6.5Hz), 3.20 (2H, b, exchangeable with D_2O), 1.77 (2H, m); ^{13}C NMR ($CDCl_3$) δ 137.8-127.8 (aromat); 73.3 (CH), 71.2, 68.2, 66.6, 32.8 (CH_2); IR (cm^{-1}, neat) 3392, 3100, 3064, 3048, 3032, 2996, 2928, 2904, 2864, 1496, 1454, 1364, 1206, 1100, 738, 698; Found: C 67.32, H 8.17, $C_{11}H_{16}O_3$ (196.249): requires C 67.32, H 8.22.

(R)-4-O-(Methylthiomethyl)butane-1,2,4-triol (9b).

$[\alpha]_D^{22}$ = 12.9 (*c* 1, EtOH); ^1H NMR (d_6-acetone) δ 4.61 (2H, s), 3.90 (2H, s, exchangeable with D_2O), 3.70 (2H, m), 3.62 (2H, m), 3.48 (1H, dd, J=10.9Hz, 6.6Hz), 3.40 (1H, dd, J=10.9Hz, 4.3Hz), 2.00 (3H, s), 1.68 (2H, m, J=2.5Hz); ^{13}C NMR (d_6-acetone) δ 75.7 (CH), 70.2, 67.3, 65.8, 34.1 (CH_2), 13.9 (CH_3); IR (cm^{-1}, neat) 3412, 2924, 1710, 1572, 1508, 1430, 1348, 1304, 1268, 1080, 970, 948, 892, 864, 730, 714, 680; Found: C 43.62, H 8.69, $C_6H_{14}O_3S$ (166.241): requires C 43.35, H 8.49.

(R)-4-O-[2'-(Trimethylsilyl)eth-1'-oxymethyl]butane-1,2,4-triol (9c).

$[\alpha]_D^{22}$ = -1.2 (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 4.65 (2H, s), 3.85 (1H, m), 3.72 (2H, m), 3.60 (3H, m), 3.45 (1H, dd, J=10.9Hz, 6.7Hz), 2.95 (2H, b, exchangeable with D_2O), 1.82 (2H, m), 0.89 (2H, t, J=8.4Hz), -0.03 (9H, s); ^{13}C NMR ($CDCl_3$) δ 94.8 (CH_2), 70.6 (CH), 66.4, 65.4, 65.3, 32.7, 18.0 (CH_2), -1.50 (CH_3); IR (cm^{-1},CH_2Cl_2) 3454, 3056, 2957, 2307, 1265, 1108, 1059, 896, 860, 837; Found: C 50.61, H 10.10, $C_{10}H_{24}O_4Si$ (236.389): requires C 50.81, H 10.23.

***General procedure for the ditosylation of the diols* 9a-c.**

To a solution of the diol (10 mmol) in pyridine (10 ml) cooled in an ice bath, p-toluenesulfonyl chloride (4.19 g, 22 mmol) was added. After stirring overnight at ambient temperature the mixture was poured in ice water (300 ml). The water was extracted with CH_2Cl_2 (3x200 ml). The combined organic solution was washed with aqueous 5 % HCl (3x50 ml), 5 % aqueous $NaHCO_3$ solution (50 ml) and finally with H_2O (50 ml). After drying (Na_2SO_4) the solvent was removed under reduced pressure and the residue subjected to flash chromatography (n-hexane:ethyl acetate = 4:1) to give the ditosylates as colourless oils.

(R)-4-O-Benzyl-1,2-O-ditosyl-butane-1,2,4-triol (10a).

Yield 76 %; $[\alpha]_D^{22}$ = 18.6 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.78-7.27 (13H, aromat), 4.85 (1H, m), 4.30 (2H, AB, J=12.2Hz), 4.15 (1H, dd, J=11.2Hz, 3.5Hz), 4.06 (1H, dd, J=11.2Hz, 5.1Hz), 3.40 (2H, m), 2.43 (3H, s), 2.41 (3H, s), 1.92 (2H, m); ^{13}C NMR ($CDCl_3$) δ 145.0-127.5 (aromat), 76.7

(CH), 72.9, 70.0, 64.9, 31.5 (CH_2), 21.7 (CH_3); IR (cm^{-1}, neat) 3064, 3032, 2924, 2908, 2868, 1598, 1496, 1454, 1370, 1308, 1292, 1212, 1204, 1174, 1096, 1020, 1014, 996, 966, 908, 816, 796, 752, 700, 692, 666; Found: C 59.76, H 5.89, $C_{25}H_{28}O_7S_2$ (504.626): requires C 59.50, H 5.59.

(R)-4-O-Methylthiomethyl-1,2-O-ditosyl-butane-1,2,4-triol (10b).

Yield 75 %; $[\alpha]_D^{21}$ = 1.4 (*c* 1.06, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.78-7.27 (8H, aromat), 4.76 (1H, m), 4.37 (2H, AB, J=11.5Hz), 4.05 (2H, m), 3.47 (1H, m), 3.28 (1H, m), 2.38 (3H, s), 2.37 (3H, s), 2.02 (3H, s), 1.92 (2H, m); ^{13}C NMR ($CDCl_3$) δ 148.3-127.5 (aromat), 76.5 (CH), 75.4, 69.7, 62.9, 31.2 (CH_2), 21.7, 14.2 (CH_3); IR (cm^{-1}, KBr) 3065, 2959, 2923, 1366, 1306, 1241, 1178, 1090, 1078, 1044, 1019, 994, 910, 815, 667, 577, 554; Found: C 50.42, H 5.49, $C_{20}H_{26}O_7S_3$ (474.622): requires C 50.61, H 5.52.

(R)-1,2-O-Ditosyl-4-O-[2'-(trimethylsilyl)eth-1'-oxymethyl]butane-1,2,4-triol (10c).

Yield 79 %; $[\alpha]_D^{23}$ = 11.2 (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.72-7.30 (8H, aromat), 4.78 (1H, m), 4.40 (2H, AB J=6.7Hz), 4.12 (1H, dd, J=11.3Hz, 3.6Hz), 4.03 (1H, dd, J=11.3Hz, 4.9Hz), 3.32 (4H, m), 2.44 (3H, s), 2.40 (3H, s), 1.87 (2H, m), 0.98 (2H, t, J=8.2Hz), -0.03 (9H, s); ^{13}C NMR ($CDCl_3$) δ 145.1-127.9 (aromat), 94.7 (CH_2), 76.4 (CH), 69.8, 65.2, 62.3 (CH_2), 31.4 (CH_3), 21.6, 18.0 (CH_2), -1.50 (CH_3); IR (cm^{-1}, neat) 2955, 1599, 1368, 1293, 1249, 1191, 1178, 1097, 1059, 916, 835, 734; Found: C 59.92, H 7.54, $C_{24}H_{36}O_8S_2Si$ (480.641): requires C 59.98, H 7.55.

***General procedure for the preparation of the phosphine boranes* 12a-c.**

A solution of lithium diphenylphosphide was generated from lithium strips (37 mg, 5.3 mmol) and freshly distilled chlorodiphenylphosphine (0.28 ml, 1.51 mmol) in THF (4 ml). The resultant deep red solution was added at 0 °C to a solution of the ditosylate (0.532 mmol) in THF (10 ml) over a period of 15 min. The solution was stirred for a further 2 h at room temperature and then the solvent removed. The residue was dissolved in CH_2Cl_2 (10 ml), washed with water (10 ml) and dried (Na_2SO_4). The solution was concentrated under reduced pressure to give the impure phosphines **11a-c**.

The crude phosphines (1mmol) were redissolved in THF (5 ml) and cooled to 0 °C. A 1M BH_3-THF-solution (2 ml, 2 mmol) was added under stirring, and then the mixture was allowed to warm to ambient temperature. After evaporation of the solvent *in vacuo* the residue was subjected to flash chromatography (n-hexane:ethyl acetate = 9:1) to give the phosphine boranes.

(S)-4-Benzyloxy-but-1,2-diyl-bis(diphenylphosphine-borane) (12a).

Yield 60 %; m.p. 105-112°C, $[\alpha]_D^{21}$ = 6.0 (*c* 1.25, $CHCl_3$); ^{31}P NMR ($CDCl_3$) δ 26.2 (m), 17.7 (m); ^1H NMR ($CDCl_3$) δ 7.82-7.00 (25H, aromat), 3.85 (2H, AB, J=11.7Hz), 3.27 (1H, m), 2.80 (2H, m), 2.58 (1H, dd, J=11.3 Hz, 2.4 Hz), 2.22 (1H, m), 2.00-0.0 (8H, b); ^{13}C NMR ($CDCl_3$) δ 138.5-127.3 (aromat), 72.3 (CH_2), 67.7 (CH_2, d, J=4.5Hz), 30.4 (CH_2), 27.5 (CH, d, J=32.2Hz), 25.8 (CH_2, d, J=33.1Hz); IR (cm^{-1}, KBr) 3078, 3055, 2854, 2386, 2353, 1437, 1105, 1063, 740, 693; Found: C 74.70, H 7.45, $C_{35}H_{40}B_2P_2O$ (560.276): requires C 75.03, H 7.20.

(S)-4-(Methylthiomethyloxy)but-1,2-diyl-bis(diphenylphosphine-borane) (12b).

Colourless oil; Yield 46 %; ^{31}P NMR ($CDCl_3$) δ 30.1 (s), 17.7 (s); ^1H NMR ($CDCl_3$) δ 7.95-7.95 (20H, aromat), 4.02 (2H, AB, J=11.3Hz), 3.28 (1H, m), 2.80 (1H, m), 2.68 (1H, d, J=7.6Hz), 2.55 (1H, ddd, J=14.7Hz, 6.0Hz, 2.2Hz), 2.22 (1H, ddd, J=27.1Hz, 14.3Hz, 1.3Hz), 2.00 (2H, s), 1.85 (3H, s), 2.00-0.0 (6H, b); ^{13}C NMR ($CDCl_3$) δ 74.6 (CH_2), 65.5 (CH_2, d, J=4.2Hz), 29.9 (CH_2), 27.4 (CH, d, J=32.4Hz), 26.0 (CH_2, d, J=33.2Hz), 13.9 (CH_3); Found: C 68.12, H 7.45, $C_{30}H_{38}OB_2P_2S$ (530.271): requires C 67.95, H 7.22.

(S)-4-[2'-(Trimethylsilyl)eth-1'-(oxymethoxy)]but-1,2-diyl-bis(diphenylphosphine-borane) (12c).

Colourless oil; Yield 53 %; $[\alpha]_D^{22}$ = 1.4 (*c* 1.03, $CHCl_3$); ^{31}P NMR ($CDCl_3$) δ 26.4 (m), 17.7 (m); ^1H NMR ($CDCl_3$) δ 7.85-7.30 (20H, m, aromat), 4.17 (2H, m), 3.35 (2H, m), 2.70-3.00 (3H, m), 2.27 (2H, m), 2.0-0.0 (10H, b), 0.0 (9H, s); ^{13}C NMR ($CDCl_3$) δ 133.0-127.3 (aromat), 94.3 (CH_2), 65.0 (CH_2, d, J=4Hz), 64.7, 30.6 (CH_2), 27.5 (CH, dd, J=32.8Hz, 4.7Hz), 25.7 (CH_2, dd, J=34.4Hz, 1.5Hz), 18.0 (CH_2), -1.3 (CH_3); IR (cm^{-1}, nujol) 3060, 3032, 2388, 2352, 2348, 2300, 1588, 1484, 1438, 1248, 1190, 1168, 1108, 1086, 1064, 1006, 1000, 938, 860, 850, 836, 738, 714, 694; Found: C 67.70, H 8.01, $C_{34}H_{48}O_2B_2P_2Si$ (600.417): requires: C 68.02, H 8.06.

(S)-1,2-Bis(diphenylphosphino)-4-O-benzyl-butane-4-ol (11a).

Bis(phosphine-borane) **12a** (0.56 g, 1 mmol) was dissolved in degassed Et_2NH (4 ml), and the solution was kept at 50 °C for 10 h under argon. Excess Et_2NH was removed *in vacuo*, and the residue was passed through a short column of basic alumina eluting with degassed benzene under argon to give practically pure **11a**. Yield 80 %; m.p. 70-75°C, $[\alpha]_D^{23}$ = -67.6 (*c* 1, $CHCl_3$); ^{31}P NMR ($CDCl_3$) δ -1.2 (d, J=25.5Hz), -20.0 (d); ^1H NMR ($CDCl_3$) δ 7.31-7.20 (25H, aromat), 4.28 (2H, m), 3.50 (2H, m), 2.38-1.88 (5H, m); ^{13}C NMR ($CDCl_3$) δ 138.7-127.4 (aromat), 72.7 (CH_2), 68.4 (CH_2, dd, J=10.0Hz, 3.2Hz), 31.5 (CH_2, dd, J=13.4Hz, 8.9Hz), 31.1 (CH, dd, J=16.5Hz, 13.3Hz), 29.2 (CH_2, dd, J=14.9Hz, 12.5Hz); Found: C 78.91, H 6.42, $C_{35}H_{34}OP_2$ (532.609): requires C 78.93, H 6.43.

(S)-4-Benzyloxy-but-1,2-diyl-bis(diphenylphosphine-oxide) (13).

To a solution of **11a** (1.0 g, 1.9 mmol) in acetone (5 ml) at 0°C some drops aqueous 30 % hydrogen peroxide were added. The mixture was allowed to stand overnight. Then the solvent was removed under reduced pressure. The residue was treated with ethyl acetate to give the phosphine oxide as a white solid. Yield 80%; m.p. 187-189°C; $[\alpha]_D^{26}$ = -10.4 (*c* 1, $CHCl_3$); ^{31}P NMR ($CDCl_3$) δ 37.3 (d, J=46.7Hz), 31.3 (d); ^1H NMR ($CDCl_3$) δ 7.68-7.0 (25H, aromat), 4.01 (2H, AB, J=12.5Hz), 3.18 (3H, m), 2.62 (2H, m), 1.95 (2H, m); ^{13}C NMR ($CDCl_3$) δ 138.2-127.5 (aromat), 72.5 (CH_2), 67.4 (CH_2, d, J=6.7Hz), 29.3 (CH_2), 28.8 (CH, dd, J=69.2Hz, 4.1Hz), 28.7 (CH_2, d, J=68.6Hz); IR (cm^{-1}, KBr) 3050, 2920, 2882, 3850, 1418, 1188, 1105, 722, 708, 685; Found: C 74.18, H 5.79, $C_{35}H_{34}O_3P_2$ (564.609): requires C 74.46, H 6.07.

(S)-4-Hydroxy-but-1,2-diyl-bis(diphenylphosphine-oxide) (14).

Catalytic hydrogenation. A mixture of benzyl ether **13** (0.4 g, 0.71 mmol) and 0.1 g preequilibrated 10 % Pd/C in ethanol was hydrogenated at ambient temperature and atmospheric pressure for 3 d. The mixture was filtered and the filtrate evaporated to give the alcohol **14** as colourless crystals (95 %). m.p. 170-72°C; $[\alpha]_D^{24}$ = -33.8 (*c* 1, $CHCl_3$); ^{31}P NMR ($CDCl_3$) δ 38.9 (d, J=43.4Hz), 34.4 (d); ^1H NMR ($CDCl_3$) δ 7.82-7.00 (20H, aromat), 3.48-3.00 (4H, m), 2.57 (2H, m), 2.02 (2H, m); ^{13}C NMR ($CDCl_3$) δ 132.1-128.6 (aromat), 58.6 (CH_2, d, J=8.5Hz), 31.7 (CH_2), 26.8 (CH, dd, J=69.7Hz, 3.4Hz), 26.1 (CH_2, d, J=68.0Hz); MS *m/e* (Ion, rel. Int.) 474 ($M^{\cdot+}$, 1), 457 (0.8), 430 (8), 397 (M^+-C_6H_5,12), 381 (M^+-C_6H_5-16, 8), 273 (100), 262 (M^+-$(CH_2)_2OH$, 18); IR (cm^{-1}, KBr) 3420, 3062, 2908, 2875, 1420, 1175, 1154, 1105, 735, 687; $C_{28}H_{28}O_3P_2$ (474.483), requires: C 70.88, H 5.95, Found: C 70.93, H 5.98.

Electrolysis. A solution of the benzyl ether **13** (0.1 g, 0.18 mmol) in THF (10 ml) was electrolyzed in the presence of $(n\text{-}Bu)_4NBF_4$ as supporting electrolyte for 4 d. The mixture was evaporated and the residue extracted with CH_2Cl_2 (50 ml), washed with H_2O (10 ml) and dried (Na_2SO_4). The solution was concentrated under reduced pressure to give **14** (90 %).

(S)-1,2-Bis(diphenylphosphino)butane-4-ol (1).

Reduction with Cl_3SiH. To a mixture of the phosphine oxide **14** (0.23 g, 0.48 mmol) and Et_3N (0.41 ml, 2.89 mmol) in toluene (10 ml) was added Cl_3SiH at 0°C. The reaction was stirred at 80 °C for 3 d. After being cooled to room temperature, the mixture was carefully quenched with aqueous 30 % NaOH-solution (8 ml). The mixture was extracted with CH_2Cl_2 (3x25 ml), washed with H_2O (10 ml) and dried (Na_2SO_4). The solution was concentrated under reduced pressure to give the crude hydroxy phosphine (80 %).

Conversion to the phosphine borane. The crude phosphine (1 mmol) was redissolved in THF (5 ml) and cooled to 0°C. A 1M BH_3-THF-solution (2 ml, 2 mmol) was added under stirring, and then the mixture was allowed to warm to ambient temperature. After evaporation of the solvent *in vacuo* the residue was subjected to flash chromatography (n-hexane:ethyl acetate=9:1) to give the phosphine borane **15** as a colourless oil in quantitative yield. $[\alpha]_D^{26}$ = -4.5 (*c* 0.44, $CHCl_3$); ^{31}P NMR ($CDCl_3$) δ 26.3 (b), 17.2 (b); ^1H NMR ($CDCl_3$) δ 7.80-7.22 (20H, aromat), 3.41-3.22 (2H, m), 3.01 (2H, m), 2.62-2.19 (2H, m), 2.00-0.0 (8H, b); ^{13}C NMR ($CDCl_3$) δ 132.9-127.3 (aromat), 60.1 (CH_2, d, J=4.5Hz), 33.1 (CH_2, d, J=2.6Hz), 27.0 (CH, d, J=32.6Hz), 25.5 (CH_2, d, J=32.9Hz); Found: C 71.81, H 7.44, $C_{28}H_{34}OP_2B_2$ (470.153): requires C 71.53, H 7.29.

Cleavage of the phosphine borane **15**. The reaction was performed as described for the preparation of **11a** to give **1** as highly air sensitive colourless oil (83 %). $[\alpha]_D^{24}$ = -64.6 (*c* 0.53, $CHCl_3$); ^{31}P NMR ($CDCl_3$) δ -0.2 (d, J=22.3Hz), -19.9 (d); ^1H NMR ($CDCl_3$) δ 7.32-7.23 (20H, aromat), 3.63 (2H, t, J=6.2Hz), 2.40-2.12 (2H, m), 1.95-1.76 (4H, m, 1H exchangeable with D_2O); ^{13}C NMR ($CDCl_3$) δ 138.8-127.8 (aromat), 60.6 (CH_2, dd, J=10.1Hz, 3.0Hz), 34.4 (CH_2, dd, J=14.1Hz, 8.0Hz), 30.6 (CH, dd, J=16.1Hz, 13.1Hz), 29.0 (CH_2, dd, J=14.8Hz, 13.0Hz); MS *m/e* (Ion, rel. Int.) 442 ($M^{\cdot+}$, 33), 370 (80), 333 (M^+-1-PPh, 27), 262 (72), 185 (80), 183 (PPh_2-2, 100), 107 (PPh-1, 30); IR (cm^{-1}, KBr) 3424, 3070, 3052, 2925, 2856, 1585, 1480, 1433, 1306, 1262, 1094, 1026, 921, 802, 741, 696, 508, 482; Found: C 75.71, 6.21, $C_{28}H_{28}OP_2$ (442.483) requires C 76.00, H 6.38.

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