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Derivatives of α,α,α',α'-Tetraaryl-2,2-dimethyl-1,3-dioxolan-4,5-dimethanol (TADDOL) Containing Nitrogen, Sulfur, and Phosphorus Atoms. New Ligands and Auxiliaries for Enantioselective Reactions.

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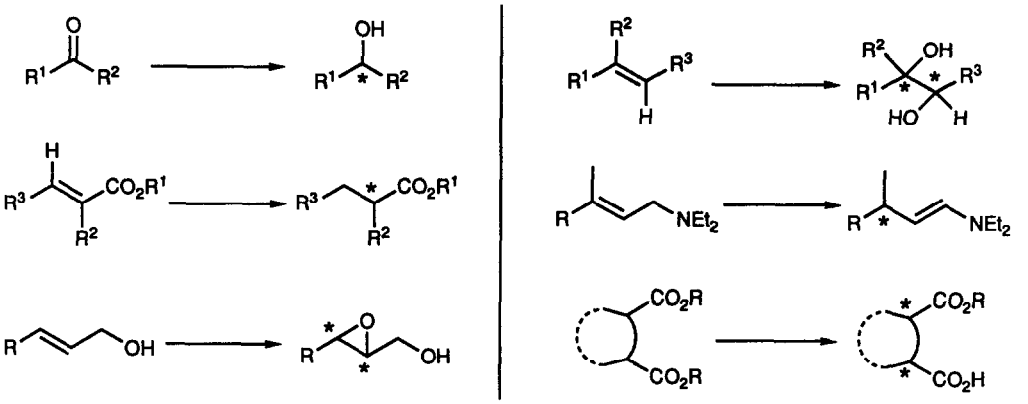
Abstract: α,α,α',α'-Tetraaryl-2,2-dimethyl-1,3-dioxolan-4,5-dimethanols are converted to bicyclic phosphites and phosphonites (**2a-2e**) by reaction with Cl_2PR and Cl_2POR derivatives. - One or both OH groups of the parent TADDOL can be replaced by Cl (→ **4a, 5a**), and the halide in turn substituted by azide (→ **4b, 5b**), thiocyanide (→ **6**), or sulfide (→ **8**). Reduction of the azido group(s) to NH_2 and *N*-alkylation or acylation furnishes a variety of amino alcohols (**4c-4f**) and diamines (**5c-5f**), as well as a bis(trifluoroacetamide) (**5g**). Cyclization of the aminoalcohol (**4c**) produces a bicyclic system (**7**), containing a pyrrolidine ring (structure determination by X-ray diffraction). - The new chiral compounds containing nitrogen and phosphorus atoms might be useful ligands and auxiliaries for enantioselective syntheses.

The title of the Symposium-in-Print of which this article is part is not only dedicated - appropriately so - to S. Yamada but also challenges authors to look into the 21st century which happens to be the beginning of a new millenium as well. One of us has wagered on the issue "Organic Synthesis - Where now?" in a recent article[3]. Among the major conclusions was the prediction that the use of transition metal derivatives in synthesis and the development of better methods for the preparation of enantiopure compounds would be main areas of thrust in the years to come. Considering that the most attractive enantioselective processes are the catalytic ones, we note that these two areas merge: with the exception of some enzymatic and main-group organometallic conversions, the most efficient, useful, and generally applicable enantioselective reactions involve transition metal centers!

The list of reactions in *Scheme 1* includes enantioselective reductions of unsymmetrical ketones[4,5], hydrogenations of the double bond in α, β–unsaturated esters[4,6,7], the epoxidation of allylic alcohols[8], the hydroxylation of olefins[9], olefin isomerization[10], and saponification of ester groups[11]. All of these transformations are *functionalizing* ones: the required substrate must contain all the carbon atoms of the desired product. Furthermore, with one exception, the substrates must be prepared stereoselectively: the double bonds to which addition occurs must be of *E* or *Z* configuration, and the diesters to be saponified of *meso* configuration[12].

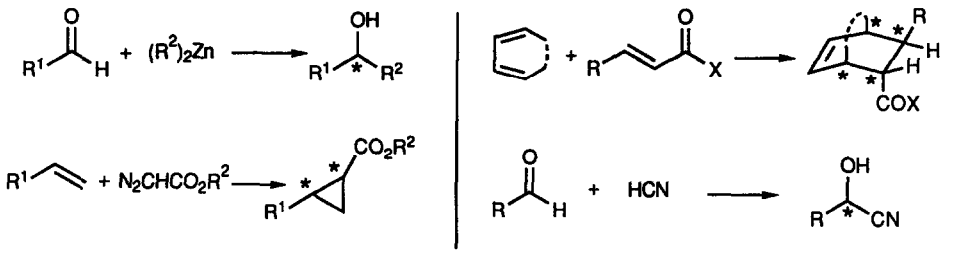
There are much fewer examples known of highly efficient (ee >95%), catalytic enantioselective C,C-bond-forming processes ("truly *synthetic*", or convergent!), see *Scheme 2*. These include addition of dialkyl zinc to aldehydes[13,14], cyclopropanation of C,C double bonds by diazo compounds[7,15], most notably the Diels-Alder reaction[16], and the enzymatic cyanohydrin formation[11,17].

It is important to realize that structurally and functionally very different systems are employed to achieve the processes shown in *Schemes 1* and *2*; a catalyst is custom-made and optimized for a particular reaction. A recently published[18] list of chiral ligands made from the pool of chiral building blocks[19] and used for various



Scheme 1. Processes which can be performed by enantioselective catalysis. The carbon skeleton is not changed in these ("functionalizing") reactions.

metals and the respective conversions their complexes catalyze demonstrates this fact. It is probably a dream of all researchers working in the field of enantioselective reactions that, once upon a time, they will find a ligand system which - by slight variations of a parent compound - is capable of functioning for most of the principal



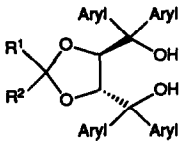
Scheme 2. C,C-Bond-forming reactions which can be carried out highly efficiently by enantioselective catalysis.

reactions of organic synthesis. From these dreams we should sometimes wake up and realize that nature uses a set of 20 building blocks to make her catalysts! The ligand system which has so far been useful for the largest variety of reactions is the 2, 2'-disubstituted 1, 1'-binaphthyl skeleton[4]. In the following sections we describe investigations aimed at an applicability extension of a chiral ligand we have been studying for ten years[20,21].

Since we first described the use[20] and preparation[21-23] of diols of type **1** (TADDOLs), there has been a number of new applications of such ligands in stoichiometric[20-22,24-26], catalytic[14,27-31] and Lewis-acid mediated[32,33] enantioselective reactions, including nucleophilic additions to aldehydes[14, 20-22,24] and ketones[33], cyanohydrin additions[25], aldol additions[24], Diels-Alder reactions[27,28], (2+2) cycloadditions[29,32], and ene-

reactions[30,31]. As may be expected for a ligand binding with an alkoxide oxygen, the metals involved so far are the polar ones (alkali, alkaline earth, early transition metals), notably titanium[14,20-25,27-32] and magnesium[33].

The number of possible applications of the simple TADDOL derivatives, readily available from tartrate acetonide, would increase if other heteroatoms could be incorporated into this system. Previously, we and others



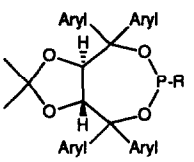
1

1a ($R^1 = R^2 = CH_3$, Aryl = Ph)
1b ($R^1 = R^2 = CH_3$, Aryl = 2-Naphth)

have demonstrated that the structure can be greatly varied by introducing different groups R^1, R^2 in the 2-position of the dioxolane ring and by varying the aryl groups; a list containing all TADDOLs known as of June 1992 has just been published[34]. While C_1-symmetrical TADDOLs (**1**, $R^1 \neq R^2$) turn out to be superior to C_2-symmetrical ones, in some cases, the modification of the aryl groups tends to lead to improvements rather than to spectacular leaps. With nitrogen, sulfur and phosphorus atoms attached to or built into the TADDOL system, however, ligands for other metals should result, and thus quite different transformations might be rendered enantioselective.

Originally, we hesitated to do reactions involving the benzhydrylic C-O bond. S_N2 substitutions with replacement of the diarylmethanol oxygen are not favorable, S_N1 reactions, on the other hand, could possibly lead to destruction of the entire molecule (elimination with loss of one of the stereogenic centers, rearrangement to a 1,3-dioxane ring, or fragmentation in a *retro*-Prins reaction). Also, the alkoxides resulting from OH deprotonation of a TADDOL might undergo fragmentation with formation of carbonyl compounds. Fortunately, we were able to find conditions under which good yields of TADDOL conversions can be realized, although colors developing in some of the reaction mixtures indicate that such destructive processes might be going on to some extent.

We first prepared cyclic phosphonites **2a**, **2b**, **2e** and phosphites **2c** and **2d**. Especially when containing impurities, these compounds are very sensitive to air. In pure, crystalline form they can be kept in an oxygen-containing atmosphere at room temperature without being oxidized, their solutions, however, always have to be kept with rigorous exclusion of oxygen. The best procedure for the preparation of bicyclic phosphonites and



2

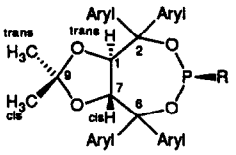
2	Aryl	R
a	Ph	CH_3
b	Ph	Ph
c	Ph	OCH_3
d	Ph	OPh
e	2-Naphth	Ph

phosphites of type **2** turned out to involve the following steps: treating the diol **1** with 2 equivalents of BuLi in THF at -70 °C, warming to +20 °C, cooling again to -70 °C, adding neat Cl_2PR or Cl_2POR, warming again to

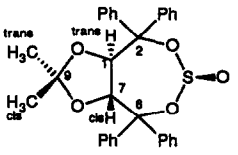
room temperature, and working up after five hours. For removal of the LiCl formed, the resulting solution is evacuated to dryness by pumping off all the solvent (final pressure *ca.* 0.1 Torr) and dissolving the product in toluene. Finally, the products are recrystallized (**2a** - **c**) or flash chromatographed (**2d**, **e**) on SiO_2. All these steps should be carried out under an inert atmosphere. Under optimized conditions the yields of crystalline products **2** range from 50 to 80%; they melt above 175 °C and have high optical rotations. Unfortunately, they also tend to include varying amounts of solvent which is hard to remove completely. This fact, together with the sensitivity to oxygen precluded our obtaining correct elemental analyses of the substances **2**.

It is appropriate to note at this point an interesting feature of the ^{1}H-NMR spectra of the phosphorus derivatives **2** which, in contrast to the C_2-symmetrical diols they are prepared from, belong to the C_1 point group: the diastereotopic methyl groups on C(9) and hydrogens on C(1) and C(7) show differences in their chemical shifts of up to 1.5 ppm, see *Table 1*. As compared to the C_2-symmetrical TADDOLs in which the geminal methyl groups appear around $\delta = 1$ ppm, the compounds **2** show one methyl group signal shifted to higher (up to 0.16 ppm) and the other one to lower field (down to 1.67 ppm).

Table 1. ^{1}H-NMR Chemical shift differences of the hydrogens H-C(1) (*trans*) and H-C (7) (*cis* to R on phosphorus) and of the hydrogen of the *cis* and *trans* CH_3 groups on C(9) of compounds **2**. For comparison, the corresponding values obtained for the cyclic sulfite **3** are also included. All values in [ppm].



2



3

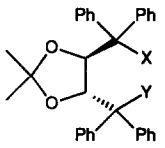
compound	Δδ H-C(1) / C(7)	δ H_3C-C(9)		Δδ H_3C-C(9)
2a	0.76	0.18	1.49	1.31
2b	0.84	0.21	1.55	1.34
2c	0.06	0.49	0.96	0.47
2d	0.45	0.67	0.76	0.09
2e	0.88	0.16	1.67	1.51
3	0.23	0.32	1.48	1.16

Chiral and achiral monodentate and bidentate phosphites, phosphonites, and phosphinites have been used for many different types of transition metal-catalyzed reactions[35], and our bicyclic TADDOL derivatives **2** are now being tested for application in some of those reactions.

For a substitution of the OH groups in TADDOLs by other heteroatoms [36,37] which are capable to serve as ligands on metal centers we decided to prepare the dichloride **5a** from the parent compound **1a** as a strategic intermediate, and we chose thionyl chloride/triethyl amine as the reagent for the OH/Cl replacement reaction. Depending on the conditions (ratio of reactants, mode and rate of addition, temperature) we were able to prepare either the cyclic sulfite **3** (see *Table 1*) or the dichloride **5a** in *ca.* 80% yield[37,38]. The rather labile chloro alcohol[37] **4a**, on the other hand, was formed by treatment of the dilithium alkoxide from **1a** with two

equivalents of methanesulfonyl chloride[39].

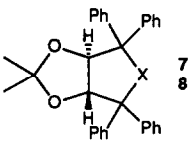
Since the monochloride **4a** was formed in high purity and in essentially quantitative yield as a crude product, and since attempts to purify it led to great losses, we used this chloro alcohol directly for a substitution reaction with NaN_3. The corresponding azido alcohol **4b**, in turn, was reduced ($LiAlH_4$) to the amino alcohol **4c** which served as a starting material for the preparation of the *N*-methyl- (**4d**), the *N, N*-dimethyl- (**4e**) and



4-6

	X	Y
4a	OH	Cl
4b	OH	N_3
4c	OH	NH_2
4d	OH	$NHCH_3$
4e	OH	$N(CH_3)_2$
4f	OH	$NHCH_2Ph$

	X	Y
5a	Cl	Cl
5b	N_3	N_3
5c	NH_2	NH_2
5d	$NHCH_3$	$NHCH_3$
5e	$N(CH_3)_2$	$NHCH_3$
5f	$N(CH_3)_2$	$N(CH_3)_2$
5g	$NHCOCF_3$	$NHCOCF_3$
6	SCN	SCN



7, 8

7 (X=NH)
8 (X=S)

the *N*-benzyl-derivatives (**4f**). The monomethylation (**4c** → **4d**) and monobenzylation (**4c** → **4f**) were achieved by using a stoichimetric amount of MeI or an excess of BnBr in dimethyl formamide (DMF), with $NaHCO_3$ as the base. All other *N*-alkylations described in this paper were carried out in the solvent 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidin-2-one ("*N, N*-dimethyl propylene urea" = DMPU)[40], using excess alkyl halide (cf. **4c** → **4e**)[41]. Like the unsymmetrical phosphorus derivatives **2**, compounds **3** and **4** show two ^{1}H-NMR signals (up to 0.8 ppm apart) for the diastereotopic Me groups in the 2-position of the dioxolane ring.

Upon treatment of the amino alcohol **4c** with tosyl chloride/*N, N*-dimethyl-4-aminopyridine (DMAP) in pyridine at 80 °C cyclization took place with formation of a pyrrolidine ring (→ **7**), which is part of a highly strained bicyclo[3,3,0]octane skeleton. The X-ray crystal structure of **7** is shown in *Figure 1*.

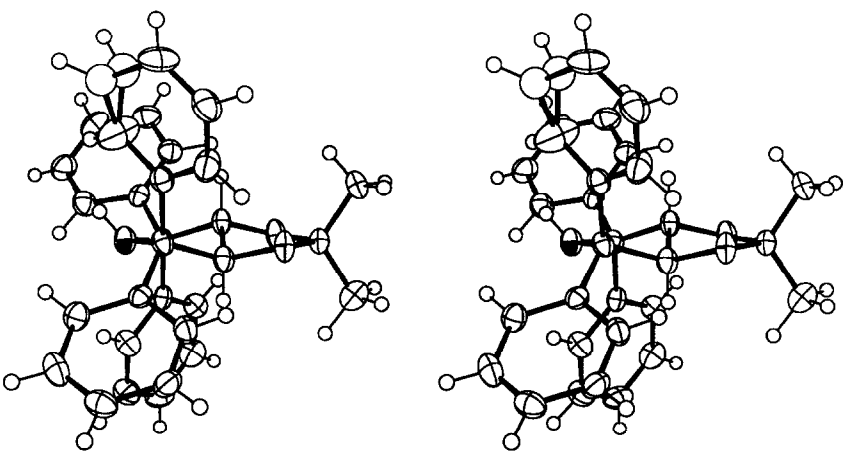


Figure 1. Stereoscopic ORTEP[42] drawing of **7**. Vibrational ellipsoids for the non-*H*-atoms are drawn at the 50% probability level. Shown is one of the two symmetrically independent molecules. Two positions were located for a disordered *C*-atom in one of the phenyl groups. The four bulky phenyl substituents block the formation of a hydrogen bond to the amino group.

It confirms the *trans* fusion of the two five-membered rings and the fact that the ring closure has occurred without racemization (also evident from the -222 specific rotation of **7**). An ananlogous cyclization of the chloro alcohol **4a** to a tetrahydrofuran was not observed. Such cyclizations should be favored by the presence of the two pairs of geminal phenyl groups,[43] and disfavored by the strain of the bicyclo[3,3,0]octane system. It is conceivable, that the tetrahydrofuran formation from TADDOLs is a reversible process, and it might actually be involved in the reactions responsible for the lability[37b] of the chloro alcohol **4a**. Since the secondary amine **7** is readily available, its use in enantioselective reactions[44,45] and as a synthetic equivalent of "chiral NH_3"[46] is being considered.

From the dichloride **5a** we have prepared the diamine **5c** through the diazide **5b**; the Cl/N_3 substitution reaction was carried out in DMF, and the diazido compound reduced with LiAlH, in tetrahydrofuran (THF). Methylations of **5c** performed under suitable conditions led to the *N*, *N'*-dimethyl- (**5d**), the *N*, *N*, *N'*-trimethyl- (**5e**) and the *N*, *N*, *N'*, *N'*-tetramethyl- (**5f**) diamines (see the experimental procedures), and acylation of **5c** with trifluoroacetic acid anhydride (TFAA) gave the diamide **5g**.

Reactions of the dichloride **5a** with sulfur nucleophiles[36] furnished the bis-thiocyanate **6** (55%, with KSCN in DMF) and the bicyclic thioether **8** (40%, with NaSH in DMF).

All the compounds **2** - **8** described herein are solid, and with one exception (**4b**) they could be purified by recrystallization and most of them were fully characterized (IR, ^{1}H- and ^{13}C-NMR spectroscopy, elemental analyses). X-Ray crystal structures were also obtained for the diazide **5b** and the diamine **5c**; they will be described in a forthcoming paper.

Acknowlegements: We thank Mr. O. Greter for determining the composition of the phosphorus compounds by high-resolution MS and Dr. E. Zass for helpful discussion. *Sandoz Pharma AG* (Basel, Switzerland) continues to support our research generously.

Experimental Part

General. Abbreviations: THF (tetrahydrofuran), DMSO (dimethylsulfoxide), BuLi (*n*-butyllithium). Solvents and reagents: THF was distilled over potassium. DMF and DMPU were distilled over CaH_2 under reduced pressure and stored over molecular sieves (4Å). All other solvents and reagents used were of p.a. quality. Indicated reaction temperature was measured with PT 100 thermometers. Flash chromatography (FC): performed at 0.3 bar, silica gel (230-400 mesh, *Merck*), aluminum oxide basic (*Alumina Woelm B*). Mp: *Büchi* 510, uncorrected. Optical rotations: *Perkin-Elmer* 241 polarimeter, in 10 cm cells. IR: *Perkin-Elmer* 983 or *Perkin-Elmer* 297, in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra: *Varian Gemini* 200 (200 or 50 MHz, respectively) or *Bruker WM* 300 (300 or 75 MHz, respectively), ^{31}P-NMR spectra: *Bruker AMX* 400 (162 MHz) or *Varian XL* 300 (121 MHz); δ in ppm downfield of TMS ($\delta = 0$), *J* in Hz. MS: *Hitachi-Perkin-Elmer* RMU-6M. Elemental analyses were performed by the Microanalytical Service Laboratory of ETH-Zürich.

Preparation of Phosphorus Ligands **2a-e** (General Procedure): To a stirred solution of 20 mmol of **1a**[21-23] or **1b**[23] in 80 ml of THF was added 42 mmol of BuLi (1.55 M solution in hexane) under argon atmosphere at -70 °C. During this addition the temperature rose up to -50 °C. The mixture was cooled again to -70 °C and stirred at this temperature for 5 min, and then warmed up to room temperature within 1 h. The reaction mixture was cooled again to -70 °C and 22 mmol of dichlorophosphorus reagent was added slowly without allowing the temperature to rise. The mixture was warmed up again to room temperature within 1h and stirred for 5 h at this temperature. After evaporation of the solvent under reduced pressure, to the residue obtained was added 50 ml of pentane. The suspension was stirred for 1h and filtered through a pressure filter funnel under argon atmosphere. To this solid residue was added 100 ml of toluene. The suspension was stirred for 10 h and filtered

through a pressure filter funnel again to remove insoluble LiCl. The filtrate was concentrated *in vacuo* to give a solid which was purified as described for the individual compound. The ligands obtained were stored under argon atmosphere.

(1*R*, 7*R*)-4,9,9-Trimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (**2a**): The general procedure was applied with 2.80 g of **1a** (6 mmol) and 0.59 ml of $MePCl_2$ (6.6 mmol). Purification by recrystallization (ethyl acetate/$CHCl_3$) provided 2.32 g (76%) of **2a** as a colourless solid. Mp 193.0-196.0 °C (decomp.). $[\alpha]_D^{RT}$ = –87.4 (c = 1.07, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.81-7.77 (m, 2H, arom H), 7.57-7.51 (m, 2H, arom H), 7.46-7.40 (m, 4H, arom H), 7.35-7.15 (m, 12H, arom H), 5.44 (dd, *J* = 8.63, 4.54 Hz, 1H, CH), 4.68 (d, *J* = 8.63 Hz, 1H, CH), 1.53 (d, *J* = 8.01 Hz, 3H, PCH_3), 1.49 (s, 3H, CH_3), 0.18 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 146.98, 146.09, 146.03, 142.04, 141.47, 130.13, 130.01, 129.33, 129.17, 129.09, 128.84, 128.48, 128.32, 128.24, 128.06, 127.80, 127.61, 127.46, 127.28, 127.16, 127.00, 111.22, 83.68, 82.84, 82.76, 82.64, 82.33, 81.91, 27.81, 24.83, 21.75, 21.50. ^{31}P-NMR ($CDCl_3$, 162 MHz): δ = 176.5. IR: ($CHCl_3$) υ = 3000, 1495, 1490, 1445, 1385, 1250, 1225, 1195, 1165, 1100, 1085, 1045, 1035, 1020, 1000, 915, 880, 865, 830, 805, 700. MS (EI), m/z (%) = 510 (M^+, <1), 452 (<1), 430 (<1), 374 (11), 237 (38), 207 (24), 180 (16), 179 (100), 178 (41), 167 (19), 166 (11), 165 (28), 105 (19), 77 (17), 28 (39). $C_{32}H_{31}O_4P$ (HRMS, $[M]^+$) Calcd. 510.1960. Found 510.1949.

(1*R*, 7*R*)-9,9-Dimethyl-2,2,4,6,6-pentaphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (**2b**): The general procedure was applied with 9.32 g of **1a** (20 mmol) and 3.0 ml of $PhPCl_2$ (22 mmol). Purification by recrystallization (ethyl acetate/$CHCl_3$) provided 5.38 g (47%) of **2b** as a colourless solid. Mp 206.0-209.0 °C (decomp.). $[\alpha]_D^{RT}$ = –85.9 (c = 1.14, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.92-7.15 (m, 25H, arom H), 5.62 (dd, *J* = 8.63, 4.69 Hz, 1H, CH), 4.78 (d, *J* = 8.63 Hz, 1H, CH), 1.55 (s, 3H, CH_3), 0.21 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 146.77, 145.90, 145.83, 141.88, 141.35, 141.21, 141.07, 130.72, 130.05, 129.74, 129.38, 128.56, 128.38, 128.12, 127.94, 127.64, 127.44, 127.32, 127.16, 111.36, 83.91, 83.25, 83.16, 82.71, 82.41, 82.18, 27.86, 24.76. ^{31}P-NMR ($CDCl_3$, 162 MHz): δ = 157.0. IR: ($CHCl_3$) υ = 3010, 1495, 1445, 1385, 1255, 1200, 1100, 1085, 1050, 1035, 1020, 1000, 880, 835, 810, 700. MS (EI), m/z (%) = 572 (M^+, <1), 514 (<1), 430 (<1), 238 (26), 237 (75), 236 (36), 208 (23), 207 (57), 180 (48), 179 (100), 178 (79), 167 (48), 166 (33), 165 (58), 152 (21), 105 (47), 77(28). $C_{37}H_{34}O_4P$ (HRMS, $[M+1]^+$) Calcd. 573.2195. Found 573.2097.

(1*R*, 7*R*)-4-Methoxy-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (**2c**): The general procedure was applied with 6.99 g of **1a** (15 mmol) and 1.56 ml of $MeOPCl_2$ (16.5 mmol). Purification by recrystallization (ethyl acetate) provided 6.25 g (79%) of **2c** as a colourless solid. Mp 190.0-192.0 °C (decomp.). $[\alpha]_D^{RT}$ = –236.7 (c = 1.17, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.61-7.17 (m, 20H, arom H), 5.14 (d, *J* = 8.30 Hz, 1H, CH), 5.08 (dd, *J* = 8.30, 1.89 Hz, 1H, CH), 3.52 (d, *J* = 9.89 Hz, 3H, $POCH_3$), 0.96 (s, 3H, CH_3), 0.49 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 146.16, 141.57, 141.34, 128.99, 128.77, 128.22, 127.91, 127.74, 127.33, 127.15, 127.05, 112.78, 84.84, 84.74, 82.55, 82.25, 82.03, 81.12, 49.49, 27.06, 26.03. ^{31}P-NMR ($CDCl_3$, 162 MHz): δ = 133.1. IR: ($CHCl_3$) υ = 3010, 1495, 1450, 1385, 1165, 1100, 1090, 1050, 1030, 1010, 885, 835, 805, 700. MS (EI), m/z (%) = 526 (M^+, <1), 468 (<1), 430 (<1), 374 (40), 344 (21), 237 (67), 208 (49), 207 (76), 180 (37), 179 (100), 178 (78), 167 (49), 165 (57), 152 (20), 105 (45), 77 (24), 28 (20). $C_{32}H_{31}O_5P$ (HRMS, $[M]^+$) Calcd. 526.1909. Found 526.1942.

(1*R*, 7*R*)-9,9-Dimethyl-4-phenoxy-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (**2d**): Following the general procedure, the reaction was performed with 2.33 g of **1a** (5 mmol) and 0.79 ml of $PhOPCl_2$ (5.5 mmol). After the reaction, THF was removed under reduced pressure and 20 ml of toluene was added to the residue directly. The suspension was stirred for 3 h and filtered through a pressure filter funnel to remove insoluble LiCl. The filtrate was concentrated *in vacuo*. The solid residue obtained was purified by FC (ø = 3 cm, 80 g silica gel, pentane/ether = 20/1) to give 2.09 g (71%) of **2d** as a colourless solid. Mp 177.0-177.5 °C (decomp.). $[\alpha]_D^{RT}$ = –172.8 (c = 1.09, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.60-7.07 (m, 22H, arom H), 6.99-6.94 (m, 1H, arom H), 6.56-6.52 (m, 2H, arom H), 5.55 (d, *J* = 8.30 Hz, 1H, CH), 5.10 (dd, *J* = 8.30, 0.77 Hz, 1H, CH), 0.76 (s, 3H, CH_3), 0.67 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 152.11, 152.04, 145.96, 141.34, 129.12, 129.03, 128.75, 128.32, 128.12, 127.90, 127.73, 127.57, 127.50, 127.36, 127.19, 126.90, 126.76, 123.20, 120.00, 119.88, 113.10, 86.66, 86.50, 85.04, 84.94, 82.25, 82.09, 80.28, 80.19, 26.62, 26.48. ^{31}P-NMR ($CDCl_3$, 121 MHz): δ = 127.4. IR: ($CHCl_3$) υ = 3008, 1593, 1492, 1448, 1383, 1373, 1248, 1166, 1088, 1051, 1035, 1016, 968, 890. MS (EI), m/z (%) = 588 (M^+, 2), 530 (6), 430 (2), 393 (11), 375 (27), 374 (89), 348 (13), 322 (10), 266 (11), 265 (23), 238 (11), 237 (68), 236 (23), 208 (22), 207 (50), 180 (18), 179 (100), 178 (33), 167 (26), 165 (18), 105 (11). $C_{37}H_{33}O_5P$ (HRMS, $[M]^+$) Calcd. 588.2066. Found 588.2061.

(1*R*, 7*R*)-9,9-Dimethyl-2,2,6,6-tetra(naphth-2-yl)-4-phenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]-decane (**2e**): Following the general procedure, the reaction was performed with 2.0 g of **1b** (3 mmol) and 0.45 ml of $PhPCl_2$ (3.3 mmol). After the reaction, THF was removed under reduced pressure and 20ml of toluene was added to the residue directly. The suspension was stirred for 3 h and filtered through a pressure filter funnel to remove insoluble LiCl. The filtrate was concentrated *in vacuo* and the residue was purified by FC (ø = 3 cm, 80 g silica gel, pentane/ether = 10/1) to give a pale yellow solid. To a solution of this solid in 20 ml of ether was added 1.0 g of activated carbon. The mixture was stirred for 3 min at room temperature and filtered off. The filtrate was evaporated *in vacuo* to give 1.85 g (75%) of **2e** as a colourless solid. Mp 174.5-176.0 °C (decomp.). $[\alpha]_D^{RT} = -140.9$ (c = 1.18, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.78-7.36 (m, 33H, arom H), 6.02 (dd, *J* = 8.57, 4.94 Hz, 1H, CH), 5.14 (d, *J* = 8.57 Hz, 1H, CH), 1.67 (s, 3H, CH_3), 0.16 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 143.73, 143.00, 141.23, 138.96, 138.75, 132.83, 132.66, 132.53, 130.85, 130.13, 129.81, 128.79, 128.60, 128.51, 128.16, 127.97, 127.85, 127.61, 127.39, 127.17, 126.50, 126.38, 126.02, 125.83, 111.88, 83.94, 83.74, 83.64, 82.87, 82.80, 82.55, 28.03, 25.29. ^{31}P-NMR ($CDCl_3$, 121 MHz): δ = 158.1. IR: ($CHCl_3$) υ = 3061, 3008, 1600, 1506, 1436, 1383, 1273, 1161, 1126, 1087, 1028, 998, 946, 901, 880, 862, 823. MS (EI), m/z (%) = 772 (M^+, <1), 714(<1), 632 (12), 631 (24), 630 (50), 545 (34), 544 (74), 417(10), 415 (14), 366 (32), 365 (93), 337 (15), 336 (23), 309 (12), 308 (34), 307 (100), 296 (15), 294 (19), 281 (27), 280 (30), 279 (85), 278 (38), 277 (23), 276 (21), 268 (25), 267 (94), 266 (54), 265 (91), 264 (29), 263 (32), 252 (21), 155 (11), 153 (10). $C_{53}H_{41}O_4P$ (HRMS, $[M]^+$) Calcd. 772.2742. Found 772.2662.

(1*R*, 7*R*)-9,9-Dimethyl-4-oxide-2,2,6,6-tetraphenyl-4-thia-3,5,8,10-tetraoxabicyclo[5.3.0]decane (**3**): A solution of 0.84 ml triethylamine (6 mmol) in 10 ml CH_2Cl_2 was added to the solution of 466 mg **1a** (1 mmol) in 10 ml CH_2Cl_2 at -40 °C. After stirring for 30 min at this temperature, a solution of 0.24 ml thionyl chloride (3.3 mmol) in 4 ml CH_2Cl_2 was slowly added, the mixture stirred for a further 3 h, then poured into 50 ml ice-water. The organic layer was separated, and the aqueous layer was extracted twice with 40 ml CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and then evaporated. The residue was recrystallized from pentane/ CH_2Cl_2 to give 410 mg (80%) of **3**. Mp 165-168 °C. $[\alpha]_D^{RT} = -87.6$ (c = 0.69, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.89-7.80 (m, 2H, arom H), 7.70-7.60 (m, 2H, arom H), 7.51-7.24 (m, 16H, arom H), 5.23 (d, *J* = 10.0 Hz, 1H, CH), 5.00 (d, *J* = 10.0 Hz, 1H, CH), 1.48 (s, 3H, CH_3), 0.32 (s, 3H, CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 144.7, 143.0, 140.2, 138.8, 129.2, 129.0, 128.9, 128.8, 128.4, 128.2, 127.9, 127.5, 127.4, 112.5, 86.6, 85.6, 82.5, 81.7, 27.7, 25.0. IR ($CHCl_3$): υ = 3670, 3560, 3100, 3060, 3000, 2940, 2910, 1960, 1900, 1820, 1600, 1580, 1500, 1450, 1390, 1380, 1360, 1320, 1300, 1250, 1170, 1090, 1050, 1030, 980, 950, 910, 870. Anal. Calcd for $C_{31}H_{28}O_5S$: C 72.63, H 5.51. Found: C 72.85, H 5.49.

(4*R*, 5*R*)-5-(Chloro-diphenyl-methyl)-2,2-dimethyl-α,α-diphenyl-1,3-dioxolan-4-methanol (**4a**) and (4*R*, 5*S*)-5-(Azido-diphenyl-methyl)-2,2-dimethyl-α,α-dipheny-1,3-dioxolan-4-methanol (**4b**): A solution of 4.66 g **1a** (10 mmol) in 50 ml THF was cooled to –78 °C and 13 ml BuLi (20 mmol, 1.54 M in hexane) were slowly introduced. The solution was warmed to –30 °C, then cooled again to –78 °C. At this temperature 1.56 ml methanesulfonyl chloride (20 mmol) was added. After 5 h the volatiles were directly evaporated to give crude **4a**. Since **4a** is not stable, the residue was dissolved in 50 ml DMF without further purification. To this solution was added 2.6 g NaN_3 (40 mmol), then the reaction mixture was stirred at 80 °C for 12 h. After cooling to room temperature, the reaction mixture was poured into 300 ml ether, then washed four times with 100 ml water. The organic layer was dried over Na_2SO_4, then evaporated. The residue was purified by FC (ø = 5 cm, 340 g silica gel, pentane/ether = 10:1) to give 3.4 g (70%) of **4b.**

4a: ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.52-7.19 (m, 20H, arom H), 5.36 (d, *J* = 5.0 Hz, 1H, CH), 5.11 (d, *J* = 5.0 Hz, 1H, CH), 1.81 (s, 1H, OH), 1.07 (s, 3H, CH_3), 0.91 (s, 3H, CH_3).

4b: $[\alpha]_D^{RT} = -52.5$ (c = 0.59,$CHCl_3$), ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.51-7.20 (m, 20H, arom H), 4.84 (d, *J* = 8.0 Hz, 1H, CH) 4.59 (d, *J* = 8.0 Hz, 1H, CH), 3.65 (s, 1H, OH), 1.07 (s, 6H, $2CH_3$). ^{13}C-NMR (50MHz, $CDCl_3$): δ = 146.1, 144.1, 141.3, 139.4, 130.0, 128.6, 128.5, 128.4, 128.2, 128.1, 127.8, 127.7, 127.5, 110.3, 82.4, 79.9, 78.0, 73.8, 27.6, 27.3. IR($CHCl_3$): υ = 3390, 3060, 3000, 2120, 1490, 1450, 1370, 1240, 1220, 1170, 1080, 1050, 880.

(4*R*, 5*S*)-5-(Amino-diphenyl-methyl)-2,2-dimethyl-α,α-diphenyl-1,3-dioxolan-4-methanol (**4c**): To a suspension of 0.6 g $LiAlH_4$ (15.8 mmol) in 30 ml THF at 0 °C (ice bath) was added dropwise a solution of 2.68 g **4b** (5.5 mmol) in 30 ml THF. After 12 h stirring at room temperature, 5 ml 1 N NaOH was added carefully, then the mixture was diluted with *ca.* 20 ml ether and *ca.* 20 g Na_2SO_4 was added. The reaction mixture was stirred for further 2 h at room temperature, then filtered through a pad of celite with the aid of ether. The filtrate was dried over K_2CO_3 and evaporated. The residue was purified by FC (ø = 3 cm, 50 g silica gel, pentane/ether = 3:1) to give 2.15 g (85%) of **4c**. Mp 211-212 °C. $[\alpha]_D^{RT} = -59.9$ (c = 1.12, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 8.92 (br s, 1H, OH), 7.76-7.72 (m, 2H, arom H), 7.48-7.16 (m, 18H, arom H), 4.30 (d, *J* = 8.0

Hz, 1H, CH), 4.19 (d, J = 8.0 Hz, 1H, CH), 2.23 (br s, 2H, NH_2), 1.27 (s, 3H, CH_3), 0.90 (s, 3H, CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 149.6, 146.3, 143.9, 140.6, 129.3, 128.1, 128.0, 127.5, 127.4, 127.3, 127.0, 126.9, 126.7, 126.5, 107.8, 81.9, 79.5, 75.9, 62.2, 27.0, 26.3. IR($CHCl_3$): υ = 3670, 3364, 3300, 3060, 3000, 2900, 2830, 1950, 1880, 1800, 1600, 1500, 1450, 1380, 1370, 1350, 1170, 1080, 1060, 1050, 1030, 1010, 970, 960, 920, 900, 880. Anal. Calcd for $C_{31}H_{31}NO_3$: C 79.97, H 6.71, N 3.01. Found: C 79.64, H 6.78, N 3.03.

(4*R*, 5*S*)-2,2-Dimethyl-5-(methylamino-diphenyl-methyl)-α,α-diphenyl-1,3-dioxolan-4-methanol (**4d**): 74 µl Iodomethane (1.2 mmol) was added to the suspension of 466 mg **4c** (1 mmol) and 0.5 g $NaHCO_3$ in 5 ml DMF at room temperature, then stirred 3 days at this temperature. The reaction mixture was poured into 50 ml ether and washed five times with 30 ml water. The organic layer was dried over K_2CO_3 and then evaporated. The residue was purified by FC (ø = 3 cm, 80 g silica gel, pentane/ether = 4:1) to give 317 mg (66%) of **4d.** An analytically pure sample was obtained by recrystallization from pentane/ether. Mp 189-191 °C. $[\alpha]_D^{RT}$ = -63.7 (c = 2.62, CHCl3). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 9.20 (s, 1H, OH), 7.91-7.88 (m, 2H, arom H), 7.50-7.13 (m, 18H, arom H), 4.40 (d, J = 8.6 Hz, 1H, NCH), 4.22 (d, J = 8.6 Hz, 1H, CH), 2.08 (q, J = 6.2 Hz, 1H, NH), 1.85 (d, J = 6.2 Hz, 3H, CH_3), 1.32 (s, 3H, CH_3), 0.82 (s, 3H, CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 147.2, 144.8, 143.8, 141.4, 130.6, 129.5, 128.6, 128.1, 128.0, 127.8, 127.7, 127.5, 127.3, 127.0, 108.1, 83.1, 76.7, 75.7, 67.7, 30.4, 27.6, 26.6. IR ($CHCl_3$): υ = 3060, 3010, 2810, 2640, 1600, 1500, 1450, 1380, 1370, 1340, 1250, 1170, 1080, 1050, 890, 820. Anal. Calcd for $C_{32}H_{33}NO_3$: C 80.14, H 6.94, N 2.92. Found: C 80.04, H 6.95, N 2.92.

(4*R*, 5*S*)-2,2-Dimethyl-5-(dimethylamino-diphenyl-methyl)-α,α-diphenyl-1,3-dioxolan-4-methanol (**4e**): 0.8 ml Iodomethane (13 mmol) was added to the suspension of 466 mg **4c** (1 mmol) and 1 g $NaHCO_3$ in 5 ml DMPU at room temperature, then stirred 3 days at this temperature. The reaction mixture was poured into 50 ml ether and washed five times with 30 ml water. The organic layer was dried over K_2CO_3 then evaporated. The residue was purified by FC (ø = 3 cm, 80 g silica gel, pentane/ether = 10:1-4:1) to give 316 mg (64%) of **4e.** An analytically pure sample was obtained by recrystallization from ethanol. Mp 181-183 °C. $[\alpha]_D^{RT}$ = –23.0 (c = 1.15, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 8.91 (s, 1H, OH), 8.10-8.03 (m, 2H, arom H), 7.40-6.88 (m, 18H, arom H), 4.81 (d, J = 8.7 Hz, 1H, CH), 4.27 (d, J = 8.7 Hz, 1H, CH), 2.31 (s, 3H, NCH_3), 1.55 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 0.52 (s, 3H, CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 146.7, 144.2, 137.7, 135.8, 130.6, 129.2, 128.0, 127.4, 127.2, 126.9, 126.8, 126.4, 126.2, 107.1, 83.4, 75.8, 74.6, 73.1, 40.8, 27.2, 25.5. IR ($CHCl_3$): υ = 3670, 3060, 3010, 2940, 2880, 2800, 2640, 1960, 1600, 1490, 1450, 1410, 1380, 1370, 1350, 1250, 1170, 1010, 1070 1050, 1050, 1000, 995, 920, 890, 870, 810, 640, 600. Anal. Calcd for $C_{33}H_{35}NO_3$: C 80.29, H 7.15, N 2.84. Found: C 79.89, H 7.15, N 2.80.

(4*R*, 5*S*)-5-(Benzylamino-diphenyl-methyl)-2,2-dimethyl-α,α-diphenyl-1,3-dioxolan-4-methanol (**4f**): 0.48 ml Benzyl bromide (4 mmol) was added to the suspension of 466 mg **4c** (1 mmol) and 1 g $NaHCO_3$ in 5 ml DMF at room temperature, then stirred 2 days at 80 °C. After cooling to room temperature, the reaction mixture was poured into 50 ml ether and washed five times with 30 ml water. The organic layer was dried over K_2CO_3, then evaporated. The residue was purified by FC (ø = 3 cm, 80 g silica gel, pentane/ether = 10:1) to give 525 mg (92%) of **4f.** An analytically pure sample was obtained by recrystallization from pentane/ether. Mp 204-206 °C. $[\alpha]_D^{RT}$ = –32.3 (c = 0.74, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 8.79 (s, 1H, OH), 7.82-7.72 (m, 2H, arom H), 7.65-7.55 (m, 2H, arom H), 7.45-7.10 (m, 21H, arom H), 4.43 (d, J = 11.6Hz, 1H, CH), 4.18 (d, J = 11.6Hz, 1H, CH), 3.30-3.06 (m, 2H, CH_2), 1.95 (t, J = 6.5 Hz, 1H, NH), 1.38 (s, 3H, CH_3), 0.84 (s, 3H, CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 146.7, 144.5, 144.2, 140.4, 138.6, 130.9, 129.33, 129.2, 128.5, 128.5, 128.3, 128.0, 127.9, 127.5, 127.4, 127.2, 108.1, 83.4, 78.8, 75.9, 68.3, 47.3, 27.6, 26.6. IR ($CHCl_3$): υ = 3670, 3060, 3010, 2820, 1950, 1600, 1500, 1450, 1380, 1370, 1340, 1250, 1170, 1080, 1060, 1030, 980, 890, 820, 640, 610. Anal. Calcd for $C_{38}H_{37}NO_3$: C 82.13, H 6.71, N 2.56. Found: C 81.85, H 6.43, N 2.56.

(4*R*, 5*R*)-4,5-Bis(chloro-diphenyl-methyl)-2,2-dimethyl-1,3-dioxolane (**5a**): To a solution of 4.66 g **1a** (10 mmol) in 60 ml CH_2Cl_2 was added 2.2 ml thionyl chloride (30 mmol) at room temperature. The resulting solution was then heated under reflux while a solution of 7 ml triethylamine (42 mmol) in 60 ml CH_2Cl_2 was introduced over a period of 3 h. The reaction solution was poured into chilled 200 ml sat. $NaHCO_3$, then stirred vigorously for 5 h. The organic layer was then separated and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by FC (ø = 3 cm, 100 g Basic aluminium oxide, pentane/ether = 10:1) to give 3.7 g (73%) of **5a.** An analytically pure sample was obtained by recrystallization from pentane/CH_2Cl_2. Mp 165-170 °C. $[\alpha]_D^{RT}$ = –11.2 (c = 0.51, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.51-7.12 (m, 20H, aromH.), 5.45 (s, 2H, 2CH), 0.98 (s, 6H, $2CH_3$). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 144.7, 143.5, 130.6, 129.2, 129.0, 128.9, 128.8, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 113.5, 84.1, 77.9, 28.7. IR ($CHCl_3$): υ = 3590, 3090, 3060, 3010, 2940, 1950, 1900, 1810, 1600, 1490, 1450, 1380, 1370, 1320, 1300, 1180,

1080, 1060, 1040, 1020, 1000, 960, 930, 900, 870, 840, 650, 630. Anal. Calcd for $C_{31}H_{28}O_2Cl_2$: C 73.96, H 5.61. Found: C 73.82, H 5.85.

(4*S*, 5*S*)-4,5-Bis(azido-diphenyl-methyl)-2,2-dimethyl-1,3-dioxolane (**5b**): To a solution of 9.1 g **5a** (17.7 mmol) in 50 ml DMF was added 4.6 g NaN_3. The reaction mixture was stirred at 80 °C for 72 h. After cooling to room temperature, the reaction mixture was poured into 300 ml water, then extracted three times with 150 ml ether. The combined organic layers were washed three times with 100 ml water, then dried over Na_2SO_4. After evaporation, the residue was crystallized from ethanol, then dried under reduced pressure to give 7.4 g of **5b** (79%). Mp 127-129 °C. $[\alpha]_D^{RT} = -13.1$ (c = 0.53, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.38–7.25 (m, 20H, arom H), 4.92 (s, 2H, 2CH), 1.12 (s, 6H, $2CH_3$). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 142.2, 140.5, 130.0, 129.0, 128.5, 128.2, 128.0, 110.7, 80.8, 73.4, 27.6. IR($CHCl_3$): υ = 3060, 3010, 2930, 2110, 1490, 1450, 1380, 1370, 1260, 1170, 1070, 1020, 980, 940, 910, 880. Anal. Calcd for $C_{31}H_{28}N_6O_2$: C 72.09, H 5.43, N 16.26. Found: C 72.25, H 5.70, N 15.99.

(4*S*, 5*S*)-2,2-Dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolan-4,5-dimethylamine (**5c**): To a cooled suspension of 2.4 g $LiAlH_4$ (63 mmol) in 60 ml THF was added, dropwise, to a solution of 5.6 g **5b** (10.6 mmol) in 60 ml THF. After 4 h stirring at 0 °C, 5 ml 1 N NaOH was added carefully. The mixture was diluted with *ca.* 20 ml ether and *ca.* 20 g Na_2SO_4 was added. After stirring for a further 2 h at room temperature, the mixture was filtered through a pad of celite with the aid of ether. The filtrate was dried over K_2CO_3 and evaporated. The residue was crystallized from hot hexane to give 3.5 g of **5c** (71%). Mp 200-201 °C. $[\alpha]_D^{RT}$ = –42.96 (c = 0.68, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.60-7.50 (m, 4H, arom H), 7.40-7.30 (m, 6H, arom H), 7.28-7.10 (m, 10H, arom H), 4.25 (s, 2H, 2CH), 2.50 (br s, 4H, $2NH_2$), 1.11 (s, 6H, $2CH_3$). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 150.3, 144.2, 129.7, 128.3, 127.9, 127.6, 127.5, 127.3, 126.8, 107.8, 82.1, 62.8, 27.4. IR ($CHCl_3$): υ = 3360, 3150, 3090, 3060, 3010, 2990, 2940, 1950, 1890, 1820, 1600, 1500, 1450, 1380, 1370, 1350, 1170, 1070, 1030, 1000, 950, 920, 890, 860, 660. Anal. Calcd for $C_{31}H_{32}N_2O_2$: C 80.14, H 6.94, N 6.03. Found: C 80.33, H 6.97, N 5.92.

(4*S*, 5*S*)-2,2,*N*,*N*′-Tetramethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolan-4,5-dimethylamine (**5d**) and (4*S*, 5*S*)-2,2,*N*,*N*,*N*′-Pentamethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolan-4,5-dimethylamine (**5e**): 130 µl Iodomethane (2.1 mmol) was added to the suspension of 466 mg **5c** (1 mmol) and 1 g $NaHCO_3$ in 5 ml DMPU at room temperature, then stirred for 24 h at this temperature. The reaction mixture was poured into 50 ml ether and washed five times with 30 ml water. The organic layer was dried over K_2CO_3, then evaporated. The residue was purified by FC (ø = 3 cm, 80 g silica gel, pentane/ether = 4:1-1:1) to give 218 mg (44%) of **5d** and 168 mg (33%) of **5e**. To obtain analytically pure samples of **5d** and **5e**, they were recrystallized from ethanol.

5d: Mp 201-203 °C. $[\alpha]_D^{RT} = -49.2$ (c = 0.52, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.60-7.55 (m, 4H, arom H), 7.37-7.03 (m, 16H, arom H), 4.12 (s, 2H, 2CH), 3.15 (br s, 2H, 2NH), 1.98 (s, 6H, $2CH_3N$), 0.99 (s, 6H, $2CH_3$). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 144.5, 141.8, 130.8, 129.8, 127.6, 127.3, 126.6, 107.1, 80.3, 67.7, 30.9, 27.2. IR ($CHCl_3$): 3230, 3090, 3060, 3010, 2990, 2940, 2800, 1600, 1490, 1450, 1380, 1370, 1340, 1170, 1100, 1080, 1020, 1000, 880, 830, 640. Anal. Calcd for $C_{33}H_{38}N_2O_2$: C 80.45, H 7.37, N 5.69. Found: C 80.02, H 7.33, N 5.56.

5e: Mp 161-163 °C. $[\alpha]_D^{RT} = -39.5$ (c = 0.62, $CHCl_3$). ^{1}H-NMR (200 MHz, (D_6)-DMSO at 100 °C): δ = 7.73-7.62 (m, 2H, arom H), 7.59-7.48 (m, 2H, arom H), 7.48-7.00 (m, 16H, arom H), 4.52 (d, *J* = 8.0 Hz, 1H, CH), 4.45 (d, *J* = 8.0 Hz, 1H, CH), 4.09 (br q, *J* = 6.0 Hz, 1H, NH), 2.08 (d, *J* = 6.0 Hz, 3H, CH_3N), 2.00 (s, 6H, $2CH_3N$), 0.95 (s, 3H, CH_3), 0.55 (s, 3H, CH_3). ^{13}C-NMR (50 MHz, (D_6)-DMSO at 100 °C): δ = 144.5, 141.8, 138.8, 136.7, 133.2, 130.7, 128.8, 129.3, 127.3, 127.1, 126.9, 126.5, 126.4, 126.2, 106.3, 82.8, 76.8, 74.2, 67.2, 41.3, 30.7, 27.1, 26.5. IR ($CHCl_3$): υ = 3250, 3090, 3060, 3010, 2940, 2880, 2840, 2800, 1600, 1490, 1440, 1380, 1370, 1340, 1170, 1100, 1070, 1030, 1020, 1010, 890, 870, 640. Anal. Calcd for $C_{34}H_{38}N_2O_2$: C 80.60, H 7.56, N 5.53. Found: C 80.32, H 7.69, N 5.44.

(4*S*, 5*S*)-2,2,*N*,*N*,*N*′,*N*′-Hexamethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolan-4,5-dimethylamine (**5f**): 1.2 ml Iodomethane (20 mmol) was added to the suspension of 464 mg **5c** (1 mmol) and 1 g $NaHCO_3$ in 5 ml DMPU at room temperature, then stirred for 3 days at this temperature. The reaction mixture was poured into 50 ml ether and washed five times with 30 ml water. The organic layer was dried over K_2CO_3 then evaporated. The residue was purified by FC (ø = 3 cm, 80 g silica gel, pentane/ether = 20:1) to give 284 mg (55%) of **5f**. Mp 239 °C (decomp.). $[\alpha]_D^{RT} = -95.4$ (c = 0.81, $CHCl_3$). ^{1}H-NMR (200 MHz, (D_6)-DMSO at 100 °C): δ = 7.72-6.99 (m, 20H, arom H), 5.43 (s, 2H, CH), 2.08 (s, 12H, $4CH_3N$), 0.19 (s, 6H, $2CH_3$). ^{13}C-NMR (50 MHz, (D_6)-DMSO at 100°C): δ = 139.6, 138.2, 132.7, 132.5, 129.7, 127.4, 127.2, 126.7, 126.6, 126.3, 108.8, 78.8, 75.4, 40.7, 27.8. IR ($CHCl_3$): υ = 3090, 3060, 3010, 2940, 2870, 2830, 2790, 1960, 1600, 1500, 1440, 1410, 1380, 1370, 1320, 1170, 1060, 1030, 1010, 940, 920, 890, 860, 660, 640. Anal. Calcd for $C_{35}H_{40}N_2O_2$: C 80.73, H 7.74, N 5.38. Found: C 80.63, H 7.70, N 5.35.

(4*S*, 5*S*)-*N*,*N*'-[2,2-Dimethyl-1,3-dioxolan-4,5-diyl-bis(diphenylmethylene)]bis(trifluoroacetamide) (**5g**): To a solution of 9.28 g **5c** (20 mmol) in CH_2Cl_2 was added 9.6 ml pyridine (120 mmol), then 480 mg DMAP (4 mmol). The solution was cooled to 0 °C (ice bath) and then 8 ml TFAA (60 mmol) was added. After 12 h stirring at room temperature, the reaction mixture was directly evaporated. The residue was dissolved in 400 ml ether and washed with 400 ml 1 N HCl, sat. $NaHCO_3$, then water. The organic layer was dried over Na_2SO_4, evaporated, and the residue was purified by FC (ø = 8 cm, 650 g silica gel, pentane/ether = 20:1-10:1-4:1) giving 11.02 g (84%) of **5g**. An analytically pure sample was obtained by recrystallization from ethanol (clathrate with ethanol was obtained), followed by repeated azeotropic distillation with toluene (to remove ethanol) and drying at 80 °C/0.5 Torr. Mp 104-107 °C. $[\alpha]_D^{RT} = -26.13$ (c = 0.93, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.40 (s, 12H, arom H), 7.32-7.14 (m, 10H, arom H and 2NH), 5.05 (s, 2H, 2CH), 1.08 (s, 6H, $2CH_3$). ^{13}C-NMR (50MHz, $CDCl_3$): δ = 157.3 (q, *J* = 40 Hz, carbonyl), 140.0, 139.0, 128.7, 128.5, 128.3, 128.2, 115.8 (q, *J* = 280 Hz,CF_3), 108.0, 81.1, 67.7, 26.9. IR($CHCl_3$): υ = 3410, 3310, 3060, 3010, 1730, 1530, 1500, 1450, 1380, 1390, 1330, 1170, 1080, 1050, 1000, 990, 900, 840, 640. Anal. Calcd for $C_{35}H_{30}N_2O_4F_6$: C 64.02, H 4.61, N4.27. Found: C 63.72, H 4.69, N 4.30.

(4*R*, 5*R*)-2,2-Dimethyl-α,α,α',α'-tetraphenyl-1,3-dioxolan-4,5-dimethylthiocyanate (**6**): To a solution of 1.03 g dichloride **5a** (2.01 mmol) was added 1 g KSCN (10.3 mmol) in 40 ml DMF. This reaction mixture was stirred at 80 °C for 12 h. After cooling to room temperature, the reaction mixture was poured into 300 ml ether, then washed three times with 100 ml water. The organic layer was dried over Na_2SO_4, then evaporated. The residue was recrystallized from CH_2Cl_2 /pentane to give 0.98 g (55%) of **6**. Mp 196-197 °C. $[\alpha]_D^{RT} = +12.6$ (c = 0.27, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.42–7.15 (m, 20H, arom H), 5.00 (s, 2H, 2CH), 1.20 (s, 6H, $2CH_3$). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 142.3, 141.2, 129.0, 128.8, 128.6, 128.4, 128.2, 127.06, 112.2, 81.6, 74.2, 28.1. IR($CHCl_3$): υ = 3060, 3010, 2940, 2030, 1600, 1490, 1450, 1380, 1370, 1160, 1090, 880. Anal. Calcd for $C_{33}H_{28}S_2N_2O_2$: C 72.23, H 5.14, N 5.11. Found: C 72.41, H 5.08, N 4.84.

(1*S*, 5*S*)-3,3-Dimethyl-6, 6, 8, 8-tetraphenyl-2,4-dioxa-7-azabicyclo[3.3.0]octane (**7**): To a solution of 2.15 g **4c** (4.6 mmol) in 35 ml pyridine was added 3.5 g DMAP (28.6 mmol) followed by 2.3 g *p*-toluenesulfonyl chloride (12 mmol). The reaction mixture was stirred at 80 °C for 12 h, cooled to room temperature then poured into 200 ml ether. The mixture was washed twice with 200 ml 1 N HCl, then with sat. $NaHCO_3$. The organic layer was dried over Na_2SO_4, then evaporated. Purification of the residue by FC (ø = 5 cm, 270 g silica gel, pentane/ether = 40:1-30:1) yielded 1.03 g (50%) of **7**. Mp 140-141 °C. $[\alpha]_D^{RT} = -222.6$ (c = 0.5, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.50-7.09 (m, 20H, arom H), 4.71 (s, 2H, 2CH), 3.54 (brs, 1H, NH), 1.35(s, 6H, $2CH_3$). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 147.9, 144.0, 128.9, 128.0, 127.7, 127.2, 126.7, 126.6, 121.5, 85.3, 65.3, 27.2. IR($CHCl_3$): υ = 3400, 3090, 3060, 2990, 2930, 1950, 1880, 1810, 1600, 1580, 1490, 1450, 1380, 1370, 1180, 1150, 1110, 1080, 1060, 1030, 970, 940, 910, 830, 650, 620. Anal. Calcd for $C_{31}H_{29}NO_2$: C 83.18, H 6.54, N 3.13. Found: C 82.78, H 6.58, N 3.10.

(1*R*, 5*R*)- 3,3-Dimethyl-6, 6, 8, 8-tetraphenyl-2,4-dioxa-7-thiabicyclo[3.3.0]octane(**8**): A solution of 2.56 g **5a** (5 mmol) in 50 ml DMF, was treated with 1.5 g NaSH-H_2O (20.2 mmol). The solution was stirred at 80 °C for 12 h. After cooling to room temperature, the reaction mixture was poured into 200 ml ether, then washed twice with 200 ml water. The organic layer was dried over Na_2SO_4, then evaporated. The residue was purified by FC (ø = 5 cm, 270 g silica gel, pentane/ether = 40:1), affording 0.98 g (39%) of **8**. An analytically pure sample was obtained by recrystallization from *t*-butyl methyl ether. Mp 179 °C. $[\alpha]_D^{RT} = -428.3$ (c = 1, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.65-7.55 (m, 4H, arom H), 7.38-7.15 (m, 16H, arom H), 5.00 (s, 2H, 2CH), 1.21(s, 6H, $2CH_3$). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 146.3, 141.1, 130.6, 128.8, 127.6, 127.3, 127.2, 127.1, 119.8, 83.0, 62.0, 27.3. IR($CHCl_3$): υ = 3670, 3090, 3060, 3010, 2990, 2930, 1950, 1900, 1810, 1600, 1580, 1550, 1450, 1380, 1320, 1170, 1130, 1080, 1040, 1030, 1000, 970, 930, 910, 900, 820, 650, 640, 630. Anal. Calcd for $C_{31}H_{28}SO_2$: C 80.14, H 6.08, S 6.89. Found: C 80.07, H 6.08, S 6.85.

X-Ray analysis of **7**: Monoclinic space group $P2_1$, Z = 4, cell dimensions *a* = 8.930(3), *b* = 33.817(7), *c* = 9.039(2) Å, β = 119.04(2). Intensities were measured at -100 °C. with an *Enraf Nonius CAD4* diffractometer (graphite monochromator, Mo*Kα*, λ = 0.7107 Å). Of the 5290 independent reflections (θ < 27°), 3160 with *I* > 3 σ(I) were used in the refinement. The structure was solved by direct methods with SHELXS86[47] and refined by full-matrix least squares analysis (SHELXL92[48]). Non hydrogen atoms were refined anisotropically. The positions of the H-atoms were calculated and included in the final least-squares cycles with the exception of the hydrogens on the disordered carbon atoms. The weighting scheme used was $\sigma(F)^{-2}$. The refinement converged at *R* = 0.038. Atomic positional and anisotropic displacement parameters for the non-H atoms are deposited with the Cambridge Crystallographic Data Centre, Cambridge, England.

References.

1. Part of the projected Ph. D. Thesis of M. H., ETH-Zürich. We thank for a Bundesstipendium granted to M. H. by the Eidgenössische Stipendienkommission für Ausländische Studierende.
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3. Seebach, D. *Angew. Chem.* **1990**, *102*, 1363-1409; *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1320-1367.
4. Noyori, R.; Kitamura, M. in "*Modern Synthetic Methods 1989*"", Ed. Scheffold, R. Springer-Verlag, Berlin, Heidelberg **1989**, Vol. 5, 115-198.
5. Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551-5553.
6. Kagan, H. B. in "*Comprehensive Organometallic Chemistry*", Eds. Wilkinson, G.; Stone, F. G. A.; Abel, E. W. Pergmon Press **1982**, *8*, 463-498.
7. Pfaltz, A. in "*Modern Synthetic Methods 1989*", reference[4], pg. 199-248.
8. Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974-5976.
9. Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K. S.; Kwong, H. L.; Morikawa, K.; Wang, Z. M.; Xu, D.; Zhang, X-L. *J. Org. Chem.* **1992**, *57*, 2768-2771, and earlier papers of this group cited therein.
10. Otsuka, S.; Tani, K. in "*Asymmetric Synthesis*", Ed. Morrison, J. D. Academic Press **1985**, Vol. 5, 171-191.
11. Crout, D. H. G.; Christen, M. in "*Modern Synthetic Methods 1989*", reference[4], pg. 1-114.
12. This is not true of malonates: $R^1R^2C(CO_2R^3)_2$.
13. Noyori, R.; Kitamura, M. *Angew. Chem.* **1991**, *103*, 34-55; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 46-67.
14. Schmidt, B.; Seebach, D. *Angew. Chem.* **1991**, *103*, 100-101; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 99-101; Schmidt, B.; Seebach, D. *Angew. Chem.* **1991**, *103*, 1383-1385; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1321-1323; Seebach, D.; Behrendt, L.; Felix, D. *Angew. Chem.* **1991**, *103*, 991-992; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1008-1009; von dem Bussche-Hünnefeld, L.; Seebach, D. *Tetrahedron* **1992**, *48*, 5719-5730.
15. Evans, D. A.; Woerpel, K. A.; Hinman, M. N.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726-728.
16. For a review see: Narasaka, K. *Synthesis* **1991**, 1-11; Kagan, H. B.; Rinant, O. *Chem. Rev.* **1992**, *92*, 1007-1019.
17. Effenberger, F.; Gutterer, B.; Ziegler, T.; Eckardt, E.; Aichholz, R. *Liebigs Ann. Chem.* **1991**, 47-54.
18. Blaser, H.-U. *Chem. Rev.* **1992**, *92*, 935-952.
19. Seebach, D.; Kalinowski, H.-O. *Nachr. Chem. Techn.* **1976**, *24*, 415-418.
20. Seebach, D.; Beck, A. K.; Schiess, M.; Widler, L.; Wonnacott, A. *Pure & Appl. Chem.* **1983**, *55*, 1807-1822.
21. Seebach, D.; Weidmann, B.; Widler, L. "*Modern Synthetic Methods 1983*", Ed. Scheffold, R. Salle & Sauerländer (Aarau, Switzerland) and J. Wiley and Sons (New York, USA), **1983**, Vol. 3, 217-353.
22. Seebach, D.; Beck, A. K.; Imwinkelried, R.; Roggo, S.; Wonnacott, A. *Helv. Chim. Acta* **1987**, *70*, 954 - 974.
23. Beck, A. K.; Bastani, B.; Plattner, D. A.; Petter, W.; Seebach, D.; Braunschweiger, H.; Gysi, P.; La Vecchia, L. *Chimia* **1991**, *45*, 238-244.

24. Duthaler, R. O.; Hafner, A. *Chem. Rev.* **1992**, *92*, 807-832.
25. Minamikawa, H.; Hayakawa, S.; Yamada, T.; Iwasawa, N.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 4379-4389.
26. There are also interesting applications of TADDOLs in solid-state reactions, see Toda´s work: Toda, F.; Tanaka, K. *Tetrahedon Lett.* **1988**, *29*, 4299-4302; Toda, F.; Mori, K. *J. Chem. Soc., Chem. Commun.* **1989**, 1245-1246.
27. Narasaka, K.; Tanaka, H.; Kanai, F. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 387-391; Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340-5345; Iwasawa, N.; Sugimori, J.; Kawase, Y.; Narasaka, K. *Chem. Lett.* **1989**, 1947-1950; Narasaka, K.; Inoue, M.; Okada, N. *Chem. Lett.* **1986**, 1109-1112.
28. Corey, E. J.; Matsumura, Y. *Tetrahedron Lett.* **1991**, *32*, 6289-6292.
29. Hayashi, Y.; Narasaka, K. *Chem. Lett.* **1989**, 793-796; Hayashi, Y.; Narasaka, K. *Chem. Lett.* **1990**, 1295-1298; Ichikawa, Y.; Narita, A.; Shiozawa, A.; Hayashi, Y.; Narasaka, K. *J. Chem. Soc., Chem. Commun.* **1989**, 1919-1921; Hayashi, Y.; Niihata, S.; Narasaka, K. *Chem. Lett.* **1990**, 2091-2094.
30. Narasaka, K.; Hayashi, Y.; Shimada, S. *Chem. Lett.* **1988**, 1609-1612.
31. Mikami, K.; Terada, T.; Nakai, T. *J. Am. Chem. Soc.* **1990**, *112*, 3949-3954.
32. Engler, Th. A.; Letavic, M. A.; Reddy, J. P. *J. Am. Chem. Soc.* **1991**, *113*, 5068-5070.
33. Weber, B.; Seebach, D. *Angew. Chem.* **1992**, *104*, 96-97; *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 84-86.
34. Seebach, D.; Plattner, D. A.; Beck, A. K.; Wang, Y.; Hunziker, D.; Petter, W. *Helv. Chim. Acta* **1992**, *75*, in print.
35. See the examples and the corresponding references in the review article: ref. 18.
36. Reaction of **1a** with Lawesson's reagent produces in *ca.* 30% yield a monothiol (**4**, X = OH, Y = SH) from which a number of derivatives [acetal with CH_2O, ketal with $(CH_3)_2CO$, methylthioether, sulfoxide and sulfone] were prepared: Lucchi, O. D.; Maglioli, P.; Delogu, G.; Valle, G. *Synlett* **1991**, 841-844.
37. a) Unsuccessful attempts to prepare the cyclic sulfite **3** and the formation of the chloro alcohol **4a** are mentioned in: Rebiere, F.; Samuel, O.; Ricard, L.; Kagan, H. B. *J. Org. Chem.* **1991**, *56*, 5991-5999. b) When solutions of **4a** are passed through SiO_2 columns or analysed by TLC, formation of the TADDOL **1a** can be detected.
38. Experiments to use **3** for the preparation of enantiomerically pure sulfoxides following Kagan´s method[37a] were unsuccessful: in a 1:1 reaction of **3** with Grignard reagent, the symmetrical products R_2SO were formed. Thus, it looks like the intermidiate sulfinates are more reactive than the original cyclic sulfite **3**.
39. Of course, this experiment was carried out in order to prepare the bis-mesylate of **1a**. May be the mono-mesylate is reacting much faster with Cl^- than the second mesylation occurs.
40. Mukhopadhyay, T.; Seebach, D. *Helv. Chim. Acta* **1982**, *65*, 385-391; Seebach, D. *Chem. Britain* **1985**, *21*, 632-633.
41. The use of HMPA as a solvent and $NaHCO_3$ was recently recommended for the preparation of cyclic amines from anilines and bifunctional alkylating reagents of type $X\text{-}(CH_2)_n\text{-}X$: Juaristi, E.; Madrigal, D. *Tetrahedron* **1989**, *45*, 629-636.
42. Johnson, C. K. *Program ORTEP, Oak Ridge National Laboratory Report ORNL* **1965**, 3794.
43. See the structures described or referred to in ref.34.

44. See table 9 in: Seebach, D. *Angew. Chem.* **1988**, *100*, 1685-1715; *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1624-1654.
45. Cox, P. J.; Simpkins, N. S. *Tetrahedron : Asymmetry* **1991**, *2*, 1-26.
46. Estermann, H.; Seebach, D. *Helv. Chem. Acta* **1988**, *71*, 1824-1839; Davies, S. G.; Ichihara, O. *Tetrahedraon : Asymmetry* **1991**, *2*, 183-186; Juaristi, E.; Escalante, J.; Lamatsch, B.; Seebach, D. *J. Org. Chem.* **1992**, *57*, 2396-2398.
47. Sheldrick, G. M.; Krüger, C.; Goddard, R. in *"Crystallographic Computing 3"*, Oxford University Press, **1985**, 175-189.
48. Sheldrick, G. M. SHELXL92. (β-version) Program for Crystal Structure Refinement, University of Göttingen, Germany.