Synthesis and Application of Chiral Phosphorus Ligands Derived from TADDOL for the Asymmetric Conjugate Addition of Diethyl Zinc to Enones

Alexandre Alexakis,*[a] Jonathan Burton,[a] Johann Vastra,[a] Cyril Benhaim,[a] Xavier Fournioux,[a] Alexandra van den Heuvel,[a] Jean-Marc Levêque,[a] Frédérique Mazé,[a] and Stephane Rosset[a]

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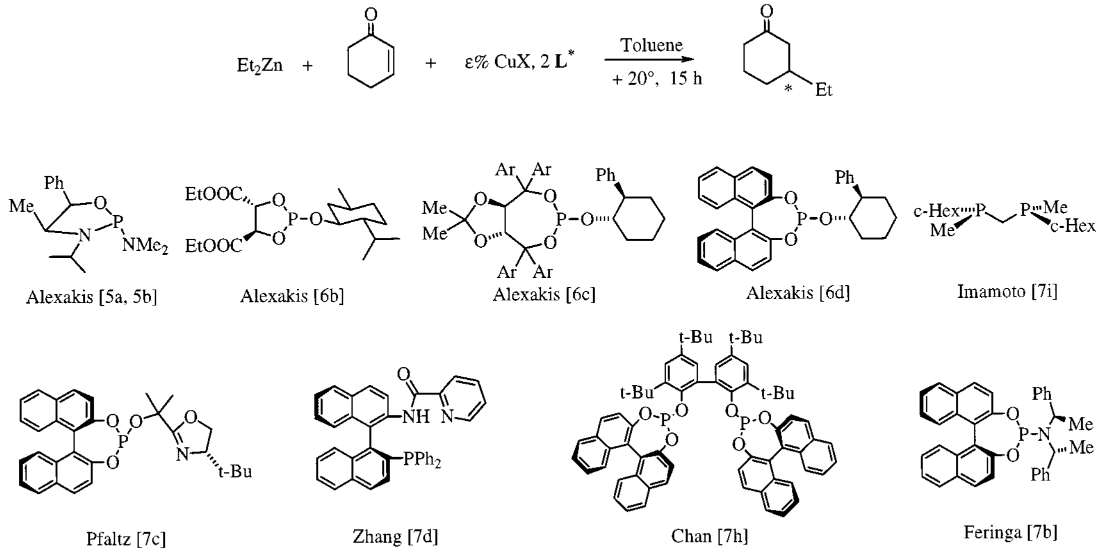
Asymmetric conjugate addition of diethylzinc to cyclohexen-2-one, chalcone, and benzalacetone has been found to occur with 0.5% copper(II) triflate *and* 1% chiral phosphite. Cyclic phosphites derived from TADDOL gave excellent to moderate enantiomeric excesses. The nature of the exocyclic substituent of the dioxaphospholane ring is important, but the chiral induction is imposed by the TADDOL framework. Syntheses of all the TADDOL ligands are described.

Introduction

Carbon−carbon bond formation through conjugate addition is best achieved by the use of organocopper reagents.[1] The asymmetric version of this reaction is an actively studied topic.[2] Although there have been several successful examples involving the use of stoichiometric chiral auxiliaries on the enone partner, much effort is currently being directed towards the development of catalytic processes based on the modification of the organometallic partner,[3] particularly with chiral external ligands.[4] In this context, chiral trivalent phosphorus ligands have emerged as being among the most efficient reagents.[5] In the catalytic reactions, the primary organometallic is either a Grignard or a dialkylzinc reagent. This latter possibility, introduced by us in 1993,[5b] has found increasing popularity and several chiral phosphorus ligands have since been developed both by ourselves[6] and by other authors.[7] Some of the most efficient are shown in Scheme 1.

The copper catalyst CuX is extremely important in these reactions. Although in our first report[5b] we used CuI as the copper source, we later found $Cu(OTf)_2$ to be a superior catalyst.[8] Furthermore, we showed that a trivalent phosphorus ligand has a strong accelerating effect. Hence, the possibility of a *ligand-accelerated asymmetric catalysis* arises when a chiral trivalent phosphorus ligand is employed. As little as 0.5% of copper salt and 1% of chiral ligand are sufficient to furnish a high yield of the conjugate adduct.[8] The reaction is fast in poorly or non-coordinating solvents such as toluene, dichloromethane, or even diethyl ether.



Scheme 1. Ligands used for asymmetric conjugate additions

As far as the chiral trivalent phosphorus ligand is concerned, we first used a ligand that had proved very success-

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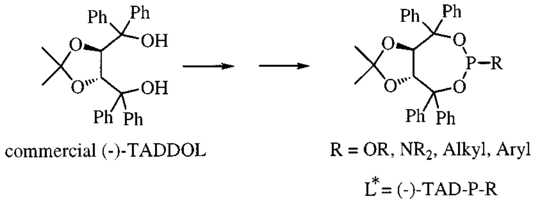
[a] Department of Organic Chemistry, University of Geneva,
30 quai Ernest Ansermet, 1211 Genève 4, Switzerland
Fax: (internat.) + 41-22/328-7396
E-mail: alexandre.alexakis@chiorg.unige.ch

ful with stoichiometric lithium diorganocuprates.[5a,5b] During our work on extending the class of chiral phosphorus ligands to chiral phosphanes[6a] and to C_2-symmetrical phosphites derived from tartrates,[6b] several other reports have described excellent results obtained with aminophosphinites and phosphites derived from binaphthol.[7a−7c,7e,7h,7l,7m] For our part, we became interested in another class of C_2-symmetrical diols, namely the TADDOLS (2,3-*O*-isopropylidene-1,1,4,4-tetraphenylthreitol).[5c,5d,7f] These chiral auxiliaries were first used by Seebach's group with several impressive applications in asymmetric synthesis.[9] We report herein our full results in this field of investigation.[10] TADDOL is easily prepared from tartaric acid esters, is ten times cheaper than chiral binaphthol,[11] and its trivalent phosphorus derivatives are rather stable towards moisture and oxidation. The preparation of these trivalent phosphorus derivatives is described in the last part of the article.

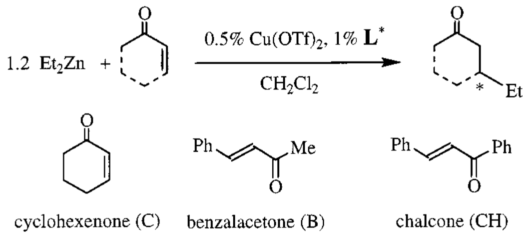
Results and Discussion

All the ligands used in this study have the same basic skeleton (Scheme 2). We have varied the exocyclic substituent from alcohols, to amines and carbon derivatives. Several structural variations have been tested in order to gain insight into the relative importance of the TADDOL part and of the steric influence or coordinative ability of the exocyclic part of the ligand.



Scheme 2. TADDOL ligands

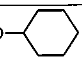
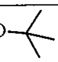
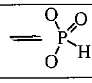
All the experiments were performed under the same conditions. First, the complex between $Cu(OTf)_2$ (0.025 mmol) and the chiral ligand (0.05 mmol) was formed (in a 1:2 ratio) by stirring the mixture at room temperature for 30 min, Et_2Zn (7 mmol) was then added at −20 °C, followed finally by the enone (5 mmol). Usually, the reactions were performed at −20 °C and were allowed to proceed for the times indicated in the tables. Most often, the reactions were run in CH_2Cl_2 solution, in which slightly higher enantiomeric excesses are generally achieved than in toluene. However, with certain classes of ligands, the best *ee* values were obtained only in toluene. Typically, three enones were tested: cyclohexenone as a representative of cyclic *s-trans* enones, benzalacetone as a representative of acyclic *s-cis* enones, and chalcone, the most extensively tested substrate in the literature, albeit a very atypical one (Scheme 3).



Scheme 3. Enones used in the present study

The results with simple achiral alcohol derivatives in the exocyclic position are shown in Table 1. With these ligands, the chirality is imposed solely by the TADDOL framework. As regards the cyclic enone, cyclohexenone, a comparison of Entries 1 and 2 or 3 shows that a bulky alcohol slightly increases the enantioselectivity. A phenyloxy group gave no significant result (Entry 4). Ligands **1** and **4** were already known to give very low asymmetric inductions in Rh-catalyzed hydroformylation reactions.[12] In all cases, the absolute stereochemistry of the conjugate adduct proved to be the same. With benzalacetone, an acyclic enone, all these ligands led only to poor *ee* values. The last Entry (5) refers to an attempt to use the diphosphite, which is in tautomeric equilibrium with the P^V form. The results are similarly disappointing. Thus, it is clear that the effect of the TADDOL moiety as the sole source of chirality is insufficient to produce high levels of asymmetric induction with both cyclic and acyclic enones.

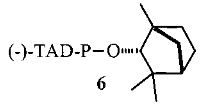
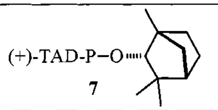
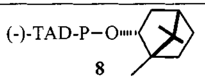
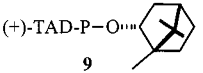
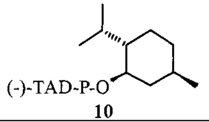
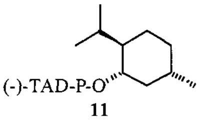
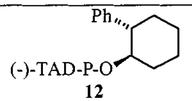
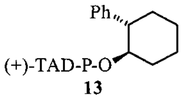
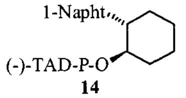
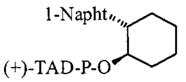
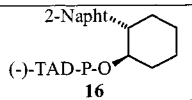
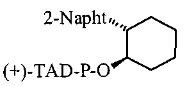
Table 1. TADDOL phosphites with an achiral exocyclic alcohol derivative

Entry	Ligand	Enone	Conditions	Yield[a] %	ee[b]	Abs. Conf.
1a	(-)-TAD-P−O-CH₃ **1**	C	-20° to -10°, 3h	93	4	S
1b		B	-20° to -10°, 5h	80	3	R
2a	(-)-TAD-P−O–  **2**	C	-20°, 1 h	86	18	S
3a	(-)-TAD-P−O–  **3**	C	-15°, 2 h	86	16	S
3b		B	-10°, 9 h	<20	4	R
4a	(-)-TAD-P−O-Ph **4**	C	0° to r.t. 1 h	97	8	S
4b		B	-20° to 0°, 2 h	97	5	R
5a	(-)-TAD-P−O-H  **5**	C	-20°, 1.5 h	71	17	S
5b		B	-20° to 0°, 6 h	86	3	R

[a] Yield of isolated adduct. − [b] *ee* determined by G.C. with chiral capillary column (Lipodex E-0.2 μm, 50 m, 0.25 mm).

A more complex ligand may be prepared by combining (−)-TADDOL with a chiral exocyclic alcohol (Table 2), thereby introducing a second source of chiral information. Hence, the possibility of matched and mismatched combinations arises. Both have been tested, with the two enantiomeric alcohols, or, where the chiral alcohol was only available in a single enantiomeric form, we replaced (−)-TADDOL by its enantiomer (+)-TADDOL. Thus, for cyclohexenone, the ligands prepared with (+)-fenchol (Entries 6 and 7) and (−)-borneol (Entries 8 and 9) gave similar or slightly better results than the simpler ligand with just cyclohexanol (**2**)

Table 2. TADDOL phosphites with a chiral non-functionalized exocyclic alcohol derivative

Entry	Ligand	Enone	Conditions	Yield^a %	ee^b	Abs. Conf.
6a	 **6**	C	-30°, 4.5 h	81	34	S
6b		B	-10° to r.t. 16 h	56	10	R
7a	 **7**	C	-30°, 4 h	90	28	R
7b		B	-10° to r.t. 16 h	40	13	R
8a	 **8**	C	-30° to r.t. 16 h	86	11	S
8b		B	-10° to r.t. 16 h	41	6	R
9a	 **9**	C	-30°, 4 h	98	32	R
9b		B	-10° to r.t. 16 h	15	-	-
10a	 **10**	C	-20° to 10°, 1 h	95	5	S
10b		CH	-20° to -10°, 2h	64	0	-
10c		B	-20° to -10°, 7h	<20	20	R
11a	 **11**	C	-20° to 10°, 1 h	95	50	S
11b		C	-20°, 1 h	90^c	40^c	S
11c		C	-20°, 1 h	97^d	54^d	S
11d		CH	-20° to 10°, 3 h	51	21	R
11e		B	-10°, 6 h	<20	0	-
12a	 **12**	C	-30° to r.t. 16 h	82	0	-
12b		B	-10° to r.t. 16 h	27	0	-
13a	 **13**	C	-30°, 3 h	92	60	R
13		C	-30°, 1h	95^c	96^c	R
13c		C	-30°, 1h	98^e	88^e	R
13d		C	-30°, 1h	94^f	80^f	R
13^e		CH	-20° to -10°, 3h	96^c	50^c	S
13f		B	-10° to r.t. 16 h	20	0	-
13g		B	-10° to 0°, 12h	92^c	35^c	S
14a	 **14**	C	-30°, 4 h	40	0	R
14b		C	-30°, 2 h	90^c	14^c	R
14c		CH	-20° to -10°, 3h	90c	17c	R
14d		B	-30° to r.t. 16 h	15	0	-
14e		B	-15°, 1 h	88c	17c	R
15a	 **15**	C	-30°, 4 h	50	8	R
15b		C	-30°, 1 h	98c	82c	R
15c		CH	-20° to -10°, 3h	99c	30c	S
15d		B	-30° to r.t. 16 h	5	0	-
15e		B	-15°, 1 h	89c	15c	S
16a	 **16**	C	-30°, 1 h	98c	20c	S
16b		B	-30°, 2 h	98c	25^c	S
17a	 **17**	C	-30°, 6 h	60	14	R
17b		C	-30°, 6 h	98^c	86^c	R
17c		CH	-20° to -10°, 3h	84^c	25^c	S
17d		B	-15°, 1 h	98^c	21^c	S

[a] Yield of isolated adduct. – [b] *ee* determined by G.C. with chiral capillary column (Lipodex E-0.2 μm, 50 m, 0.25 mm). – [c] Reaction is performed in toluene. – [d] 10 mol-% MeOH is added to the mixture. – [e] Reaction is performed in diethyl ether. – [f] 4-Å molecular sieves were added.

(Table 1, Entry 2, 18% *ee*). A small but significant difference in *ee* is apparent between ligands **8** and **9**, corresponding to matched and mismatched combinations. This difference is even more striking with ligands **10** and **11** derived from (−)- and (+)-menthol (5% and 50% *ee*, respectively). In both cases, the same absolute configuration of the adduct is obtained. Thus, although the sense of the asymmetric induction is imposed by the TADDOL part, the degree of enantioselection is strongly affected by the exocyclic moiety.

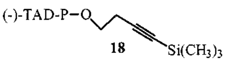
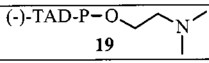
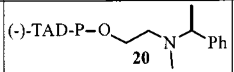
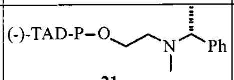
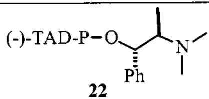
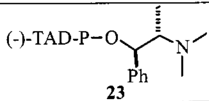
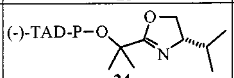
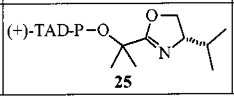
Some experimental modifications were then attempted using the aforementioned matched ligand **11**, which led to the highest *ee* yet achieved. For example, the use of toluene as solvent showed, once again, that CH_2Cl_2 is somewhat better (cf. Entries 11a and 11b). The addition of a small amount of MeOH (10%) led to a small but not insignificant improvement (Entry 11c). The aim of this experiment was to check whether aged solutions of Et_2Zn (containing alcoholates) may affect the enantioselectivity. Conversely, we also tested the addition of small or large amounts of 4-Å molecular sieves, as such an additive has been reported to improve the enantioselection.[7f] In the present case, using ligand **13** (Entry 13d) or ligand **33** (Entry 33c, Table 5), no such effect was observed.

Arylcyclohexanols are generally excellent chiral auxiliaries,[13] much better than menthol, and sometimes even better than phenylmenthol. We recently described a facile preparation of this class of compounds in highly enantioenriched form through enantioselective nucleophilic ring-opening of cyclohexene oxide.[14] Indeed, ligand **13**, prepared from phenylcyclohexanol, gave a better *ee* (60%, Entry 13a) than ligand **11** (with menthol, Entry 11a) in CH_2Cl_2 solution. However, to our surprise, this ligand behaved much better in toluene solution (Entry 13b), giving ethylcyclohexanone with up to 96% *ee*. Et_2O also proved to be a good solvent in this case (88% *ee*, Entry 13c). This unusual behavior in toluene was likewise observed with all the ligands derived from arylcyclohexanols. The results obtained with the 1-naphthyl (ligands **14** and **15**) and 2-naphthyl series (ligands **16** and **17**) are comparable. Again, marked differences were observed between the matched and mismatched combinations of ligands. In all these cases, toluene appeared to be a better solvent, perhaps due to the better solubility of these ligands. Their lower solubility in CH_2Cl_2 may also account for the low chemical yields obtained with chalcone and benzalacetone.

Generally speaking, acyclic enones gave poor enantioselectivities. The best results were obtained with ligand **13** (chalcone: 50% *ee*, Entry 13d; benzalacetone: 35% *ee*, Entry 13f). Thus, another general trend emerges: A ligand that improves the enantioselection with cyclohexenone also improves it with chalcone. In contrast, benzalacetone seems to be less sensitive to the matched or mismatched combinations of the ligand.

In order to ascertain whether interactions other than steric ones may be useful for improved enantioselection, we introduced several functionalized alcohols in the exocyclic position (see Table 3). The homopropargylic system (ligand **18**) was selected for π interactions with the Cu atom (Entry 18), but the result achieved was comparable to those obtained with the non-functionalized alcohols (see Table 1), indicating a rather low influence of the triple bond. The β-dimethylamino group (ligand **19**) was chosen for its ability to coordinate to the organometallic reagent through the nitrogen atom (Entry 19). Although the *ee* was of the usual low magnitude, a noteworthy reversal of the absolute configuration was observed. Therefore, strong coordination of the nitrogen atom to the Cu or Zn atom seems to be involved.

Table 3. TADDOL phosphites with a functionalized exocyclic alcohol derivative

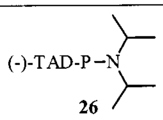
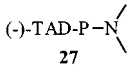
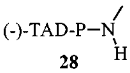
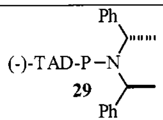
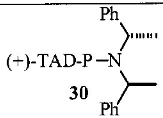
Entry	Ligand	Enone	Conditions	Yield[a] %	ee[b]	Abs. Conf.
18a	 (-)-TAD-P–O … Si(CH₃)₃ **18**	C	-20, 2 h	98	12	S
18b		B	-20° to r.t. 16 h	45	8	S
19a	 (-)-TAD-P–O … N **19**	C	-20° to -10°,3 h	95	13	R
19b		B	-20° to r.t. 8 h	98	15	R
20a	 (-)-TAD-P–O … N … Ph **20**	C	-20°, 2.5 h	98	5	R
20b		B	-20° to 0°, 6.5 h	98	3	S
21a	 (-)-TAD-P–O … N … Ph **21**	C	-20°, 3 h	98	38	R
21b		B	-20° to 0°, 6.5 h	47	3	S
22a	 (-)-TAD-P–O … N … Ph **22**	C	-20° to -10°, 1h	98	8	R
22b		B	-20° to 0°, 5 h	14	29	R
23a	 (-)-TAD-P–O … N … Ph **23**	C	-20° to r.t. 21 h	41	16	S
23b		C	-20° to r.t. 10 h	98[c]	10[c]	S
23c		B	-20° to r.t. 21 h	0	-	-
24a	 (-)-TAD-P–O … O … N **24**	C	-20°, 6 h	84	13	S
24b		C	-20° to r.t. 10 h	98[c]	4[c]	R
24c		B	-20° to r.t. 21 h	34	16	R
25a	 (+)-TAD-P–O … O … N **25**	C	-20°, 6 h	85	2	R
25b		C	-20° to r.t. 10 h	98[c]	10[c]	S
25c		B	-20° to 0°, 7 h	7	2	R

[a] Yield of isolated adduct. – [b] *ee* determined by G.C. with chiral capillary column (Lipodex E-0.2 µm, 50 m, 0.25 mm). – [c] Reaction is performed in toluene. – [d] 1 mol-% MeOH is added to the mixture. – [e] Using CuI instead of Cu(OTf)$_2$.

In the other examples in Table 3, a heteroatom *and* an additional source of chiral information are combined. Again, matched and mismatched combinations may be formed, both of which had to be checked. When a chiral center was introduced in the substituents at the nitrogen atom, a matched combination boosted the *ee* to 38% (ligand **21**, Entry 21a), again with a reversal of the absolute configuration, whereas the *ee* with the mismatched combination amounted to just 5% (Entry 20a). The situation was not so clear-cut with derivatives of (+)- or (−)-ephedrines (ligands **22** and **23**), nor with the chiral oxazolines (ligands **24** and **25**), both combinations giving low to very low *ee* values. It is interesting to note that the latter ligands (**24** and **25**) gave excellent results in the Rh-catalysed hydrosilylation of ketones.[15]

It has been shown that the chiral phosphorus amidites derived from binaphthol (see Scheme 1) are capable of inducing very high levels of enantiocontrol in conjugate addition reactions.[7a,7b] Therefore, a number of TADDOL-derived phosphorus amidites were tested under the standard conditions; the results are shown in Table 4. It should be noted that during the course of our work, ligands **26** and **27** were also described by Feringa et al. and tested with cyclohexenone and cyclopentenone.[7f] A bulky diisopropylamino group (ligand **26**, Entry 26) gives a moderate degree of enantioselectivity with the usual absolute configuration, i.e. that imposed by the chirality of (−)-TADDOL. Interestingly, a small dimethylamino group (ligand **27**, Entry 27) not only leads to a higher *ee* (35%), but also inverts the enantioselection! The reason for the switch in absolute induction is unclear at the present time. The divergence from the reported value of 54% *ee* for the same experiment[7f] could be due to slight differences in the experimental procedure. Two other examples (Entries 29 and 30) correspond to a matched and mismatched combination with a chiral exocyclic amine. Although this exocyclic amino group markedly improved the results with binaphthol instead of TADDOL,[7b] ligands **29** and **30** were completely inefficient in the TADDOL case. Thus, all the above ligands gave poor to moderate results with cyclohexenone. In contrast to the aforementioned results, ligand **28**, with an even smaller methylamino group (Entry 28), gave the highest *ee* (49%) of this study for benzalacetone. In this case, coordination of the metal center by a nitrogen atom cannot be invoked and other effects must be operative.

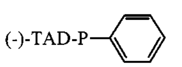
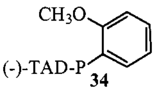
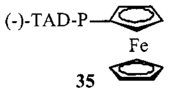
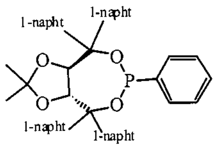
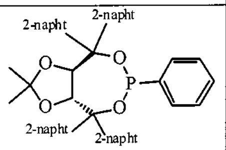
Table 4. TADDOL phosphonamidite with an exocyclic amino derivative

Entry	Ligand	Enone	Conditions	Yield[a] %	ee[b]	Abs. Conf.
26a	 (-)-TAD-P–N **26**	C	-20°, 1 h	94	17	S
26b		CH	-20° to -10°, 6h	37	13	R
26c		B	-20° to 10°, 5 h	60	8	R
27a	 (-)-TAD-P–N **27**	C	-20°, 1 h	98	35	R
27b		CH	-20°, 4.5 h	60	3	S
27c		B	-20°, 4.5 h	51	10	R
28a	 (-)-TAD-P–N–H **28**	C	-20°, 2 h	98	11	S
28b		B	-20°, 4.5 h	98	49	R
29a	 Ph (-)-TAD-P–N Ph **29**	C	-20°, 1.5 h	98	15	-
29b		B	-20° to 0°, 5 h	91	0	
30a	 Ph (+)-TAD-P–N Ph **30**	C	-20°, 50 mn	98	17	R

[a] Yield of isolated adduct. – [b] *ee* determined by G.C. with chiral capillary column (Lipodex E-0.2 µm, 50 m, 0.25 mm). – [c] Reaction is performed in toluene. – [d] 1 mol-% MeOH is added to the mixture. – [e] Using CuI instead of Cu(OTf)$_2$.

Finally, Table 5 shows the results of some tests with alkyl and aryl phosphinites. Phosphinite **33** has already been successfully used in Rh-catalyzed asymmetric hydroformylation and hydrosilylation reactions.[12] On the other hand, alkyl phosphinamidites gave a moderate degree of enantioselectivity in the copper-catalyzed conjugate addition to cyclohexenone.[7g] As seen in Entries 31 and 33, a simple

Table 5. TADDOL phosphonites with an exocyclic carbon framework

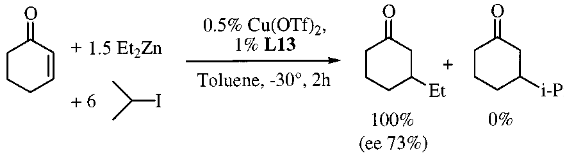
Entry	Ligand	Enone	Conditions	Yield[a] %	ee[b]	Abs. Conf.
31a	(-)-TAD-P—*n*-Bu **31**	C	-20°, 2 h	95[c]	48[c]	S
32a	(-)-TAD-P—*t*-Bu **32**	C	-20°, 2 h	98[c]	17[c]	S
33a	 **33**	C	-5°, 1 h	95	48	S
33b		C	-20°, 2 h	97[c]	54[c]	S
33c		C	-20°, 2 h	94[f]	50[f]	S
33d		CH	-5° to r.t. 24 h	55	7	R
33e		B	-5° to r.t. 24 h	8	-	-
34a	 **34**	C	-20°, 1 h	97	2	S
34b		CH	-20°, 7 h	48	8	R
34c		B	-20°, 7 h	83	8	R
35a	 **35**	C	-20°, 1 h	97	33	S
35b		C	-5° to r.t. 20h	20[e]	7[e]	S
36a	 **36**	C	-20°, 3 h	50	0	-
36b		C	-30°, 3 h	98[c]	33	S
37a	 **37**	C	-20°, 2 h	98[c]	45[c]	S

[a] Yield of isolated adduct. – [b] *ee* determined by G.C. with chiral capillary column (Lipodex E-0.2 µm, 50 m, 0.25 mm). – [c] Reaction is performed in toluene. – [d] 1 mol-% MeOH is added to the mixture. – [e] Using CuI instead of Cu(OTf)$_2$. – [f] 4-Å molecular sieves were added.

exocyclic *n*-butyl (ligand **31**) or phenyl group (ligand **33**) leads to some of the highest *ee* values in this study, with values of 48–54% with cyclohexenone. This is quite a surprising result, since the only stereochemical information comes from TADDOL itself! The absolute configuration is that usually observed with (–)-TADDOL as sole source of stereochemical information. Attempts to improve the *ee* through the use of a bulkier alkyl substituent (ligand **32** with *t*Bu) or other aryl substituents such as *o*-anisyl (ligand **34**) or ferrocenyl groups (ligand **35**) did not improve the enantioselection. Similarly disappointing results were obtained using 1-naphtho-TADDOL (ligand **36**) or 2-naphtho-TADDOL (ligand **37**), although the latter has been reported to be more efficient in other kinds of reactions.[12] Nevertheless, this represents a quite promising means of introducing new variations in this class of TADDOL ligands.

Except in the case of the TADDOL-arylcyclohexanol ligands **13**, **15**, and **17**, the above results are not among the best ones in the asymmetric conjugate addition of diethylzinc to enones. However, they allow a better understanding of the various factors that affect the efficiency of these TADDOL-derived chiral phosphites. Due to the modular nature of these ligands, it should be a facile task to further vary the nature of the aromatic group on the TADDOL moiety as well as the nature of the acetal protecting group. Therefore, ligand tuning should be possible, allowing access to highly selective catalysts.

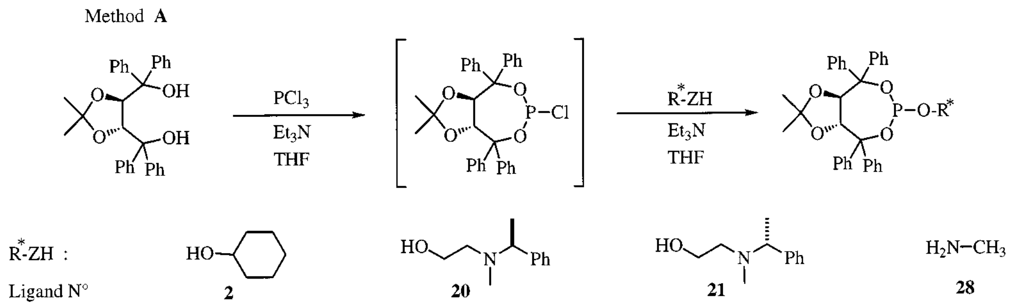
A final series of experiments was carried out with the aim of checking whether any radical-type mechanism might be involved in the above reactions. Indeed, a recent report showed that in the presence of oxygen diethylzinc may undergo conjugate addition to cyclohexenone.[16] If isopropyl iodide (up to 6 equivalents) is admixed, only the *i*Pr moiety is transferred, and not the Et group. In the experiment shown in Scheme 4, we did not observe any trace of the *i*Pr adduct. This clearly demonstrates that no radical mechanism is involved in our copper-catalyzed reactions.



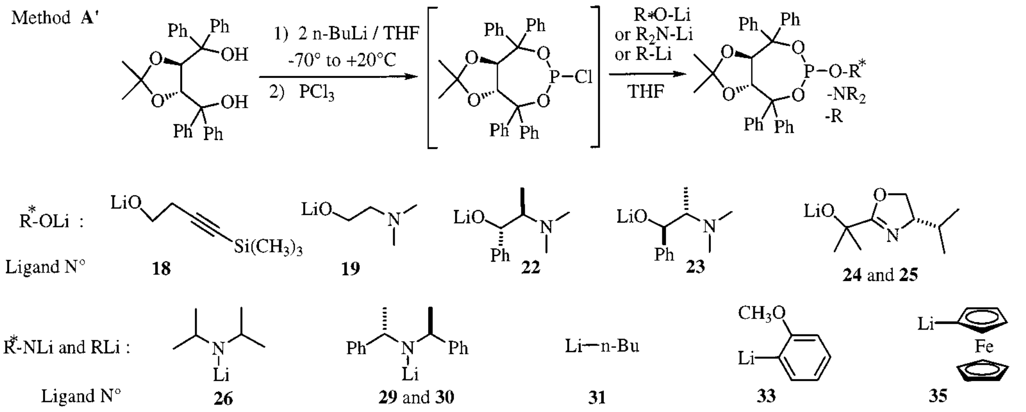
Scheme 4. Proof of non-radical mechanism

Synthesis of the TADDOL Ligands

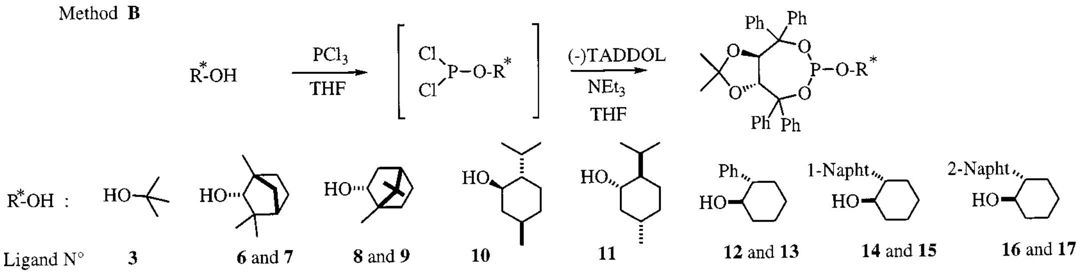
The synthesis of all of the above ligands is not as trivial as it might appear at first glance. Due to the pronounced steric congestion between the phenyl groups of TADDOL and the exocyclic substituent, different methods were applied according to the specific ligand needed. The most obvious and classical method (Method **A**) is summarized in Scheme 5 and the ligands prepared in this way are shown. It involves initial preparation of the TADDOL-P–Cl intermediate in the presence of NEt$_3$ as an HCl scavenger, followed



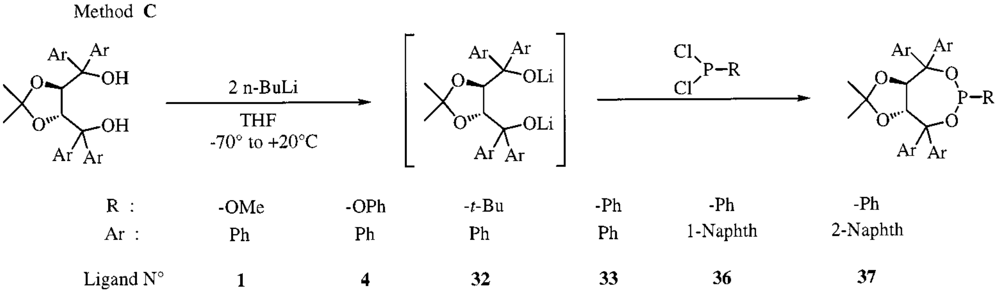
Scheme 5. Synthesis of TADDOL ligands according to Method **A**



Scheme 6. Synthesis of TADDOL ligands according to Method **A**′



Scheme 7. Synthesis of TADDOL ligands according to Method **B**



Scheme 8. Synthesis of TADDOL ligands according to Method **C**

by addition of the required alcohol.[17] The course of both steps of the reaction could easily be monitored by ^{31}P NMR spectroscopy.

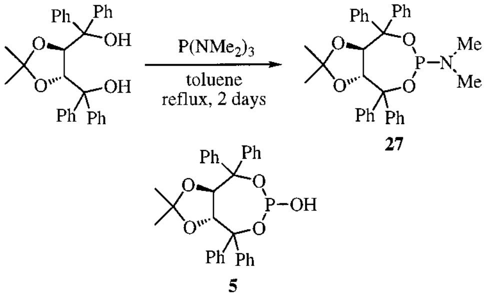
An alternative to the above method is to use the alcoholates instead of the free alcohol. Thus, the bis(lithium) alcoholate of TADDOL is prepared and treated with PCl_3. In a separate flask, the lithium alcoholate, lithium amide, or organolithium reagent is prepared and then added to the TADDOL-P−Cl intermediate. This method (Method **A**′) avoids the formation of triethylammonium chloride (which is sometimes difficult to filter off) since it generates only LiCl salts. It is also the only method possible when an alkyl or aryl group is required in an exocyclic position. Scheme 6 summarizes the ligands prepared in this way.

A reverse method (Method **B**) was used when a bulky alcohol was needed in the exocyclic position. It involves the construction of the seven-membered ring in the last step, thereby taking advantage of cyclization as a driving force.[18] The reaction of the secondary or tertiary alcohol with PCl_3 to give the $RO-PCl_2$ species has to be carried out in the absence of NEt_3 to avoid the formation of the corresponding chloride (R−Cl) and/or di- or triphosphites. The formation of the $RO-PCl_2$ intermediate could easily be monitored by ^{31}P NMR. NEt_3 was then added, followed immediately by solid TADDOL. This method is particularly well suited for ligands bearing an aryl cyclohexanol moiety. The ligands prepared according to this method are shown in Scheme 7.

In a few particular cases, we took advantage of the commercial availability of some intermediates ($MeO-PCl_2$, $PhO-PCl_2$, tBu−PCl_2, $Ph-PCl_2$). These ligands have already been prepared by Seebach,[19] and we followed the described procedure exactly (Method **C**), as shown in Scheme 8.

Finally, two ligands were prepared in a different way. Ligand **27** was obtained by reaction of TADDOL with

HMPT,[7f,19] while ligand **5** was isolated as a by-product from the various ligand preparations (see Scheme 9).



Scheme 9. Synthesis of TADDOL ligands **5** and **27**

Conclusion

The TADDOL class of chiral trivalent phosphorus ligands would seem to be very promising for copper-catalyzed enantioselective conjugate addition. Although the chirality of the TADDOL backbone is insufficient for achieving high levels of enantiocontrol, the external chirality introduced by a chiral alcohol moiety attached to the phosphorus atom allows an increase of the enantiomeric excess of the conjugate adduct up to 96% in the best case. Steric factors play an essential role and a computational model for the design of new ligands may be expected on this basis. Some of these ligands have already been used in the literature for other transition metal catalyzed reactions. All the new ligands described in this study may also be tested in these reactions, thus widening the scope of their potential applications.

Experimental Section

General Remarks: ^{1}H NMR spectra were recorded with Bruker AC-200 (200 MHz) and AC-400 (400 MHz) spectrometers. Chemical shifts are quoted in ppm relative to tetramethylsilane ($\delta = 0$) and were referenced to the residual protons in the solvent. Proton-decoupled ^{13}C-NMR spectra were recorded with Bruker AC-200 (50 MHz) and AC-400 (100 MHz) spectrometers in the solvent indicated. Chemical shifts are quoted relative to tetramethylsilane ($\delta = 0$). − Mass spectra were recorded at the Université Pierre et Marie Curie, Paris, under chemical ionization (CI) conditions using NH_3 as the carrier gas. − Optical rotations were measured with a Perkin−Elmer 241 polarimeter, using a cell of 1 dm path length. The concentration (*c*) is expressed in g/100 mL. − Microanalyses were carried out by the staff of the Université Pierre et Marie Curie Microanalytical Department. − Melting points (m.p.) were determined using a Büchi SMP-20 melting point apparatus and are uncorrected. − Analytical thin-layer chromatography (TLC) was carried out on Merck pre-coated 0.25 mm thick plates of Kieselgel 60 F_{254}; TLC plates for use with phosphorus ligands were first neutralized by exposing them to the vapour from an open bottle of ammonia. Gravity chromatography was carried out using Merck Kieselgel and POLYGRAM® SIL G/UV_{254}. − Enantiomeric excesses for the conjugate addition products derived from 2-cyclohexenone and benzalacetone were measured by chiral GC (chiral capillary column − Lipodex E, 0.2 µm, 50 m, 0.25 mm). The enantiomeric excess for the conjugate addition product derived from chalcone was measured by comparison of the optical rotation with the literature value for the optically pure material, $[\alpha]_D^{23} = +10.5$ ($c = 2.5$ in EtOH).[21] − Chalcone was recrystallized from ethanol and benzalacetone from pentane; 2-cyclohexenone was used as received. Dry THF was distilled from sodium in a recycling still using benzophenone ketyl as indicator. Other solvents were purified by standard techniques.[22] Reactions in non-aqueous media were carried out under dry nitrogen or dry argon unless indicated otherwise.

Typical Procedure for the Conjugate Addition: A 25-mL three-necked flask was charged with Cu(OTf)$_2$ (9 mg, 0.025 mmol), CH_2Cl_2 (3 mL), and the appropriate ligand (0.05 mmol) either neat or as a 1 M solution in toluene. The resulting mixture was stirred for 30 min and then cooled to −40 °C, whereupon diethylzinc (7 mL of a 1 M solution in hexane, 7 mmol) was added. The solution was allowed to warm to −20 °C, whereupon a solution of the appropriate enone (5 mmol) in CH_2Cl_2 (3 mL) was added dropwise. The reaction mixture was stirred for 1−3 h at −20 °C (and for a further 4 h at 0 °C in cases where no evolution was observed) and then quenched by the careful addition of 2 M hydrochloric acid (ca. 5 mL). Diethyl ether (ca. 10 mL) was added at 0 °C and the resulting mixture was stirred until clear. The organic phases were combined, dried ($MgSO_4$), and the solvent was removed in vacuo. Where necessary, chromatography provided the pure adduct.

3-Ethylcyclohexanone: Purification by flash chromatography: $R_f = 0.48$ (silica, hexane/AcOEt, 80:20). The enantiomeric excess was measured by chiral GC: Lipodex E, 25 m, 50 cm^3·s^{-1}, $T = 60$ °C, $t_R = 24.72$ min (*R*) enantiomer, $t_R = 28.15$ min (*S*) enantiomer; yellow oil. − ^{1}H NMR: $\delta = 2.50-0.70$ (many m). − ^{13}C NMR: $\delta = 25.0$ (C-7), 28.6 (C-8), 31.0 (C-4), 36.0 (C-5), 38.8 (C-3), 41.1 (C-6), 47.9 (C-2), 210.9 (C-1).

1,3-Diphenylpentanone: Purification by flash chromatography: $R_f = 0.44$ (silica, pentane/Et$_2$O, 95:5) gave an ivory-colored solid. The enantiomeric excess was measured by polarimetry {ref.[21] $[\alpha]_D^{23} = +10.5$ ($c = 2.50$ in EtOH) pure (*S*)-(+) adduct} or by HPLC [Chiralpak AD, 250 mm, 2% *i*PrOH in hexane, 1 mL·min^{-1}, $t_R = 7.71$ min (+)-(*S*) enantiomer, $t_R = 10.04$ min (−)-(*R*) enantiomer]. − ^{1}H NMR: $\delta = 0.80$ (t, $J = 7.3$ Hz, 3 H, 5-H$_3$), 1.50−1.90 (m, 2 H, 4-H), 3.15−3.35 (m, 3 H, 2-H$_2$ and 3-H), 7.10−7.60 (m, 8 H, aryl H), 7.85−7.98 (m, 2 H, 2′-H, 6′-H). − ^{13}C NMR: $\delta = 12.2$ (CH_3CH_2), 29.3 (CH_3CH_2), 43.1 (PhCH), 45.6 (*C*H$_2$CO), 126.3 (C arom.), 127.7, 128.1, 128.5, 128.6, 132.9, 137.4, 144.8, 199.1 (CO).

4-Phenylhexanone: Purification by flash chromatography: $R_f = 0.4$ (silica, cyclohexane/EtOAc, 80:20) gave a yellow oil. − $C_{12}H_{16}O$, $M_r = 176$. The enantiomeric excess was measured by polarimetry {ref.[21] $[\alpha]_D^{22} = +30$ ($c = 2.30$ in EtOH) pure (*S*)-(+) adduct} or by chiral GC [enantiomer separation: Lipodex E, 25 m, 75 cm^{3}s^{-1}, $T = 75$ °C, $t_R = 35.05$ min (*S*) enantiomer, $t_R = 37.66$ min (*R*) enantiomer. − ^{1}H NMR: $\delta = 0.78$ (t, $J = 7.3$ Hz, 3 H, CH_3CH$_2$CH), 1.62 (m, 2 H, CH$_3$$CH_2$CH), 2.02 (s, 3 H, COCH$_3$), 2.72 (d, $J = 7.2$ Hz, 2 H, CH$_2$COPh), 3.03 (m, 1 H, PhCH), 7.33−7.15 (m, 10 H, ArH). − ^{13}C NMR: $\delta = 11.9$ (CH_3CH_2), 29.3 (CH_3CH_2), 30.6 (COCH$_3$), 42.9 (PhCH), 50.5 (CH$_2$COPh), 126.3 (C arom.), 127.5, 128.4, 144.2 (C$_q$), 208.0 (CO).

Synthesis of the Ligands

(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 (1); Method C: Preparation according to the literature.[18] To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) in THF (10 mL) at −70 °C, butyllithium (3.4 mL of a 1.5 M solution in hexanes, 5.13 mmol) was added at such a rate as to keep the internal temperature below −50 °C. The reaction mixture was then stirred at −70 °C for 10 min, allowed to warm to room temperature, and maintained under these conditions for 3 h. It was then cooled to −70 °C once more, whereupon neat MeOPCl$_2$ was added dropwise at such a rate as to keep the internal temperature below −70 °C. The resulting mixture was allowed to warm to room temperature, stirred for 1 h, and then the solvent was removed in vacuo. The resulting semi-solid residue was stirred with toluene (10 mL) for 1 h and then filtered through Celite. The solvent was subsequently removed in vacuo; purification of the residue by flash chromatography (cyclohexane/diethyl ether/triethylamine, 95:5:1) followed by crystallization from pentane furnished the title compound as a white crystalline solid (1.13 g, 2.1 mmol, 86%); m.p. 189−191 °C (from pentane) (ref.[19] 190−192 °C). − $[\alpha]_D^{18}$ = −223 (*c* = 1.05 in CH_2Cl_2) {ref.[18] $[\alpha]_D^{r.t.}$ = −236.7 (*c* = 1.17 in $CHCl_3$)}. − ^{1}H NMR: δ = 0.61 (s, 3 H, CH_3-TADDOL), 0.88 (s, 3 H, CH_3-TADDOL), 3.28 (d, 3 H, CH_3O), 5.49 (dd, *J* = 8.2 and 1.5 Hz, 1 H, 7-H), 5.62 (d, *J* = 8.2 Hz, 1 H, 1-H), 7.12−6.95 (m, 12 H, ArH), 7.82−7.66 (m, 8 H, ArH). − ^{13}C NMR: δ = 26.6, 27.2, 49.4, 81.5, 82.8, 82.9, 83.4, 85.9, 86.0, 113.3 (C-9), 128.3, 129.3, 142.2, 146.8, 147.0. − ^{31}P NMR: δ = 133.80.

(1*R*,7*R*)-4-Cyclohexyloxy-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (2); Method A: To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) and triethylamine (1.24 mL, 8.5 mmol) in THF (10 mL) at 0 °C was slowly added PCl_3 (236 μL, 2.6 mmol). A white precipitate was deposited and the resulting mixture was stirred at room temperature for 10 min and then cooled to 0 °C once more. A solution of cyclohexanol (270 mg, 2.7 mmol) in THF (10 mL) was then added and stirring was continued for 1 h at room temperature. The reaction mixture was diluted with diethyl ether and filtered through a pad of Celite. The solvent was removed in vacuo, and the residue was taken-up in diethyl ether and filtered through Celite; this procedure was repeated until addition of ether produced a clear solution. Purification by flash chromatography (cyclohexane/diethyl ether/triethylamine, 95:5:1) followed by crystallization from a mixture of diethyl ether and pentane furnished the title compound as a white solid (693 mg, 1.16 mmol, 47%); m.p. 189−191 °C (pentane/diethyl ether). − $[\alpha]_D^{18}$ = −154.8 (*c* = 0.75 in $CHCl_3$). − ^{1}H NMR: δ = 0.65 (s, 3 H, CH_3-TADDOL), 0.93 (s, 3 H, CH_3-TADDOL), 1.34−1.12 (m, 6 H, cyclohexyl), 1.70−1.58 (m, 3 H, cyclohexyl), 1.81−1.75 (br. m, 1 H, cyclohexyl), 4.28−4.22 (m, 1 H, CHO-cyclohexyl), 5.07 (dd, *J* = 8.3 and 1.4 Hz, 1 H, 7-H), 5.29 (d, 1 H, *J* = 8.3 Hz, 1-H), 7.37−7.28 (m, 12 H, ArH), 7.63−7.50 (m, 8 H, ArH). − ^{13}C NMR: δ = 23.9, 25.3, 26.2, 26.8, 34.1, 73.3, 73.4, 81.1, 82.2, 82.5, 84.4, 84.5, 112.3 (C-9), 127.0, 127.2, 127.4, 127.7, 128.0, 128.7, 129.0, 141.7, 146.4. − ^{31}P NMR: δ = 134.10. − MS (CI, NH_3): *m/z* (%) = 595 $[M + H]^+$ (< 1), 373 (100). − $C_{37}H_{39}O_5P$ (594.7) calcd. C 74.73, H 6.61; found C 74.88, H 6.76.

(1*R*,7*R*)-4-(*tert*-Butyloxy)-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (3); Method B: To a stirred solution of PCl_3 (218 μL, 2.5 mmol) and triethylamine (1.08 mL, 7.8 mmol) in THF (10 mL) at 0 °C, a solution of *tert*-butyl alcohol (185 mg, 2.5 mmol) in THF (10 mL, 1 mL rinse) was added over a period of 0.5 h. The reaction mixture was then allowed to warm to ambient temperature and maintained under these conditions for 1.5 h. Solid (−)-TADDOL (1.16 g, 2.5 mmol) was then added and stirring was continued for 1.5 h. Diethyl ether was added, the resulting precipitate was removed by filtration through Celite, and the solvent removed in vacuo. Purification of the residue by flash chromatography (cyclohexane/EtOAc/triethylamine, 95:5:1) followed by crystallization from pentane furnished the title compound as a white solid (1.22 g, 2.15 mmol, 86%); m.p. 174−176 °C (pentane). − $[\alpha]_D^{18}$ = −133.4 (*c* = 1.06 in $CHCl_3$). − ^{1}H NMR: δ = 0.54 (s, 3 H, CH_3-TADDOL), 0.89 [s, 9 H, $(CH_3)_3C$], 1.01 (s, 3 H, CH_3-TADDOL), 5.33 (d, *J* = 8.5 Hz, 1 H, 7-H), 6.12 (d, *J* = 8.5 Hz, 1 H, 1-H), 7.15−6.99 (m, 10 H, ArH), 7.89−7.68 (m, 10 H, ArH). − ^{13}C NMR: δ = 26.3, 27.1, 30.1, 30.2, 77.6, 80.2, 80.3, 82.6, 82.9, 83.5, 83.6, 84.8, 85.0, 112.3 (C-9), 127.1, 127.3, 127.4, 127.7, 127.8, 127.9, 129.2, 129.5, 142.5, 142.8, 147.1. − ^{31}P NMR: δ = 132.33. − MS (CI, NH_3): *m/z* (%) = 585 $[M + 16 + H]^+$ (5). − $C_{35}H_{37}O_5P$ (568.6): calcd. C 73.93, H 6.56; found C 73.77, H 6.96.

(1*R*,7*R*)-9,9-Dimethyl-2,2,6,6-tetraphenyl-4-phenyloxy-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (4); Method C: Preparation according to the literature.[18] To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) in THF (10 mL) at −70 °C was added butyllithium (3.4 mL of a 1.5 M solution in hexanes, 5.13 mmol) at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 3 h. It was then cooled to −70 °C once more, whereupon neat PhOPCl$_2$ was added dropwise so as to keep the internal temperature below −60 °C. The resulting mixture was allowed to warm to room temperature, stirred for 18 h (for convenience), and then the solvent was removed in vacuo. The resulting semi-solid residue was stirred with toluene (10 mL) for 1 h and then filtered through Celite. The solvent was removed in vacuo and purification of the residue by flash chromatography (cyclohexane/diethyl ether/triethylamine, 95:5:1) followed by crystallization from pentane furnished the title compound as a white solid (1.17 g, 1.99 mmol, 80%); m.p. 178−179 °C (pentane) (ref.[18] 177−177.5 °C). − $[\alpha]_D^{18}$ = −167.2 (*c* = 1.36 in $CHCl_3$) {ref.[19] $[\alpha]_D^{18}$ = −172.8 (*c* = 1.09 in $CHCl_3$)}. − ^{1}H NMR: δ = 0.70 (s, 3 H, CH_3-TADDOL), 0.79 (s, 3 H, CH_3-TADDOL), 5.13 (d, *J* = 8.3 Hz, 1 H, 7-H), 5.59 (d, *J* = 8.3 Hz, 1 H, 1-H), 6.58 (d, *J* = 8.3 Hz, 2 H, ArH), 7.63−7.01 (m, 23 H, ArH). − ^{13}C NMR: δ = 26.9, 27.0, 80.6, 82.5, 82.6, 85.4, 86.6, 113.5 (C-9), 120.3, 120.4, 127.6, 128.3, 129.1, 129.4, 129.5, 141.7, 146.3, 152.5. − ^{31}P NMR: δ = 128.12.

(1*R*,7*R*)-9,9-Dimethyl-4-hydrido-4-oxo-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (5): This compound was isolated from various ligand preparations as a white crystalline solid; m.p. 226−227 °C (decomp.) (pentane/diethyl ether). − $[\alpha]_D^{18}$ = −289.9 (*c* = 1.56 in $CHCl_3$). − ^{1}H NMR: δ = 0.59 (s, 3 H, CH_3-TADDOL), 0.79 (s, 3 H, CH_3-TADDOL), 5.24 (d, *J* = 8.0 Hz, 1 H, 7-H), 5.38 (d, *J* = 8.0 Hz, 1 H, 1-H), 7.12 (d, *J* = 7.3 Hz, 1 H, 4-H), 7.45−7.30 (m, 16 H, ArH), 7.65−7.61 (m, 4 H, ArH). − ^{13}C NMR: δ = 28.2, 28.7, 81.7, 72.0, 90.6, 90.7, 116.3 (C-9), 128.7, 128.8, 130.3, 130.6, 130.7, 145.1, 145.6. − ^{31}P NMR: δ = −3.13. − MS (CI, NH_3): *m/z* (%) = 530 $[M + NH_4]^+$ (1), 431 (100). − $C_{31}H_{29}O_5P$ (512.5): calcd. C 72.65, H 5.70; found C 72.51, H 5.68.

(1*R*,7*R*)-9,9-Dimethyl-2,2,6,6-tetraphenyl-4-(1,3,3-trimethylbicyclo[2.2.1]hept-2-yloxy)-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (6); Method B: To a stirred solution of (+)-fenchol (0.77 g, 5.0 mmol) in THF (5 mL) was slowly added PCl_3 (436 μL, 5.0 mmol) as a solution in THF (4 mL, 1 mL rinse) and the resulting mixture was stirred for 1 h. Thereafter, ^{31}P NMR indicated the presence of fenchol−PCl$_2$ (δ = 174.60). The reaction mixture was then cooled to −10 °C and triethylamine (2.08 mL, 15 mmol) was slowly added. A slightly exothermic process was noted, accompanied by the formation of a white precipitate. The reaction mixture was allowed to warm to room temperature, maintained under these conditions for 0.25 h, and then cooled to 0 °C. Solid (−)-TADDOL was added, the reaction mixture allowed to warm to room temperature, and stirring was continued for 2 h prior to dilution with diethyl ether. The solids were removed by filtration through a pad of Celite, the solvent was removed in vacuo, and the residue was taken up in diethyl ether. The resulting solution was filtered as before; this procedure was repeated until the addition of ether produced a clear solution. Purification by flash chromatography (cyclohexane/EtOAc/triethylamine, 98:2:1) furnished the title compound as a white foam (0.97 g, 1.5 mmol, 30%). − $[\alpha]_D^{18} = -163$ (c = 0.50 in CHCl$_3$). − ^{1}H NMR: δ = 0.37 (s, 3 H), 0.76 (s, 3 H), 0.83 (s, 3 H), 1.15 (s, 6 H), 4.10 (d, J_{HP} = 14 Hz, 1 H, CHO-fenchyl), 5.12 (m, 2 H, CHO-Taddol), 7.8−7.2 (m, 20 H, ArH). − ^{13}C NMR: δ = 18.8, 22.6, 28.6, 32.4, 36.4, 38.3, 40.4, 71.8, 71.9, 87.5, 87.6, 87.7, 126.0, 128.4, 129.0, 143.0. − ^{31}P NMR: δ = 138.41. − $C_{41}H_{45}O_5P$ (648.7): calcd. C 75.90, H 6.99; found C 76.32, H 7.21.

(1*S*,7*S*)-9,9-Dimethyl-2,2,6,6-tetraphenyl-4-(1,3,3-trimethylbicyclo[2.2.1]hept-2-yloxy)-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (7); Method B: To a stirred solution of (+)-fenchol (0.77 g, 5.0 mmol) in THF (5 mL) was slowly added PCl$_3$ (436 µL, 5.0 mmol) as a solution in THF (4 mL, 1 mL rinse) and the resulting mixture was stirred for 1 h, whereupon ^{31}P NMR indicted the presence of fenchol−PCl$_2$ (δ = 174.6). The reaction mixture was cooled to −10 °C and triethylamine (2.08 mL, 15 mmol) was slowly added. A slightly exothermic process was noted, accompanied by the formation of a white precipitate. The reaction mixture was allowed to warm to room temperature, maintained under these conditions for 0.25 h, and then cooled to 0 °C. Solid (+)-Taddol was added, the reaction mixture allowed to warm to room temperature, and stirring was continued for 2 h prior to dilution with diethyl ether. The solids were removed by filtration through a pad of Celite, the solvent was removed in vacuo, and the residue was taken-up in diethyl ether. The resulting solution was filtered as before; this procedure was repeated until the addition of ether produced a clear solution. Purification by flash chromatography (cyclohexane/EtOAc/triethylamine, 98:2:1) furnished the title compound as a white foam (1.07 g, 1.65 mmol, 33%). − $[\alpha]_D^{20} = +146$ (c = 0.50 in CHCl$_3$). − ^{1}H NMR: δ = 0.31 (s, 3 H), 0.90 (s, 3 H), 1.02 (s, 3 H), 1.10 (s, 3 H), 1.23 (s, 3 H), 1.80−1.00 (m, 9 H, CH and CH$_2$-fenchyl), 4.17 (d, J_{HP} = 13.5 Hz, 1 H, CHO-fenchyl), 5.00 (d, J = 8.44 Hz, 1 H, CHO-Taddol), 5.20 (dd, J = 8.44 Hz, J_{HP} = 2.8 Hz, 1 H, CHO-Taddol), 7.8−7.2 (m, 20 H, ArH). − ^{13}C NMR: δ = 18.8, 22.6, 28.6, 32.4, 36.4, 38.3, 40.4, 71.8, 71.9, 87.5, 87.6, 87.7, 126.0, 128.4, 129.0, 143.0. − ^{31}P NMR: δ = 138.11. − $C_{41}H_{45}O_5P$ (648.7).

(1*R*,7*R*)-9,9-Dimethyl-2,2,6,6-tetraphenyl-4-(1,7,7-trimethylbicyclo[2.2.1]hept-2-yloxy)-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (8); Method B: To a stirred solution of (−)-borneol (0.77 g, 5.0 mmol) in THF (5 mL) was slowly added PCl$_3$ (436 µL, 5.0 mmol) as a solution in THF (4 mL, 1 mL rinse) and the resulting mixture was stirred for 1 h. Thereafter, ^{31}P NMR indicated the presence of borneol−PCl$_2$ (δ = 177.80). The reaction mixture was then cooled to −10 °C and triethylamine (2.08 mL, 15 mmol) was slowly added. A slightly exothermic process was noted, accompanied by the formation of a white precipitate. The reaction mixture was allowed to warm to room temperature, maintained under these conditions for 0.25 h, and then cooled to 0 °C. Solid (−)-Taddol was added, the resulting mixture was allowed to warm to room temperature, and stirring was continued for 2 h prior to dilution with diethyl ether. The solids were removed by filtration through a pad of Celite, the solvent was removed in vacuo, the residue was taken up in diethyl ether and filtered as before; this procedure was repeated until the addition of ether produced a clear solution. Purification by flash chromatography (cyclohexane/EtOAc/triethylamine, 98:2:1) furnished the title compound as a white foam (1.07 g, 1.65 mmol, 33%). − ^{1}H NMR (400 MHz): δ = 0.50 (s, 3 H, CH$_3$-Taddol), 0.85, 0.84 (2 s, 6 H, CH$_3$-bornyl), 1.02 (s, 3 H, CH$_3$-Taddol), 2.20−1.20 (5 m, CH and CH$_2$ bornyl), 4.75 (m, 1 H, CHO-bornyl), 5.08 (dd, J = 8.3 Hz, J_{HP} = 1.8 Hz, 1 H, CHO-Taddol), 5.19 (d, J = 8.3 Hz, 1 H, CHO-Taddol), 7.6−7.2 (m, 20 H, ArH). − ^{31}P NMR: δ = 135.76. − $C_{41}H_{45}O_5P$ (648.7).

(1*S*,7*S*)-9,9-Dimethyl-2,2,6,6-tetraphenyl-4-(1,7,7-trimethylbicyclo[2.2.1]hept-2-yloxy)-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (9); Method B: To a stirred solution of (−)-borneol (0.77 g, 5.0 mmol) in THF (5 mL) was slowly added PCl$_3$ (436 µL, 5.0 mmol) as a solution in THF (4 mL, 1 mL rinse) and the resulting mixture was stirred for 1 h. Thereafter, ^{31}P NMR indicated the presence of borneol−PCl$_2$ (δ = 177.80). The reaction mixture was then cooled to −10 °C and triethylamine (2.08 mL, 15 mmol) was slowly added. A slightly exothermic process was noted, accompanied by the formation of a white precipitate. The reaction mixture was allowed to warm to room temperature, maintained under these conditions for 0.25 h, and then cooled to 0 °C. Solid (+)-Taddol was added, the reaction mixture was allowed to warm to room temperature, and stirring was continued for 2 h prior to dilution with diethyl ether. The solids were removed by filtration through a pad of Celite, the solvent was removed in vacuo, and the residue was taken up in diethyl ether and filtered as before; this procedure was repeated until the addition of ether produced a clear solution. Purification by flash chromatography (cyclohexane/EtOAc/triethylamine, 98:2:1) furnished the title compound as a white foam (0.49 g, 0.75 mmol, 15%). − $[\alpha]_D^{20} = -106$ (c = 0.50 in CHCl$_3$). − ^{1}H NMR: δ = 0.50 (s, 3 H), 0.85 (s, 3 H), 0.90 (s, 3 H), 0.92 (s, 3 H), 1.05 (s, 3 H), 2.20−1.01 (3 m, CH and CH$_2$ bornyl), 4.76 (m, 1 H, CHO-bornyl), 5.06 (dd, J = 8.3 Hz, J_{HP} = 1.8 Hz, 1 H, CHO-Taddol), 5.14 (d, 1 H, J = 8.3 Hz, CHO-Taddol), 7.8−7.2 (m, ArH). − ^{13}C NMR: δ = 13.2, 19.4, 22.6, 26.8, 28.6, 29.1, 40.4, 44.2, 55.2, 69.4, 71.8, 87.5, 102.8, 126.0, 128.4, 129.0, 143.0. − ^{31}P NMR: δ = 135.34. − $C_{41}H_{45}O_5P$ (648.7): calcd. C 75.90, H 6.99; found C 76.07, H 7.10.

(1*R*,7*R*)-4-[(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyloxy]-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (10); Method B: To a stirred solution of (−)-menthol (391 mg, 2.5 mmol) in THF (5 mL) was slowly added PCl$_3$ (218 µL, 2.5 mmol) as a solution in THF (4 mL, 1 mL rinse) and the resulting mixture was stirred for 1 h. Thereafter, ^{31}P NMR indicated the presence of menthol−PCl$_2$ (δ = 177.00).[18] The reaction mixture was then cooled to −10 °C and triethylamine (1.07 mL, 7.75 mmol) was slowly added. A slightly exothermic process was noted, accompanied by the formation of a white precipitate. The reaction mixture was allowed to warm to room temperature, maintained under these conditions for 0.5 h, and then cooled to 0 °C. Solid (−)-Taddol was added, the resulting mixture was allowed to warm to room temperature, and stirring was continued for 1 h prior to dilution with diethyl ether. The solids were removed by filtration through a pad of Celite, the solvent was removed in vacuo, and the residue was taken up in diethyl ether and filtered as before; this procedure was repeated until the addition of ether produced a clear solution. Addition of pentane induced crystallization to provide the title compound as a white solid (800 mg, 49%); m.p. 155−156 °C (pentane). − $[\alpha]_D^{18} = -176.1$ (c = 1.14 in CH$_2$Cl$_2$). − ^{1}H NMR: δ = 0.54 (s, 3 H, CH$_3$-Taddol), 0.76 (d, J = 7.2 Hz, 3 H, CH$_3$-menthyl), 0.77 (d, J = 6.6 Hz, 3 H, CH$_3$-menthyl), 0.88 (d, J = 7.0 Hz, 3 H, CH$_3$-menthyl), 0.97 (s, 3 H, CH$_3$-Taddol), 1.26−1.20 (m, 1 H, menthyl), 1.12−0.46 (m, 4 H, menthyl), 1.45−1.38 (m, 2 H, menthyl), 2.06−2.03 (m, 1 H, menthyl), 2.43−2.37 (m, 1 H, menthyl), 4.03 (dq, J = 10.0 Hz and 4.4 Hz, 1 H, CHO-menthyl), 5.58 (dd, J = 8.3 Hz and 1.6 Hz, 1 H, 7-H), 5.67 (d, J = 8.3 Hz, 1

H, 1-H), 7.16−6.97 (m, 12 H, ArH), 7.89−7.72 (m, 8 H, ArH). − ^{13}C NMR: δ = 15.9, 21.6, 22.2, 23.1, 81.4, 25.3, 25.8, 27.3, 31.6, 34.2, 44.0, 48.6, 48.7, 76.0, 76.3, 82.1, 82.5, 84.2, 112.5 (C-9), 127.1, 127.4, 127.5, 127.8, 129.2, 129.0, 141.4, 145.9, 146.5. − ^{31}P NMR: δ = 143.11. − MS (CI, NH$_3$): *m/z* (%) = 651 [M + H]$^+$ (5), 431 (100). − $C_{41}H_{47}O_5P$ (650.8): calcd. C 75.67, H 7.28; found C 75.58, H 7.36.

(1*R*,7*R*)-4-[(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyloxy]-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (11); Method B: To a stirred solution of (−)-menthol (391 mg, 2.5 mmol) in THF (5 mL) was slowly added PCl$_3$ (218 µL, 2.5 mmol) as a solution in THF (4 mL, 1 mL rinse) and the resulting mixture was stirred for 1 h. Thereafter, ^{31}P NMR indicated the presence of menthol−PCl$_2$ (δ = 177.00).[18] The reaction mixture was then cooled to −10 °C and triethylamine (1.07 mL, 7.75 mmol) was slowly added. A slightly exothermic process was noted, accompanied by the formation of a white precipitate. The reaction mixture was allowed to warm to room temperature, maintained under these conditions for 0.25 h, and then cooled to 0 °C. Solid (−)-Taddol was added and the resulting mixture was allowed to warm to room temperature and stirred for 1 h prior to dilution with diethyl ether. The solids were removed by filtration through a pad of Celite, the solvent was removed in vacuo, and the residue was taken up in diethyl ether and filtered as before; this procedure was repeated until the addition of ether produced a clear solution. Purification by flash chromatography (cyclohexane/EtOAc/triethylamine, 95:5:1) furnished the title compound as a white foam (1.15 g, 71%). − $[\alpha]_D^{18}$ = −80.2 (*c* = 0.98 in CH$_2$Cl$_2$). − ^{1}H NMR: δ = 0.48 (s, 3 H, CH$_3$-Taddol), 0.69−0.59 (m, 1 H, CH-menthyl), 0.78 (d, *J* = 6.2 Hz, 3 H, CH$_3$-menthyl), 0.86 [d, *J* = 7.0 Hz, 6 H, (CH$_3$)$_2$-menthyl], 1.06 (s, 3 H, CH$_3$-Taddol), 1.29−1.04 (m, 3 H, menthyl), 1.48−1.34 (m, 3 H, menthyl), 2.34−2.20 (m, 1 H, menthyl), 2.41−2.34 (m, 1 H, menthyl), 4.20 (dq, *J* = 10.0 Hz and 4.3 Hz, 1 H, CHO-menthyl), 5.55 (d, *J* = 8.3 Hz, 1 H, 7-H), 5.60 (dd, *J* = 8.3 Hz and 2.4 Hz, 1 H, 1-H), 7.17−6.96 (m, 12 H, ArH), 7.94−7.71 (m, 8 H, ArH). − ^{13}C NMR: δ = 16.3, 21.4, 22.3, 23.3, 25.4, 25.8, 27.1, 27.6, 32.0, 34.4, 44.3, 48.9, 49.0, 76.1, 76.3, 81.9, 82.0, 82.3, 82.7, 83.5, 112.3 (C-9), 127.4, 127.7, 127.8, 128.3, 129.0, 129.1, 129.4, 142.3, 146.2, 146.9. − ^{31}P NMR: δ = 143.50. − MS (CI, NH$_3$): *m/z* (%) = 651 [M + H]$^+$ (5), 431 (100). − $C_{41}H_{47}O_5P$ (650.8): calcd. C 75.67, H 7.28; found C 75.57, H 7.37.

(1*R*,7*R*)-9,9-Dimethyl-2,2,6,6-tetraphenyl-4-[(1*R*,2*S*)-phenylcyclohexanyloxy]-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (12); Method B: To a stirred solution of (1*R*,2*S*)-phenylcyclohexanol (0.88 g, 5.0 mmol) in THF (5 mL) was slowly added PCl$_3$ (436 µL, 5.0 mmol) as a solution in THF (4 mL, 1 mL rinse) and the resulting solution was stirred for 1 h. Thereafter, ^{31}P NMR indicated the presence of phenylcyclohexanol−PCl$_2$ (δ = 176.10). The reaction mixture was then cooled to −10 °C and triethylamine (2.08 mL, 15 mmol) was slowly added. A slightly exothermic process was noted, accompanied by the formation of a white precipitate. The reaction mixture was allowed to warm to room temperature, maintained under these conditions for 0.25 h, and then cooled to 0 °C. Solid (−)-Taddol was added, the resulting mixture was allowed to warm to room temperature, and stirring was continued for 2 h prior to dilution with diethyl ether. The solids were removed by filtration through a pad of Celite, the solvent was removed in vacuo, the residue was taken up in diethyl ether and filtered as before; this procedure was repeated until the addition of ether produced a clear solution. Purification by flash chromatography (cyclohexane/EtOAc/triethylamine, 98:2:1) furnished the title compound as a white foam (1.17 g, 1.75 mmol, 35%). − $[\alpha]_D^{20}$ = −110 (*c* = 0.55 in CHCl$_3$). − ^{1}H NMR: δ = 0.33 (s, 3 H, CH$_3$-Taddol), 1.10 (s, 3 H, CH$_3$-Taddol), 2.60−0.81 (6 m, CH and CH$_2$ phenylcyclohexyl), 4.47 (m, 1 H, CHO-phenylcyclohexyl), 4.95 (d, *J* = 8.1, 1 H, CHO-Taddol), 5.01 (dd, *J* = 8.1 Hz, J_{HP} = 2 Hz, 1 H, CHO-Taddol), 7.81−7.23 (m, 25 H, ArH). − ^{13}C NMR: δ = 25.0, 25.4, 25.6, 27.2, 33.3, 35.1, 51.3, 80.8, 81.4, 82.0, 82.1, 109.4, 112.1, 126−128 (Ph), 142.6, 145.8. − ^{31}P NMR: δ = 139.90. − $C_{43}H_{43}O_5P$ (670.8).

(1*R*,7*R*)-9,9-Dimethyl-2,2,6,6-tetraphenyl-4-[(1*S*,2*R*)-phenylcyclohexanyloxy]-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (13); Method B: To a stirred solution of (1*S*,2*R*)-phenylcyclohexanol (0.88 g, 5.0 mmol) in THF (5 mL) was slowly added PCl$_3$ (436 µL, 5.0 mmol) as a solution in THF (4 mL, 1 mL rinse) and the resulting mixture was stirred for 1 h. Thereafter, ^{31}P NMR indicated the presence of phenylcyclohexanol−PCl$_2$ (δ = 176.1). The reaction mixture was then cooled to −10 °C and triethylamine (2.08 mL, 15 mmol) was slowly added. A slightly exothermic process was noted, accompanied by the formation of a white precipitate. The reaction mixture was allowed to warm to room temperature, maintained under these conditions for 0.25 h, and then cooled to 0 °C. Solid (+)-Taddol was added, the resulting mixture was allowed to warm to room temperature, and stirring was continued for 2 h prior to dilution with diethyl ether. The solids were removed by filtration through a pad of Celite, the solvent was removed in vacuo, the residue was taken up in diethyl ether and filtered as before; this procedure was repeated until the addition of ether produced a clear solution. Purification by flash chromatography (cyclohexane/EtOAc/triethylamine, 98:2:1) furnished the title compound as a white foam (0.67 g, 1.00 mmol, 20%). − $[\alpha]_D^{20}$ = +131 (*c* = 0.55 in CHCl$_3$). − ^{1}H NMR: δ = 0.32 (s, 3 H, CH$_3$-Taddol), 1.22 (s, 3 H, CH$_3$-Taddol), 2.6−0.8 (6 m, CH and CH$_2$ phenylcyclohexyl), 4.57 (m, 1 H, CHO-phenylcyclohexyl), 4.88 (d, *J* = 8.4 Hz, 1 H, CHO-Taddol), 4.95 (dd, *J* = 8.4 Hz, J_{HP} = 2.5 Hz, 1 H, CHO-Taddol), 7.81−7.23 (m, 25 H, ArH). − ^{13}C NMR: δ = 24.9, 25.3, 25.7, 27.3, 33.5, 35.3, 51.5, 81.6, 81.9, 82.3, 82.6, 111.7, 126−128 (Ph), 140.8, 141.5, 141.5, 143.5, 145.8, 146.3. − ^{31}P NMR: δ = 140.4. − $C_{43}H_{43}O_5P$ (670.8).

(1*R*,7*R*)-9,9-Dimethyl-4-[(1*R*,2*S*)-(1-naphthyl)cyclohexanyloxy]-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (14); Method B: To a stirred solution of (1*R*,2*S*)-1-naphthylcyclohexanol (*ee* > 99%, 1.12 mg, 5 mmol) in THF (10 mL), PCl$_3$ (436 µL, 5 mmol) was added dropwise and the resulting solution was stirred for 2 h. The mixture was then cooled to −10 °C and Et$_3$N (3 equiv., freshly distilled, 2.1 mL, 15 mmol) was added dropwise leading to the formation of a white precipitate. The mixture was allowed to warm to room temperature and maintained under these conditions for 15 min. It was then cooled to 0 °C, whereupon (−)-Taddol (2.34 g, 5.0 mmol) was added in a single portion. The resulting yellowish mixture was allowed to warm to room temperature and stirred for 2 h prior to filtration with diethyl ether twice through Celite and once through a mixture of Celite and alumina. The solvents were partly removed at water-pump pressure and then completely removed by means of an oil vacuum pump. The ligand was obtained as a white foam. Purification by flash chromatography (R_f = 0.19; alumina, hexane/AcOEt, 98:2) furnished the title compound as a white foam (3.0 g, 85% yield). − $[\alpha]_D^{20}$ = −101 (*c* = 0.80 in CHCl$_3$). − ^{1}H NMR: δ = 0.29 (s, 3 H, 2-Me), 1.18 (s, 3 H, 2-Me), 0.80−2.05 (m, 9 H, cyclohex. H), 3.60−3.70 (m, 1 H), 4.75−4.88 (m, 2 H), 6.9−7.93 (m, 26 H, aryl H), 8.25 (d, *J* = 8.4 Hz, 1 H, aryl H). − ^{31}P NMR: δ = 140.40. − $C_{43}H_{43}O_5P$ (670.8).

(1*S*,7*S*)-9,9-Dimethyl-4-[(1*R*,2*S*)-(1-naphthyl)cyclohexanyloxy]-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (15); Method B: To a stirred solution of (1*R*,2*S*)-1-naphthylcyclohexanol (*ee* > 99%, 1.12 mg, 5 mmol) in THF (10 mL), PCl_3 (436 μL, 5 mmol) was added dropwise and the resulting mixture was stirred for 2 h. The mixture was then cooled to −10 °C and Et_3N (3 equiv., freshly distilled, 2.1 mL, 15 mmol) was added dropwise leading to the formation of a white precipitate. The mixture was allowed to warm to room temperature and maintained under these conditions for 15 min. It was then cooled to 0 °C and (+)-TADDOL (2.34 g, 5.0 mmol) was added in a single portion. The resulting yellowish mixture was allowed to warm to room temperature and stirred for 2 h prior to filtration with diethyl ether twice through Celite and once through a mixture of Celite and alumina. The solvents were partly removed at water-pump pressure and then completely removed by means of an oil vacuum pump. The ligand was obtained as a white foam. Purification by flash chromatography (R_f = 0.20; alumina, hexane/AcOEt, 98:2) furnished the title compound as a white foam (2.3 g, 68% yield). − $[\alpha]_D^{20}$ = +162 (*c* = 0.50 in $CHCl_3$). − ^1H NMR: δ = 0.29 (s, 3 H, 2-Me), 1.18 (s, 3 H, 2-Me), 0.80−2.05 (m, 9 H, cyclohex. H), 3.6−3.70 (m, 1 H, 3a-H or 8a-H), 4.75−4.88 (m, 2 H, 1′-H, 3a-H, or 8a-H), 6.90−7.93 (m, 26 H, aryl H), 8.25 (d, *J* = 8.4 Hz, 1 H, aryl H). − ^{31}P NMR: δ = 140.50. − $C_{43}H_{43}O_5P$ (670.8).

(1*R*,7*R*)-9,9-Dimethyl-4-[(1*R*,2*S*)-(2-naphthyl)cyclohexanyloxy]-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (16); Method B: To a stirred solution of (1*R*,2*S*)-2-naphthylcyclohexanol (*ee* > 99%, 1.12 mg, 5 mmol) in THF (10 mL), PCl_3 (436 μL, 5 mmol) was added dropwise and the resulting solution was stirred for 2 h. The mixture was then cooled to −10 °C and Et_3N (3 equiv., freshly distilled, 2.1 mL, 15 mmol) was added dropwise leading to the formation of a white precipitate. The mixture was allowed to warm to room temperature and maintained under these conditions for 15 min. It was then cooled to 0 °C and (−)-TADDOL (2 mol) was added in a single portion. The resulting yellowish mixture was allowed to warm to room temperature and stirred for 2 h prior to filtration with diethyl ether twice through Celite and once through a mixture of Celite and alumina. The solvents were partly removed at water-pump pressure and then completely removed by means of an oil vacuum pump. The ligand was obtained as a white foam. Purification by flash chromatography (R_f = 0.4; alumina, hexane/AcOEt, 95:5) furnished the title compound as a white foam (3.0 g, 86%yield). − $[\alpha]_D^{20}$ −129 (*c* = 0.55 in $CHCl_3$). − ^1H NMR: δ = 0.28 (s, 3 H, 2-Me), 1.09 (s, 3 H, 2-Me), 0.80−2.30 (m, 7 H, cyclohex. H), 2.70−2.90 (m, 1 H, cyclohex. H), 4.5−4.65 (m, 1 H, 1′-H), 4.90−5.10 (m, 3 H, 3a-H, 8a-H, 2′-H), 6.80−7.90 (m, 27 H, aryl H). − ^{31}P NMR: δ = 138.60. − $C_{43}H_{43}O_5P$ (670.8).

(1*S*,7*S*)-9,9-Dimethyl-4-[(1*R*,2*S*)-(2-naphthyl)cyclohexanyloxy]-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (17); Method B: To a stirred solution of (1*R*,2*S*)-2-naphthylcyclohexanol (*ee* > 99%, 1.12 mg, 5.0 mmol) in THF (10 mL), PCl_3 (436 μL, 5.0 mmol) was added dropwise and the resulting solution was stirred for 2 h. The mixture was cooled to −10 °C and Et_3N (3 equiv., freshly distilled, 2.1 mL, 15 mmol) was added dropwise, leading to the formation of a white precipitate. The mixture was allowed to warm to room temperature and maintained under these conditions for 15 min. It was then cooled to 0 °C and (+)-TADDOL (2.34 g, 5.0 mmol) was added in a single portion. The resulting yellowish mixture was allowed to warm to room temperature and stirred for 2 h prior to filtration with diethyl ether twice through Celite and once through a mixture of Celite and alumina. The solvents were partly removed at water-pump pressure and then completely removed by means of an oil vacuum pump. The ligand was obtained as a white foam. Purification by flash chromatography (R_f = 0.4; alumina, hexane/AcOEt, 95:5) furnished the title compound as a white foam (2.8 g, 76% yield). − $[\alpha]_D^{17}$ = +99 (*c* = 0.55 in $CHCl_3$). − ^1H NMR: δ = 0.29 (s, 3 H, 2-Me), 1.20 (s, 3 H, 2-Me), 0.80−2.00 (m, 6 H, cyclohex. H), 2.31−2.40 (m, 1 H, cyclohex. H), 2.75−2.90 (m, 1 H, cyclohex. H), 4.65−4.80 (m, 1 H, 1′-H), 4.80−4.90 (m, 3 H, 3a-H, 8a-H, 2′-H), 6.75−7.75 (m, 27 H, aryl H). − ^{31}P NMR: δ = 140.30. − $C_{43}H_{43}O_5P$ (670.8).

(1*R*,7*R*)-9,9-Dimethyl-4-(4-trimethylsilylbut-3-ynyloxy)-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (18); Method A′: To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) in THF (10 mL) at −70 °C was added butyllithium (3.5 mL of a 1.5 M solution in hexanes, 5.25 mmol) at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 1 h. A second flask was charged with THF (5 mL) and PCl_3 (228 μL, 2.63 mmol) and then cooled to −70 °C. The solution of lithium TADDOLate was slowly added by means of a cannula so as to maintain the internal temperature below −60 °C. The reaction mixture was allowed to warm to room temperature and was stirred for 1 h. Thereafter, ^{31}P NMR indicated the presence of TADDOL−PCl (δ = 148.9). A third flask was charged with 4-trimethylsilylbut-3-yn-1-ol[23] (393 mg, 2.75 mmol) and THF (5 mL) and then cooled to −10 °C. Butyllithium (1.87 mL of a 1.5 M solution in hexanes, 2.8 mmol) was added and the mixture was stirred for 10 min at room temperature and then transferred by means of a cannula to the solution of lithium TADDOLate at −70 °C, at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was then allowed to warm to room temperature and maintained under these conditions for 2 h. The solvent was then removed in vacuo, toluene (10 mL) was added, and the cloudy mixture was stirred for 18 h under argon prior to filtration through Celite. The solvent was removed in vacuo, and purification of the residue by flash chromatography (cyclohexane/diethyl ether/triethylamine, 95:5:1) followed by crystallization from a mixture of pentane and diethyl ether furnished the title compound as a white solid (870 mg, 1.37 mmol, 55%); m.p. 139−141 °C (pentane/diethyl ether). − $[\alpha]_D^{17}$ = −154 (*c* = 0.8 in $CHCl_3$). − ^1H NMR: δ = 0.17 [s, 9 H, $(CH_3)_3Si$], 0.66 (s, 3 H, CH_3-TADDOL), 0.86 (s, 3 H, CH_3-TADDOL), 2.29 (t, *J* = 7.3 Hz, 2 H, CH_2CH_2O), 3.87−3.72 (m, 2 H, CH_2O), 5.07 (dd, *J* = 8.4 Hz and 1.4 Hz, 1 H, 7-H), 5.28 (d, *J* = 8.4 Hz, 1 H, 1-H), 7.38−7.20 (m, 12 H, ArH), 7.61−7.48 (m, 8 H, ArH). − ^{13}C NMR: δ = 0.004, 22.3, 22.4, 26.2, 26.7, 61.0, 61.1, 80.9, 82.0, 82.3, 83.1, 84.8, 85.0, 86.1, 102.8, 112.6 (C-9), 126.9, 127.1, 127.6, 127.9, 128.0, 128.6, 128.9, 141.4, 146.0, 146.1. − ^{31}P NMR: δ = 132.10. − MS (CI, NH_3): *m*/*z* = 637 $[M + H]^+$, (< 1), 431 (100). − $C_{38}H_{41}O_5PSi$ (636.8): calcd. C 71.67, H 6.49; found C 71.60, H 6.37.

(1*R*,7*R*)-4-(2-Dimethylaminoethyloxy)-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (19); Method A′: To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) in THF (10 mL) at −80 °C was added butyllithium (3.4 mL of a 1.5 M solution in hexanes, 5.13 mmol) at such a rate as to keep the internal temperature below −50 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 2 h. A second flask was charged with THF (5 mL) and PCl_3 (228 μL, 2.63 mmol) and then cooled to −70 °C. The solution of lithium TADDOLate was slowly added by means of a cannula so as to maintain the internal temperature below −65 °C. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. Thereafter, ^{31}P NMR indicated the presence of Taddol−PCl (δ = 148.90). A third flask was charged with 2-dimethylaminoethanol (251 µL, 2.5 mmol) and THF (5 mL) and then cooled to −10 °C. Butyllithium (1.7 mL of a 1.5 M solution in hexanes, 2.5 mmol) was added and the mixture was stirred at room temperature for 5 min and then slowly added to the lithium TaddoLate solution at −70 °C at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was allowed to warm to room temperature and maintained under these conditions for 1 h. The solvent was then removed in vacuo, toluene (10 mL) was added, and the cloudy mixture was stirred for 18 h under argon prior to filtration through Celite. The solvent was removed in vacuo, and purification of the residue by flash chromatography (diethyl ether) followed by crystallization from a mixture of diethyl ether and pentane furnished the title compound as a white solid (1.12 g, 19.7 mmol, 79%); m.p. 139−141 °C (pentane/diethyl ether). − $[\alpha]_D^{18}$ = −186 (*c* = 0.72 in $CHCl_3$). − ^{1}H NMR: δ = 0.71 (s, 3 H, CH_3-Taddol), 0.81 (s, 3 H, CH_3-Taddol), 1.96 [s, 6 H, $(CH_3)_2N$], 2.23−2.16 (m, 2 H, CH_2N), 3.87−3.82 (m, 2 H, CH_2O), 5.47 (dd, *J* = 8.2 Hz and 1.4 Hz, 1 H, 7-H), 5.76 (d, *J* = 8.2 Hz, 1 H, 1-H), 7.14−6.99 (m, 12 H, ArH), 7.85−7.73 (m, 8 H, ArH). − ^{13}C NMR: δ = 26.2, 27.0, 45.8, 59.5, 60.4, 81.2, 82.5, 82.7, 85.0, 112.7 (C-9), 127.4, 127.8, 128.0, 128.3, 128.8, 129.2, 141.6, 146.3. − ^{31}P NMR: δ = 132.90. − MS (CI, NH_3): *m/z* (%) = 584 [M + H]$^+$ (30), 237 (100). − $C_{35}H_{38}O_5NP$ (583.7): calcd. C 72.02, H 6.56, N 2.40; found C 71.89, H 6.56, N 2.25.

(1*R*,7*R*)-9,9-Dimethyl-4-{(*S*)-2-[methyl-1-(phenylethyl)amino]-ethyloxy}-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo-[5.3.0]decane (20); Method A: To a stirred solution of (−)-Taddol (1.16 g, 2.5 mmol) and triethylamine (1.24 mL, 8.5 mmol) in THF (10 mL) at 0 °C was slowly added PCl_3 (236 µL, 2.6 mmol). A white precipitate was deposited and the reaction mixture was stirred at room temperature for 1.5 h. It was then cooled to 0 °C once more, whereupon a solution of (*S*)-2-[methyl(1-phenylethyl)amino]ethanol[24] (483 mg, 2.7 mmol) in THF (7 mL, 3 mL rinse) was added and stirring was continued for 2 h at room temperature. The reaction mixture was subsequently diluted with diethyl ether and filtered through a pad of Celite. The solvent was removed in vacuo, the residue was taken up in diethyl ether, and the resulting solution was filtered through Celite; this procedure was repeated until the addition of ether produced a clear solution. Purification by flash chromatography (cyclohexane/diethyl ether/triethylamine, 80:20:1) followed by crystallization from a mixture of diethyl ether and pentane furnished the title compound as a white solid (1.58 g, 2.3 mmol, 94%). − $[\alpha]_D^{18}$ = −169 (*c* = 1.06 in $CHCl_3$). − ^{1}H NMR: δ = 0.63 (s, 3 H, CH_3-Taddol), 0.98 (s, 3 H, CH_3-Taddol), 1.39 (d, *J* = 6.7 Hz, 3 H, CH_3CHN), 2.21 (s, 3 H, CH_3N), 2.43 (dt, *J* = 13.1 Hz and 6.3 Hz, 1 H, OCH_2CHHN), 2.57 (dt, *J* = 13.1 Hz and 6.7 Hz, 1 H, OCH_2CHHN), 3.63 (q, *J* = 6.7 Hz, 1 H, PhCHN), 3.98−3.89 (m, 2 H, CH_2O), 5.13 (br. d, *J* = 8.4 Hz, 1 H, 7-H), 5.27 (d, *J* = 8.4 Hz, 1 H, 1-H), 7.39−7.28 (m, 17 H, ArH), 7.60−7.50 (m, 8 H, ArH). − ^{13}C NMR: δ = 18.5, 26.4, 27.2, 39.4, 54.4, 61.1, 63.6, 81.2, 81.3, 82.2, 82.6, 82.9, 84.8, 84.9, 112.8 (C-9), 127.0, 127.2, 127.4, 127.5, 127.5, 127.9, 128.1, 128.3, 128.9, 129.2, 129.3, 129.2, 130.3, 141.6, 141.8, 143.7, 146.4. − ^{31}P NMR: δ = 133.31. − $C_{42}H_{44}O_5NP$ (673.8): calcd. C 74.87, H 6.58, N 2.08; found C 74.75, H 6.51, N 2.04.

(1*R*,7*R*)-9,9-Dimethyl-4-{(*R*)-2-[methyl-1-(phenylethyl)amino]-ethyloxy}-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo-[5.3.0]decane (21); Method A: To a stirred solution of (−)-Taddol (500 mg, 1.07 mmol) and triethylamine (461 µL, 3.3 mmol) in THF (5 mL) at 0 °C was slowly added PCl_3 (94 µL, 1.07 mmol). A white precipitate was deposited and the reaction mixture was stirred at room temperature for 10 min. It was then cooled to −10 °C, whereupon a solution of (*R*)-2-[methyl(1-phenylethyl)amino]ethanol[24] (192 mg, 1.07 mmol) in THF (5 mL) was added and stirring was continued for 1 h at room temperature. The reaction mixture was subsequently diluted with diethyl ether and filtered through a pad of Celite. The solvent was removed in vacuo, the residue was taken up in diethyl ether, and the resulting solution was filtered through Celite; this procedure was repeated until the addition of ether produced a clear solution. Purification by flash chromatography (cyclohexane/diethyl ether/triethylamine, 80:20:1) furnished the title compound as a white foam (600 mg, 0.89 mmol, 83%). − $[\alpha]_D^{18}$ = −140 (*c* = 0.82 in $CHCl_3$). − ^{1}H NMR: δ = 0.57 (s, 3 H, CH_3-Taddol), 0.93 (s, 3 H, CH_3-Taddol), 1.34 (d, *J* = 6.7 Hz, 3 H, CH_3CHN), 2.15 (s, 3 H, CH_3N), 2.36−2.30 (m, 1 H, OCH_2CHHN), 2.59−2.52 (m, 1 H, OCH_2CHHN), 3.57−3.55 (m, 1 H, PhCHN), 3.95−3.83 (m, 2 H, CH_2O), 5.05 (dd, *J* = 8.4 Hz and 1.7 Hz, 1 H, 7-H), 5.19 (d, *J* = 8.3 Hz, 1 H, 1-H), 7.33−7.25 (m, 21 H, ArH), 7.49−7.44 (m, 1 H, ArH), 7.52−7.51 (m, 1 H, ArH), 7.60−7.56 (m, 2 H, ArH). − ^{13}C NMR: δ = 16.7, 26.3, 27.1, 39.4, 54.3, 61.1, 63.7, 81.2, 82.2, 82.5, 82.8, 84.7, 112.7 (C-9), 127.0, 127.2, 127.3, 127.4, 127.8, 128.0, 128.3, 128.9, 129.2, 141.6, 143.8, 146.3. − ^{31}P NMR: δ = 133.20. − $C_{42}H_{44}O_5NP$ (673.8): calcd. C 74.87, H 6.58, N 2.08; found C 74.97, H 6.63, N 2.02.

(1*R*,7*R*)-9,9-Dimethyl-4-[(1*S*,2*R*)-2-dimethylamino-1-phenyl-propyloxy]-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo-[5.3.0]decane (22); Method A′: To a stirred solution of (−)-Taddol (1.16 g, 2.5 mmol) in THF (10 mL) at −70 °C was added butyllithium (3.5 mL of a 1.5 M solution in hexanes, 5.25 mmol) at such a rate as to keep the internal temperature below −50 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 2 h. A second flask was charged with THF (5 mL) and PCl_3 (228 µL, 2.63 mmol) and then cooled to −70 °C. The solution of lithium TaddoLate was slowly added by means of a cannula so as to maintain the internal temperature below −65 °C. The reaction mixture was then allowed to warm to room temperature and was stirred for 1 h. Thereafter, ^{31}P NMR indicated the presence of Taddol−PCl (δ = 148.90). A third flask was charged with (1*S*,2*R*)-2-dimethylamino-1-phenylpropanol (448 mg, 2.5 mmol) and THF (5 mL) and was cooled to −10 °C. Butyllithium (1.7 mL of a 1.5 M solution in hexanes, 2.5 mmol) was added and the mixture was stirred at room temperature for 5 min and then slowly added to the lithium TaddoLate solution at −70 °C at such a rate as to keep the internal temperature below −65 °C. The reaction mixture was then allowed to warm to room temperature and maintained under these conditions for 1 h. The solvent was then removed in vacuo, toluene (10 mL) was added, and the cloudy mixture was stirred for 18 h under argon prior to filtration through Celite. The solvent was subsequently removed in vacuo, and purification of the residue by flash chromatography (cyclohexane/diethyl ether/triethylamine, 80:20:1) furnished the title compound as a white foam (1.1 g, 1.6 mmol, 64%). − $[\alpha]_D^{18}$ = −162 (*c* = 0.56 in $CHCl_3$). − ^{1}H NMR: δ = 0.38 (s, 3 H, CH_3-Taddol), 0.99 (d, *J* = 6.8 Hz, 3 H, CH_3CHN), 1.07 (s, 3 H, CH_3-Taddol), 2.31 [s, 6 H, $(CH_3)_2N$], 2.76−2.70 (m, 1 H, CHN), 4.96 (d, *J* = 8.4 Hz, 1 H, 7-H), 5.16 (dd, *J* = 8.2 Hz and 2.0 Hz, 1 H, 1-H), 5.43 (dd, *J* = 9.4 Hz and 4.8 Hz, 1 H, PhCHOP), 7.33−7.18 (m, 25 H, ArH). − ^{13}C NMR: δ = 8.8, 25.9, 27.5, 41.7, 65.4, 81.6, 82.1, 82.5, 82.8, 112.8 (C-9), 127.1, 127.4, 127.6, 127.8, 128.2, 128.3, 128.9, 129.0, 141.3, 142.4, 145.9, 146.3. − ^{31}P NMR: δ = 142.50. − MS (CI,

NH_3): *m/z* (%) = 674 $[M + H]^+$ (70), 236 (100). − $C_{42}H_{44}O_5NP$ (673.8): calcd. C 74.87, H 6.58, N 2.08; found C 74.72, H 6.78, N 1.99.

(1*R*,7*R*)-9,9-Dimethyl-4-[(1*R*,2*S*)-2-dimethylamino-1-phenylpropyloxy]-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (23); Method A′: To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) in THF (10 mL) at −70 °C was added butyllithium (3.5 mL of a 1.5 M solution in hexanes, 5.25 mmol) at such a rate as to keep the internal temperature below −50 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 2 h. A second flask was charged with THF (5 mL) and PCl_3 (228 μL, 2.63 mmol) and then cooled to −70 °C. The solution of lithium TADDOLate was then slowly added by means of a cannula so as to maintain the internal temperature below −65 °C. The reaction mixture was then allowed to warm to room temperature and was stirred for 1 h. Thereafter, ^{31}P NMR indicated the presence of TADDOL−PCl (δ = 148.9). A third flask was charged with (1*R*,2*S*)-2-dimethylamino-1-phenylpropanol (448 mg, 2.5 mmol) and THF (5 mL) and then cooled to −10 °C. Butyllithium (1.7 mL of a 1.5 M solution in hexanes, 2.5 mmol) was added and the mixture was stirred at room temperature for 5 min and then slowly added to the lithium TADDOLate solution at −70 °C at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was then allowed to warm to room temperature and maintained under these conditions for 1 h. The solvent was removed in vacuo, toluene (10 mL) was added, and the cloudy mixture was stirred for 18 h under argon prior to filtration through Celite. The solvent was removed in vacuo, and purification of the residue by flash chromatography (cyclohexane/diethyl ether/triethylamine, 80:20:1) furnished the title compound as a white foam (650 mg, 0.97 mmol, 39%). − $[\alpha]_D^{18}$ = −217 (*c* = 0.62 in $CHCl_3$). − ^1H NMR: δ = 0.19 (s, 3 H, CH_3-TADDOL), 0.83 (d, *J* = 6.7 Hz, 3 H, CH_3CHN), 0.88 (s, 3 H, CH_3-TADDOL), 2.03 [s, 6 H, $(CH_3)_2N$], 2.58−2.50 (m, 1 H, CHN), 4.97 (d, *J* = 8.2 Hz, 1 H, 7-H), 5.02 (dd, *J* = 8.2 Hz and 1.8 Hz, 1 H, 1-H), 5.50 (dd, *J* = 9.2 Hz, *J* = 4.8 Hz, 1 H, PhCHOP), 7.38−6.78 (m, 25 H, ArH). − ^{13}C NMR: δ = 9.1, 25.9, 27.3, 41.3, 65.3, 80.9, 82.0, 82.4, 90.0, 112.7 (C-9), 126.9, 127.3, 127.5, 127.9, 128.1, 128.7, 129.1, 140.7, 142.4, 145.7, 146.3. − ^{31}P NMR: δ = 140.30. − MS (CI, NH_3): *m/z* (%) = 674 $[M + H]^+$ (80), 237 (100).

(1*R*,7*R*)-4-{(*S*)-1-[4-Isopropyl-1,3-oxazolin-2-yl]-1-methylethyloxy}-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (24); Method A′: To a stirred solution of (−)-TADDOL (582 mg, 1.25 mmol) in THF (5 mL) at −70 °C was added butyllithium (1.7 mL of a 1.5 M solution in hexanes, 2.56 mmol) at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 1.5 h. A second flask was charged with THF (5 mL) and PCl_3 (114 μL, 1.31 mmol) and then cooled to −80 °C. The solution of lithium TADDOLate was then slowly added by means of a cannula so as to maintain the internal temperature below −70 °C. The reaction mixture was allowed to warm to room temperature and was stirred for 1.5 h. Thereafter, ^{31}P NMR indicated the presence of TADDOL−PCl (δ = 148.9). A third flask was charged with (*S*)-2-hydroxydimethyl-4-isopropyl-1,3-oxazoline[25] (213 mg, 1.25 mmol) and THF (5 mL) and was cooled to 0 °C. Butyllithium (0.88 mL of a 1.5 M solution in hexanes, 1.31 mmol) was added until the solution just became yellow and then stirring was continued for 0.5 h. The resulting solution was then slowly added by means of a cannula (1 mL THF rinse) to the cold (−80 °C) solution of lithium TADDOL−PCl so as to maintain the internal temperature below −70 °C. The resulting suspension was stirred at −80 °C for 10 min, then allowed to warm to ambient temperature, and maintained under these conditions for 15 h. The solvent was subsequently removed in vacuo and purification of the residue by flash chromatography (two columns, eluting with cyclohexane/EtOAc/triethylamine, 90:10:1) furnished the title compound as a white foam (260 mg, 0.39 mmol, 31%). − $[\alpha]_D^{20}$ = −199 (*c* = 0.54 in $CHCl_3$). − ^1H NMR: δ = 0.72 (s, 3 H, CH_3-TADDOL), 0.73 (s, 3 H, CH_3-TADDOL), 0.80 [d, *J* = 6.8 Hz, 3 H, $(CH_3)_2CH$], 0.90 [d, *J* = 6.9 Hz, 3 H, $(CH_3)_2CH$], 1.20 [s, 3 H, $(CH_3)_2COP$], 1.30 [s, 3 H, $(CH_3)_2COP$], 1.77−1.68 [m, 1 H, $(CH_3)_2CH$], 3.96−3.87 (m, 2 H), 4.20−4.16 (m, 1 H), 5.05 (d, *J* = 8.3 Hz, 1 H, 7-H), 5.49 (d, *J* = 8.3 Hz, 1 H, 1-H), 7.36−7.24 (m, 10 H, ArH), 7.61−7.47 (m, 8 H, ArH). − ^{13}C NMR: δ = 17.7, 18.7, 26.5, 26.6, 26.9, 27.4, 27.6, 32.2, 70.0, 71.8, 74.7, 74.9, 80.0, 80.1, 82.0, 82.2, 83.9, 84.0, 85.1, 85.3, 112.7 (C-9), 126.9, 127.0, 127.1, 127.2, 127.4, 127.5, 127.6, 127.9, 129.0, 141.6, 142.0, 146.3, 146.5, 168.5 (C=N). − ^{31}P NMR: δ = 135.10. − MS (CI, NH_3): *m/z* (%) = 667 $[M + H]^+$ (100). − $C_{40}H_{44}NO_6P$ (665.8): calcd. C 72.16, H 6.66, N 2.10; found C 72.08, H 6.68, N 2.06.

(1*S*,7*S*)-4-{(*S*)-1-[4-Isopropyl-1,3-oxazolin-2-yl]-1-methylethyloxy}-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (25); Method A′: To a stirred solution of (+)-TADDOL (582 mg, 1.25 mmol) in THF (5 mL) at −70 °C was added butyllithium (1.7 mL of a 1.5 M solution in hexanes, 2.56 mmol) at such a rate as to keep the internal temperature below −65 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 1.75 h. A second flask was charged with THF (5 mL) and PCl_3 (114 μL, 1.31 mmol) and then cooled to −80 °C. The solution of lithium TADDOLate was slowly added by means of a cannula at such a rate as to maintain the internal temperature below −75 °C. The reaction mixture was then allowed to warm to room temperature and was stirred for 1.5 h. Thereafter, ^{31}P NMR indicated the presence of TADDOL−PCl (δ = 148.90). A third flask was charged with (*S*)-2-hydroxydimethyl-4-isopropyl-1,3-oxazoline[25] (213 mg, 1.25 mmol) and THF (5 mL) and was cooled to 0 °C. Butyllithium (0.88 mL of a 1.5 M solution in hexanes, 1.31 mmol) was added until the solution just became yellow and stirring was continued for 0.5 h. The resulting solution was then slowly added by means of a cannula (1 mL THF rinse) to the cold (−80 °C) solution of lithium TADDOL−PCl so as to maintain the internal temperature below −70 °C. The resulting suspension was stirred at −80 °C for 10 min, then allowed to warm to ambient temperature, and maintained under these conditions for 4 h. The solvent was subsequently removed in vacuo, toluene (10 mL) was added, and the resulting suspension was stirred for 18 h prior to filtration through Celite. The solvent was removed in vacuo and purification of the residue by flash chromatography (two columns, eluting with cyclohexane/EtOAc/triethylamine, 90:10:1, and then cyclohexane/diethyl ether/triethylamine, 90:10:1) furnished the title compound as a white foam (308 mg, 0.46 mmol, 37%). − $[\alpha]_D^{20}$ = +139 (*c* = 0.64 in $CHCl_3$). − ^1H NMR: δ = 0.73 (s, 3 H, CH_3-TADDOL), 0.74 (s, 3 H, CH_3-TADDOL), 0.81 [d, *J* = 6.8 Hz, 3 H, $(CH_3)_2CH$], 0.91 [d, *J* = 6.8 Hz, 3 H, $(CH_3)_2CH$], 1.26 [s, 3 H, $(CH_3)_2COP$], 1.30 [s, 3 H, $(CH_3)_2COP$], 1.77−1.69 [m, 1 H, $(CH_3)_2CH$], 3.90−3.84 (m, 1 H), 3.98−3.95 (m, 1 H), 4.15 (dd, *J* = 9.4 Hz and 8.4 Hz, 1 H), 5.06 (d, *J* = 8.3 Hz, 1 H, 7-H), 5.51 (d, *J* = 8.3 Hz, 1 H, 1-H), 7.38−7.21 (m, 10 H, ArH), 7.61−7.50 (m, 8 H, ArH). − ^{13}C NMR: δ = 17.7, 18.7, 26.8, 27.6, 32.2, 70.0, 71.6, 74.6, 74.9, 80.2, 82.2, 83.7, 85.2, 112.6 (C-9), 127.0, 127.2, 127.5, 127.8, 129.1, 141.7, 142.0, 146.2, 146.4, 168.4 (C=N). − ^{31}P NMR: δ = 135.7. − MS

(CI, NH_3): *m/z* (%) = 667 $[M + H]^+$ (100). − $C_{40}H_{44}NO_6P$ (665.8): calcd. C 72.16, H 6.66, N 2.10; found C 72.02, H 6.73, N 2.06.

(1*R*,7*R*)-4-(Diisopropylamino)-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (26); Method A′: To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) in THF (10 mL) at −70 °C was added butyllithium (3.4 mL of a 1.5 M solution in hexanes, 5.13 mmol) at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 1 h. A second flask was charged with THF (10 mL) and PCl_3 (228 μL, 2.63 mmol) and then cooled to −80 °C. The solution of lithium TADDOLate was slowly added by means of a cannula so as to maintain the internal temperature below −65 °C. The reaction mixture was allowed to warm to room temperature and was stirred for 2 h. Thereafter, ^{31}P NMR indicated the presence of TADDOL−PCl (δ = 148.9). The reaction mixture was cooled to −70 °C, whereupon a solution of LDA [prepared from diisopropylamine (350 μL, 2.5 mmol) and butyllithium (1.6 mL of a 1.5 M solution in hexanes, 2.4 mmol) in THF (5 mL)] was slowly added by means of a cannula. The reaction mixture was allowed to warm to room temperature, stirred for 2 h, and then the solvent was removed in vacuo. To the semi-solid residue was added pentane (20 mL) and the resulting suspension was stirred for 1 h prior to filtration through Celite. The solvent was removed in vacuo, toluene (10 mL) was added, and the resulting suspension was stirred for 18 h prior to filtration through Celite. Purification by flash chromatography (cyclohexane/diethyl ether/triethylamine, 95:5:1) followed by crystallization from pentane furnished the title compound as a white crystalline solid (400 mg, 0.67 mmol, 27%); m.p. 174−175 °C (pentane). − $[\alpha]_D^{18} = -83.4$ (*c* = 0.7 in CH_2Cl_2). − ^1H NMR: δ = 0.30 (s, 3 H, CH_3-TADDOL), 1.13 {d, *J* = 6.8 Hz, 6 H, $[(CH_3)_2CH]_2N$}, 1.18 {d, *J* = 6.8 Hz, 6 H, $[(CH_3)_2CH]_2N$}, 1.38 (s, 3 H, CH_3-TADDOL), 3.97−3.91 {m, 2 H, $[(CH_3)_2CH]_2N$}, 5.10 (d, *J* = 8.6 Hz, 1 H, 7-H), 5.71 (dd, *J* = 8.6 Hz and 3.9 Hz, 1 H, 1-H), 7.19−7.01 (m, 12 H, ArH), 7.74−7.72 (m, 2 H, ArH), 7.89−7.82 (m, 4 H, ArH), 8.14−8.11 (m, 2 H, ArH). − ^{13}C NMR: δ = 24.5, 24.6, 24.7, 24.8, 25.5, 28.2, 44.6, 44.7, 81.0, 81.5, 81.6, 82.9, 83.1, 83.6, 111.4 (C-9), 127.5, 127.6, 127.9, 128.2, 129.5, 142.3, 143.3, 147.4, 147.8. − ^{31}P NMR: δ = 142.31. − MS (CI, NH_3): *m/z* (%) = 612 $[M + H + 16]^+$ (100), 596 $[M + H]^+$ (20). − $C_{37}H_{42}O_4P$ (581.7): calcd. C 74.60, H 7.11, N 2.35; found C 74.80, H 7.18, N 2.27.

(1*R*,7*R*)-4-Dimethylamino-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (27): Prepared according to Scheme 8. To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) in toluene (10 mL) was added HMPT (0.54 mL, 3.26 mmol) and the resulting solution was heated under reflux for 2 d, during which a slow flow of nitrogen was passed through the top of the reflux condenser. The solvent was subsequently removed in vacuo and purification of the residue by flash chromatography (cyclohexane/EtOAc/triethylamine, 95:5:1) followed by crystallization from a mixture of diethyl ether and CH_2Cl_2 furnished the title compound as a white solid (340 mg, 0.63 mmol, 25%); m.p. > 220 °C (diethyl ether/CH_2Cl_2). − $[\alpha]_D^{18} = -151$ (*c* = 0.69 in $CHCl_3$). − ^1H NMR: δ = 0.34 (s, 3 H, CH_3-TADDOL), 1.33 (s, 3 H, CH_3-TADDOL), 2.78 [d, 6 H, *J* = 10.5 Hz, $(CH_3)_2N$], 4.87 (d, *J* = 8.4 Hz, 1 H, 7-H), 5.24 (dd, *J* = 8.4 Hz and 3.1 Hz, 1 H, 1-H), 7.37−7.28 (m, 12 H, ArH), 7.47 (d, *J* = 7.3 Hz, 2 H, ArH), 7.53 (d, *J* = 7.3 Hz, 2 H, ArH), 7.65 (d, *J* = 7.4 Hz, 2 H, ArH), 7.79 (d, *J* = 7.2 Hz, 2 H, ArH). − ^{13}C NMR: δ = 25.5, 27.4, 35.4, 35.7, 81.3, 81.5, 82.0, 82.4, 82.7, 111.9 (C-9), 127.3, 127.5, 127.7, 127.9, 128.9, 128.9, 129.2, 142.0, 142.3, 146.7, 147.1. − ^{31}P NMR: δ = 140.60. − MS (CI, NH_3): *m/z* (%) = 540 $[M + H]^+$ (100). − $C_{33}H_{34}NO_4P$ (539.6): calcd. C 73.45, H 6.35, N 2.60; found C 73.32, H 6.36, N 2.46.

(1*R*,7*R*)-4-Methylamino-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (28); Method A: To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) and triethylamine (1.24 mL, 8.5 mmol) in THF (10 mL) at 0 °C was slowly added PCl_3 (236 μL, 2.6 mmol). A white precipitate was deposited and the reaction mixture was stirred at room temperature for 1 h and then cooled to 0 °C once more. Methylamine (1.38 mL of a 2.0 M solution in THF, 2.75 mmol) was added and stirring was continued for 1 h at room temperature. The reaction mixture was diluted with diethyl ether and filtered through a pad of Celite. The solvent was removed in vacuo, the residue was taken up in diethyl ether, and the resulting solution was filtered through Celite; this procedure was repeated until the addition of ether produced a clear solution. The title compound was isolated as an unstable white foam (1.32 g, 2.5 mmol, 100%). − ^1H NMR: δ = 0.33 (s, 3 H, CH_3-TADDOL), 1.30 (s, 3 H, CH_3-TADDOL), 2.58 (dq, *J* = 33.2 Hz and 5.6 Hz, 1 H, NH), 2.83 (dd, *J* = 8.5 Hz and 5.6 Hz, 3 H, CH_3N), 4.87 (d, *J* = 8.5 Hz, 1 H, 7-H), 5.22 (dd, *J* = 8.5 Hz and 3.3 Hz, 1 H, 1-H), 7.32−7.21 (m, 16 H, ArH), 7.46 (d, *J* = 7.5 Hz, 2 H, ArH), 7.52 (d, *J* = 7.7 Hz, 2 H, ArH), 7.65 (d, *J* = 7.6 Hz, 1 H, ArH), 7.79 (d, *J* = 7.4 Hz, 2 H, ArH). − ^{31}P NMR: δ = 137.90. − MS (CI, NH_3): *m/z* (%) = 526 $[M + H]^+$ (80), 431 (100).

(1*R*,7*R*)-4-{(*S*,*S*)-[Bis(1-phenylethyl)]amino}-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (29); Method A′: To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) in THF (10 mL) at −70 °C was added butyllithium (3.4 mL of a 1.5 M solution in hexanes, 5.13 mmol) at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 1.5 h. A second flask was charged with THF (10 mL) and PCl_3 (228 μL, 2.63 mmol) and then cooled to −80 °C. The solution of lithium TADDOLate was slowly added by means of a cannula so as to maintain the internal temperature below −65 °C. The reaction mixture was then allowed to warm to room temperature and was stirred for 1.5 h. Thereafter, ^{31}P NMR indicated the presence of TADDOL−PCl (δ = 148.9). A third flask was charged with (*S,S*)-[bis(1-phenylethyl)]amine (562 mg, 2.5 mmol) and THF (5 mL) and was cooled to −10 °C. Butyllithium (1.75 mL of a 1.5 M solution in hexanes, 2.63 mmol) was added and stirring was continued for 0.5 h at −10 °C. The resulting solution was then slowly added by means of a cannula to the cold (−60 °C) solution of TADDOL−PCl so as to maintain the internal temperature below −55 °C. The brown solution was subsequently allowed to warm to room temperature and stirred for 18 h. The solvent was removed in vacuo, toluene (10 mL) was added, and the resulting suspension was stirred for 3 h prior to filtration through Celite. Purification by flash chromatography (two columns, eluting with cyclohexane/EtOAc/triethylamine, 95:5:1) furnished the title compound as a white foam (250 mg, 0.34 mmol, 14%). − $[\alpha]_D^{18} = -147.1$ (*c* = 0.21 in $CHCl_3$). − ^1H NMR: δ = 0.21 (s, 3 H, CH_3-TADDOL), 1.42 (s, 3 H, CH_3-TADDOL), 1.70 (d, *J* = 7.1 Hz, 6 H, 2 × CH_3CHN), 4.77 (d, *J* = 8.6 Hz, 1 H, 7-H), 5.03−4.85 (m, 2 H, 2 × CH_3CHN), 5.29 (dd, *J* = 8.6 Hz and 3.8 Hz, 1 H, 1-H), 7.00 (br. m, 10 H, ArH), 7.52−7.16 (m, 18 H, ArH), 7.94−7.89 (m, 2 H, ArH). − ^{13}C NMR: δ = 21.7, 25.3, 27.9, 52.5, 52.7, 81.6, 81.9, 82.3, 83.1, 111.3 (C-9), 126.4, 127.3, 127.4, 127.6, 127.9, 128.3, 129.3, 129.6, 142.2, 142.6, 143.8, 146.7, 146.9. − ^{31}P NMR: δ = 140.20. − MS (CI, NH_3): *m/z* (%) = 721 $[M + H]^+$ (8), 226 (100). − $C_{47}H_{46}NO_4P$ (719.9): calcd. C 78.42, H 6.44; found C 78.35, H 6.51.

(1S,7S)-4-{(S,S)-[Bis(1-phenylethyl)]amino}-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (30); Method A′: To a stirred solution of (+)-TADDOL (1.16 g, 2.5 mmol) in THF (10 mL) at −70 °C was added butyllithium (3.4 mL of a 1.5 M solution in hexanes, 5.13 mmol) at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 1.5 h. A second flask was charged with THF (10 mL) and PCl_3 (228 μL, 2.63 mmol) and then cooled to −80 °C. The solution of lithium TADDOLate was slowly added by means of a cannula so as to maintain the internal temperature below −65 °C. The reaction mixture was then allowed to warm to room temperature and was stirred for 1.5 h. Thereafter, ^{31}P NMR indicated the presence of TADDOL−PCl ($\delta = 148.9$). A third flask was charged with (S,S)-[bis(1-phenylethyl)]amine hydrochloride (655 mg, 2.5 mmol) and THF (5 mL) and was cooled to −10 °C. Butyllithium (3.4 mL of a 1.5 M solution in hexanes, 5.13 mmol) was added and stirring was continued for 0.5 h at −10 °C. The resulting solution was then slowly added by means of a cannula to the cold (−60 °C) solution of lithium TADDOL−PCl so as to maintain the internal temperature below −65 °C. The brown solution was allowed to warm to room temperature and was stirred for 18 h. The solvent was subsequently removed in vacuo, toluene (10 mL) was added, and the resulting suspension was stirred for 2 h prior to filtration through Celite. Purification by flash chromatography (two columns, eluting first with cyclohexane/EtOAc/triethylamine, 95:5:1, and then with pentane/EtOAc/triethylamine, 95:5:1) furnished the title compound as a white foam (180 mg, 0.25 mmol, 10%). − $[\alpha]_D^{18} = +18.2$ ($c = 1.2$ in $CHCl_3$). − ^1H NMR: $\delta = 0.24$ (s, 3 H, CH_3-TADDOL), 1.45 (s, 3 H, CH_3-TADDOL), 1.71 (d, $J = 7.1$ Hz, 6 H, 2 × CH_3CHN), 4.82 (d, $J = 8.6$ Hz, 1 H, 7-H), 5.03−4.85 (m, 2 H, 2 × CH_3CHN), 5.17 (dd, $J = 8.6$ Hz and 3.6 Hz, 1 H, 1-H), 7.70−7.10 (m, 30 H, ArH). − ^{13}C NMR: $\delta = 21.5$, 24.9, 27.6, 51.9, 52.1, 80.5, 80.6, 80.8, 81.0, 82.7, 111.0 (C-9), 126.3, 127.4, 128.9, 141.8, 143.3, 147.1. − ^{31}P NMR: $\delta = 140.70$. − MS (CI, NH_3): m/z (%) = 721 $[M + H]^+$ (11), 226 (100).

(1R,7R)-4-n-Butyl-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (31); Method A′: To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) in THF (10 mL) at −70 °C was added butyllithium (3.4 mL of a 1.5 M solution in hexanes, 5.13 mmol) at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 1 h. A second flask was charged with THF (10 mL) and PCl_3 (228 mL, 2.63 mmol) and then cooled to −80 °C. The solution of lithium TADDOLate was slowly added by means of a cannula so as to maintain the internal temperature below −65 °C. The reaction mixture was then allowed to warm to room temperature and was stirred for 2 h. Thereafter, ^{31}P NMR indicated the presence of TADDOL−PCl ($\delta = 148.9$). The mixture was then cooled to −70 °C and butyllithium (1.6 mL of a 1.5 M solution in hexanes, 2.4 mmol) was slowly added. The resulting mixture was allowed to warm to room temperature, stirred for 2 h, and then the solvent was removed in vacuo. To the semi-solid residue was added pentane (20 mL) and the resulting suspension was stirred for 1 h prior to filtration through Celite. The solvent was removed in vacuo, toluene (10 mL) was added, and the resulting suspension was stirred for 1 h prior to filtration through Celite. The solvent was removed in vacuo. Purification by flash chromatography on Al_2O_3 (pentane/diethyl ether, 80:20; $R_f = 0.8$) furnished the title compound as a white foam. − $[\alpha]_D^{20} = -67$ ($c = 0.65$ in $CHCl_3$). − ^1H NMR: $\delta = 0.19$ (s, 3 H, CH_3-TADDOL), 1.4 (s, 3 H, CH_3-TADDOL), 1.80−0.80 [6 m, CH_2 and CH_3 (nBu)], 4.67 (d, $J = 8.6$ Hz, 1 H, CHO), 5.50 (dd, $J = 8.6$ Hz and 4.6 Hz, 1 H, CHO), 7.8−7.2 (4 m, ArH). − ^{13}C NMR: $\delta = 13.8$, 14.0, 22.6, 23.7, 24.0, 24.1, 24.6, 27.7, 29.6, 31.8, 35.5, 35.6, 81.4, 82.3, 82.5, 83.7, 111.0, 129.3−127.0 (Ph), 141.6, 142.0, 146.1, 149.0. − ^{31}P NMR: $\delta = 177.40$.

(1R,7R)-4-$tert$-Butyl-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (32); Method C: To a stirred solution of (−)-TADDOL (1.86 g, 4 mmol) in THF (15 mL) at −70 °C was added butyllithium (6 mL of a 1.5 M solution in hexanes, 8.8 mmol) at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 1 h. A second flask was charged with THF (10 mL) and tBu−PCl_2 (0.636 mL, 4 mmol) and then cooled to −80 °C. The solution of lithium TADDOLate was slowly added by means of a cannula so as to maintain the internal temperature below −65 °C. The reaction mixture was then allowed to warm to room temperature and was stirred for 2 h. Thereafter, ^{31}P NMR indicated the presence of TADDOL-P−tBu ($\delta = 177$). The solvent was then removed in vacuo. To the semi-solid residue was added pentane (20 mL) and the resulting suspension was stirred for 1 h prior to filtration through Celite. The solvent was removed in vacuo, toluene (10 mL) was added, and the resulting suspension was stirred for 1 h prior to filtration through Celite. The solvent was removed in vacuo and purification of the residue by chromatography on Al_2O_3 (pentane/diethyl ether, 80:20; $R_f = 0.8$) furnished the title compound as a white foam. − $[\alpha]_D^{20} = -62$ ($c = 0.55$ in $CHCl_3$). − ^1H NMR: $\delta = 0.25$ (s, 3 H, CH_3-TADDOL), 1.31 [d, $J = 12.7$ Hz, CH_3 (tBu)], 1.60 (s, 3 H, CH_3-TADDOL), 4.74 (d, $J = 8.4$ Hz, 1 H, CHO), 5.65 (dd, 1 H, CHO), 7.9−7.3 (4 m, ArH). − ^{13}C NMR: $\delta = 22.4$, 23.7, 23.8, 24.6, 27.7, 35.0, 81.9, 82.5, 82.6, 83.6, 111.0, 129.4−126.9 (Ph), 142.1,146.6. − ^{31}P NMR: $\delta = 171.00$.

(1R,7R)-9,9-Dimethyl-2,2,4,6,6-pentaphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (33); Method C: To a stirred solution of (−)-TADDOL (1.86 g, 4 mmol) in THF (15 mL) at −70 °C was added butyllithium (6 mL of a 1.5 M solution in hexanes, 8.8 mmol) at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 1 h. A second flask was charged with THF (10 mL) and Ph−PCl_2 (0.546 mL, 4 mmol) and then cooled to −80 °C. The solution of lithium TADDOLate was slowly added by means of a cannula so as to maintain the internal temperature below −65 °C. The reaction mixture was then allowed to warm to room temperature and was stirred for 2 h. Thereafter, ^{31}P NMR indicated the presence of TADDOL-P−Ph ($\delta = 177.00$). The solvent was then removed in vacuo. To the semi-solid residue was added pentane (20 mL) and the resulting suspension was stirred for 1 h prior to filtration through Celite. The solvent was removed in vacuo, toluene (10 mL) was added, and the resulting suspension was stirred for 1 h prior to filtration through Celite. The solvent was removed in vacuo and purification of the residue by chromatography on Al_2O_3 (cyclohexane/EtOAc/triethylamine, 90:10:1) furnished the title compound as a white solid (400 mg, 0.66 mmol, 28%); m.p. > 200 °C [ref.[19] m.p. 206−209 °C (decomp.)]. − $[\alpha]_D^{22} = -87$ ($c = 1.2$ in $CHCl_3$) {ref.[19] $[\alpha]_D^{r.t.} = -85.9$ ($c = 1.14$ in $CHCl_3$)}. − ^1H NMR: $\delta = 0.21$ (s, 3 H, CH_3), 1.55 (s, 3 H, CH_3), 4.78 (d, $J = 8.6$ Hz, 1 H, CHOP), 5.62 (dd, $J = 8.6$ Hz, $J_{HP} = 4.5$ Hz, 1 H, CHOP), 7.92−7.15 (m, 25 H, ArH). − ^{13}C NMR: $\delta = 24.8$, 27.9, 82.2, 82.4, 82.7, 83.16, 83.3, 83.9, 111.4, 127.2, 127.3, 127.4, 127.6, 127.9, 128.1, 128.4, 128.6, 129.4, 129.7, 130.1, 130.7, 141.1, 141.2, 141.4, 141.9, 145.8, 145.9, 146.8. − ^{31}P NMR: $\delta = 157.70$.

(1*R*,7*R*)-4-(2-Methoxyphenyl)-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (34); Method A′: To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) in THF (10 mL) at −70 °C was added butyllithium (3.5 mL of a 1.5 M solution in hexanes, 5.25 mmol) at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 2 h. A second flask was charged with THF (5 mL) and $\mathrm{PCl_3}$ (228 µL, 2.63 mmol) and then cooled to −70 °C. The solution of lithium TADDOLate was slowly added by means of a cannula so as to maintain the internal temperature below −60 °C. The reaction mixture was then allowed to warm to room temperature and was stirred for 1.5 h. Thereafter, ^{31}P NMR indicated the presence of TADDOL-PCl ($\delta = 148.90$). A third flask was charged with 2-bromoanisole (512 mg, 2.75 mmol) and diethyl ether (10 mL) and was cooled to −40 °C. Butyllithium (1.87 mL of a 1.5 M solution in hexanes, 2.8 mmol) was added and stirring was continued for 40 min at −40 °C. The resulting solution was added by means of cannula to the solution of lithium TADDOLate at −70 °C so as to keep the internal temperature below −65 °C.[26] The reaction mixture was allowed to warm to room temperature and maintained under these conditions for 0.5 h. The solvent was then removed in vacuo, toluene (10 mL) was added, and the cloudy mixture was stirred for 18 h under argon prior to filtration through Celite. The solvent was removed in vacuo, and purification of the residue by flash chromatography (cyclohexane/EtOAc/triethylamine, 90:10:1) followed by crystallization from pentane furnished the title compound as a white solid (355 mg, 0.66 mmol, 27%); m.p. 178 °C (decomp.) (pentane). − $[\alpha]_D^{17} = -72.0$ ($c = 0.59$ in $\mathrm{CHCl_3}$). − ^{1}H NMR: $\delta = 0.22$ (s, 3 H, $\mathrm{CH_3}$-TADDOL), 1.58 (s, 3 H, $\mathrm{CH_3}$-TADDOL), 3.86 (s, 3 H, $\mathrm{CH_3O}$), 4.80 (d, $J = 8.7$ Hz, 1 H, 7-H), 5.66 (dd, $J = 8.7$ Hz and 4.4 Hz, 1 H, 1-H), 6.90−6.95 (m, 1 H, ArH), 7.54−7.15 (m, 20 H, ArH), 7.64 (d, $J = 7.4$ Hz, 1 H, ArH), 8.00 (d, $J = 7.4$ Hz, 1 H, ArH), 8.17−8.12 (m, 1 H, ArH). − ^{13}C NMR: $\delta = 24.7$, 27.9, 55.2, 81.9, 82.3, 82.8, 83.1, 84.0, 110.3, 111.2, 120.9, 127.2, 127.4, 127.6, 127.8, 127.9, 128.3, 128.6, 129.5, 129.8, 130.1, 130.3, 132.1, 132.6, 141.7, 146.0, 146.5, 161.3, 161.7. − ^{31}P NMR: $\delta = 152.20$. − MS (CI, $\mathrm{NH_3}$): *m*/*z* (%) = 603 [M + H]$^+$ (80), 373 (100). − $\mathrm{C_{38}H_{35}O_5P}$: calcd. C 75.73, H 5.85; found C 75.57, H 6.01.

(1*R*,7*R*)-4-Ferrocenyl-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (35); Method C: To a stirred solution of (−)-TADDOL (1.16 g, 2.5 mmol) in THF (10 mL) at −70 °C was added butyllithium (3.5 mL of a 1.5 M solution in hexanes, 5.25 mmol) at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 2 h. A second flask was charged with THF (5 mL) and $\mathrm{PCl_3}$ (228 µL, 2.63 mmol) and then cooled to −70 °C. The solution of lithium TADDOLate was slowly added by means of a cannula so as to maintain the internal temperature below −60 °C. The reaction mixture was allowed to warm to room temperature and was stirred for 2 h. Thereafter, ^{31}P NMR indicated the presence of TADDOL−PCl ($\delta = 148.9$). A third flask was charged with ferrocene[27] (697 mg, 3.75 mmol) and THF (5.5 mL) and was cooled to 0 °C. *tert*-Butyllithium (1.9 mL of a 1.7 M solution in pentane, 3.25 mmol) was added and the mixture was stirred for 15 min at 0 °C and then allowed to warm to room temperature. The resulting solution of ferrocenyllithium was added by means of a cannula to the solution of lithium TADDOLate at −70 °C at such a rate as to keep the internal temperature below −65 °C. The reaction mixture was allowed to warm to room temperature and maintained under these conditions for 1 h. The solvent was subsequently removed in vacuo, toluene (10 mL) was added, and the cloudy mixture was stirred for 18 h under argon prior to filtration through Celite. The solvent was removed in vacuo, and purification by flash chromatography (cyclohexane/diethyl ether/triethylamine, 95:5:1) followed by crystallization from a mixture of $\mathrm{CH_2Cl_2}$ and diethyl ether furnished the title compound as an orange solid (355 mg, 0.57 mmol, 23%); m.p. > 200 °C ($\mathrm{CH_2Cl_2}$/diethyl ether). − $[\alpha]_D^{17} = -98.5$ ($c = 0.67$ in $\mathrm{CHCl_3}$). − ^{1}H NMR: $\delta = 0.22$ (s, 3 H, $\mathrm{CH_3}$-TADDOL), 1.52 (s, 3 H, $\mathrm{CH_3}$-TADDOL), 4.14 (s, 5 H, ferrocenyl-H), 4.42 (br. m, 1 H, ferrocenyl-H), 4.45 (br. m, 1 H, ferrocenyl-H), 4.53 (br. m, 1 H, ferrocenyl-H), 4.60 (br. m, 1 H, ferrocenyl-H), 4.71 (d, $J = 8.6$ Hz, 1 H, 7-H), 5.66 (dd, $J = 8.6$ Hz and 4.7 Hz, 1 H, 1-H), 7.45−7.25 (m, 16 H, ArH), 7.77 (d, $J = 7.3$ Hz, 2 H, ArH), 7.89 (d, $J = 7.4$ Hz, 2 H, ArH). − ^{13}C NMR: $\delta = 25.0$, 27.8, 68.9, 69.5, 69.8, 70.1, 82.1, 83.0, 83.6, 111.4 (C-9), 127.2, 127.4, 127.6, 127.9, 128.2, 128.8, 129.6, 141.7, 142.5, 146.4, 146.9. − ^{31}P NMR: $\delta = 163.71$. − MS (CI, $\mathrm{NH_3}$): *m*/*z* (%) = 681 [M + H]$^+$ (50), 373 (100).

(1*R*,7*R*)-9,9-Dimethyl-2,2,6,6-tetra(1-naphthyl)-4-phenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (36); Method C: 36 was prepared according to the same procedure as that used for **33** starting from 2,2-dialkyl-α,α,α′,α′-tetra(1-naphthyl)-1,3-dioxolane-4,5-dimethanol (334 mg, 0.5 mmol). Purification by flash chromatography was not possible. Nevertheless, the ^{31}P NMR spectrum showed a single signal ($\delta = 156.02$), assumed to be attributable to the product. ^{1}H NMR showed by-products in low percentages. The compound was used without further purification.

(1*R*,7*R*)-9,9-Dimethyl-2,2,6,6-tetra(2-naphthyl)-4-phenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (37); Method C: To a stirred solution of (−)-2-naphtho-TADDOL (0.5 g, 4 mmol) in THF (3 mL) at −70 °C was added butyllithium (1.1 mL of a 1.5 M solution in hexanes, 1.7 mmol) at such a rate as to keep the internal temperature below −60 °C. The reaction mixture was stirred at −70 °C for 10 min, then allowed to warm to room temperature, and maintained under these conditions for 1 h. A second flask was charged with THF (1 mL) and Ph−$\mathrm{PCl_2}$ (4 mmol) and then cooled to −80 °C. The solution of lithium TADDOLate was slowly added by means of a cannula so as to maintain the internal temperature below −65 °C. The reaction mixture was then allowed to warm to room temperature and was stirred for 2 h. Thereafter, ^{31}P NMR indicated the presence of 2-naphtho-TADDOL−PPh ($\delta = 158.1$). After removal of the solvent, filtration through alumina, and concentration of the filtrate in vacuo, we obtained the product as a white powder in 28% yield (ref.[19]). − ^{1}H NMR: $\delta = 0.12$ (s, 3 H, $\mathrm{CH_3}$-TADDOL), 1.7 (s, 3 H, $\mathrm{CH_3}$), 5.2 (d, $J = 8.6$ Hz, 1 H, CHO), 6.0 (dd, $J = 8.6$ Hz, 1 H, CHO), 8.7−7.4 (m, ArH). − ^{13}C NMR: $\delta = 25.3$, 28.0, 82.5, 82.7, 82.8, 83.6, 83.7, 83.9, 111.8, 125.8, 126.0, 126.3, 126.5, 127.1, 127.4, 127.6, 127.8, 127.9, 128.2, 128.5, 128.6, 128.8, 129.8, 130.1, 130.8, 132.5, 132.7, 132.8, 138.7, 138.9, 141.2, 143.0, 143.7. − ^{31}P NMR: $\delta = 158.10$.

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