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Synthesis of Functionalized 1,4-Cyclohexadienes through Intramolecular Anionic Dearomatization of *N*-Alkyl-*N*-benzyldiphenylphosphinamides. Insight into the Reaction Mechanism

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A generalization of the intramolecular nucleophilic dearomatization−electrophilic alkylation reactions of *N*-alkyl-*N*-benzyldiphenylphosphinamide anions is presented. The process has been optimized by analyzing the effects of metalation and quench times, additives, the nature of the electrophiles used (MeI, CF_3SO_3Me, $Me_3O^+BF_4^-$, AllylBr, $PhCH_2Br$, $BrCH_2CO_2Me$, and RCH═O, where R = Ph, 4-Cl−C_6H_4, 4-MeO−C_6H_4, and ^{i}Pr), and the alkyl substituent linked to the nitrogen of the phosphinamide. Both HMPA and DMPU act as catalysts. The latter proved to be much more efficient for obtaining high yields of substituted tetrahydrobenzo[*c*][1,2]-1λ^5-phospholes containing a 1,4-cyclohexadiene system with very high regio- and diastereoselectivity. Steric effects in the neighborhood of the benzylic anion tend to decrease the stereoselectivity of the anionic cyclization. The optimization study also served to shed light on the reaction mechanism of the dearomatization process by identifying several intermediate species and showing the reversibility of the anionic cyclization step as well as of the reaction with aldehydes.

1. Introduction

Dearomatization reactions of arenes have considerable potential because they allow the use of stable and widely available materials as synthons in the synthesis of functionalized alicyclic compounds. A variety of methods have been devised for breaking up the conjugated π-system, which include oxidation,[1] reduction,[2] photocycloaddition,[3] and electrophilic[4] and nucleophilic addition to activated arenes. This synthetic strategy represents a valuable tool for the preparation of bioactive substances.[5]

Nucleophilic addition to arenes requires the activation of the aromatic system. This activation may be achieved by complexation to transition metals[6] or through bonding to electron-withdrawing groups. Generally, the Michael acceptors used for the activation of the aromatic ring are based on carbonyl-bearing functional groups (e.g., aldehyde and ketone,[7,8] carboxylic acid,[9] carboxylic ester,[10]

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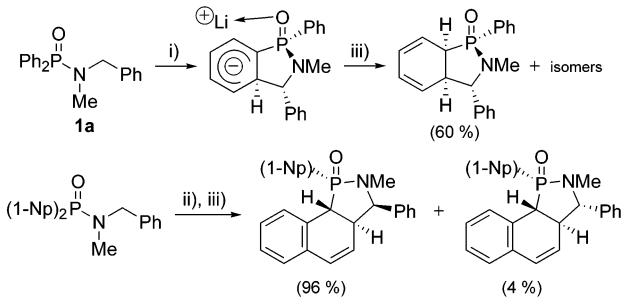
and acyl halide[11]) or some nitrogenated derivatives (e.g., imines,[12] carboxamides,[13] nitriles,[14] oxazolidines,[15] oxazolines,[16] and triazenes[17]). Clayden et al. have shown that for lithium tertiary *N*-benzylcarboxamides, the dearomatization occurs intramolecularly with excellent regio- and stereocontrol, leading to the formation of a substituted pyrrolid-2-one[18] or azepin-2-one ring.[19] The five-membered heterocycles have been used as precursors in the synthesis of natural products[20] and nonnatural analogues.[21]

Lithiated phenyl sulfones[22] and *N*-benzylsulfonamides[23] also participate in dearomatizing cyclization reactions, although their synthetic utility has not been exploited. With regard to organophosphorus compounds, nucleophilic addition to an aromatic ring has been observed only in two specific cases, the reaction of LiBu^t with *N*,*N*-dibenzyltriphenylphosphonium bromide[24] and diphenyl(2-naphthyl)phosphine oxide.[25]

SCHEME 1[a]



[a] Conditions: (i) LiBu^s (1.5 equiv), THF −90 °C, HMPA (6 equiv), 30 min; (ii) LiBu^s (2.5 equiv), THF −90 °C; (iii) MeOH, 30 min, then chromatography.

We have recently reported the dearomatization of a phenyl ring linked to the phosphorus atom of *N*-benzyl-*N*-methyldiphenylphosphinamide **1a** by treatment with LiBu^s in the presence of HMPA at −90 °C (Scheme 1). The tetrahydrobenzo[*c*][1,2]aza-1λ^5-phospholes obtained were readily transformed into γ-aminophosphinic acids and methyl esters.[26] Phosphinic acid derivatives are important compounds due to their activity as enzyme inhibitors,[27] and on GABA receptors.[28]

The phosphorus-stabilized anion resulting in the dearomatization reaction of *N*-benzyl-*N*-methyldiphenylphosphinamide was quenched with methanol, D_2O, MeI, and PhCHO. The reaction with benzaldehyde showed very high regio- and stereoselectivity. However, in the alkylation with MeI, the yield of dearomatized products was significantly reduced due to several competing processes: rearomatization, *ortho*-methylation, and the base-induced formation of the methylated phosphine oxide. A detailed study of the anionic dearomatization−protonation reaction of *N*-alkyl-*N*-benzyldiphenylphosphinamides led to an efficient route for the stereoselective synthesis of γ-aminophosphinic acids.[29]

The phosphinamide and thiophosphinamide linkage are good *ortho*-directing groups for the lithiation of an aromatic ring.[30] Apparently, the anionic cyclization observed in the dearomatization of *N*-benzyldiphenylphos-

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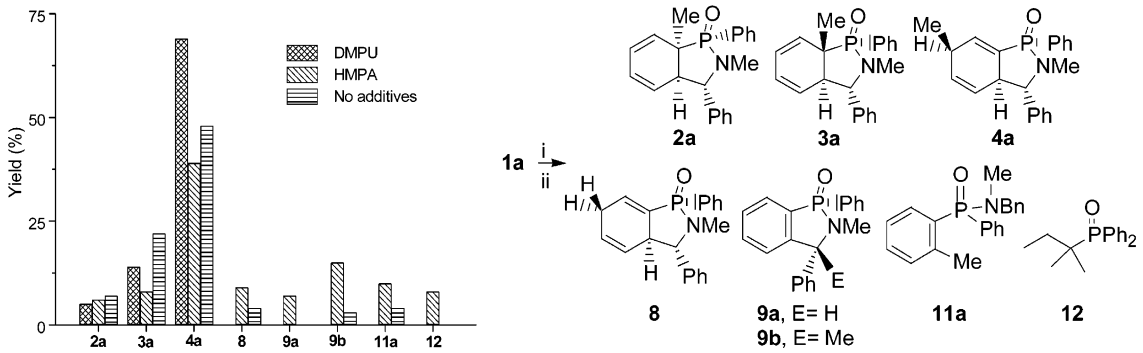

FIGURE 1. Distribution of products in the dearomatization−methyl iodide addition of **1a** as a function of the coordinating agent used. General reaction conditions: (i) LiBu^s (2.5 equiv), THF −90 °C, 30 min; (ii) MeI (2.5 equiv), 5 h.

phinamides was driven by the use of the strongly coordinating agent HMPA.[18a,b,d,31] In contrast, for *N*-benzyldinaphthylphosphinamides, the lower resonance stabilization of the naphthalene ring allowed the dearomatization to proceed via an intramolecular nucleophilic conjugate addition in THF without the addition of cosolvents (Scheme 1).[32]

In this paper, we report the extension of this synthetic methodology based on the concatenation of intramolecular nucleophilic dearomatization−electrophilic alkylation reactions to a series of *N*-alkyl-*N*-benzyldiphenylphosphinamides and electrophiles. The systematic variation of the reaction times and additives used afforded insight that allowed high yields of heterocycles containing functionalized 1,4-cyclohexadienes to be obtained with very good regio- and stereoselectivity and without the participation of carcinogenic cosolvents. The optimization procedure also gave access to open-chained compounds, whose product structures allowed the delineation of the mechanism of this process.

2. Results and Discussion

The electrophiles used to study the scope of the anionic dearomatization reaction of *N*-alkyl-*N*-benzyldiphenylphosphinamides include MeI, CF_3SO_3Me, $Me_3O^+BF_4^-$, BrAllyl, $BrCH_2Ph$, $BrCH_2CO_2Me$, and RCH=O, where R = Ph, 4-Cl−C_6H_4, 4-MeO−C_6H_4, and ^{i}Pr. The evaluation of the effects of the substituent linked to the nitrogen was also monitored through phosphinamides **1a**−**c** $Ph_2P(O)N(R^1)CH_2Ph$, where R^1 = Me (**1a**), CH_2Ph (**1b**), and Bu^t (**1c**). Compounds **1a**−**c** were prepared in multigram scale according to methods previously described.[29]

Reactions with Alkylating Reagents. Due to the low efficiency shown by the reaction of MeI with the intermediate anionic species formed in the metalation of **1a**, our first goal was to improve its performance through a systematic study of the experimental conditions. The use of the carcinogenic agent HMPA was an additional drawback of the method.

HMPA can either accelerate or inhibit the reaction, depending on the structure of the lithiated species and the particular properties of the electrophile.[33] To check this effect, the reaction was performed first in the absence of HMPA. In addition to the omission of HMPA, two additional modifications were introduced: (i) the concentration of methyl iodide was increased to 5 equiv to avoid the formation of nonmethylated byproducts and (ii) the reaction time with the electrophile (t_2)[34] was increased to 5 h, to allow the reaction to reach completeness. After aqueous workup the ^{31}P NMR spectrum of the crude reaction material revealed the presence of a complex mixture. The major compounds **3a** (11%), **4a** (12%), and **11a** (15%) (Figure 1) where identified on the basis of their ^{31}P chemical shift.[35] The major component, however, was unreacted starting phosphinamide (16%). One may conclude from these results that dearomatization in absence of HMPA is possible, although the methylation proceeds in a rather indiscriminate way. Consequently, HMPA acts as a catalyst in the anionic cyclization of lithiated phosphinamides **1**. Decreasing the temperature of the MeI reaction to −120 °C did not produce significant changes in the distribution of products. The formation of the *ortho*-methylated phosphinamide **11a** suggested that the metalation time was too short to complete a translocation of aryl anion to benzylic anion. However, by extending the lithiation period to 10 h at −90 °C and the subsequent alkylation with MeI to 12 h, 96% of **1a** was converted, with the methylated dearomatized compounds accounting for the majority of the product formation (77%). The major components of the reaction mixture were **2a** (7%), **3a** (22%), and **4a** (48%) (relative ratio of 9:28:63).

Next, additive alternatives to HMPA were assayed. The use of TMEDA under the same reaction conditions was disappointing due to the intractable mixture of compounds formed. Accordingly, no additional experiments were performed with TMEDA. However, the use of DMPU showed an increase in the selective formation of **4a**. The optimal conditions involved the treatment of a THF solution of **1a** and DMPU (6 equiv) with LiBu^s (2.5 equiv) at −90 °C for 12 h, followed by addition of MeI (2.5 equiv) and additional stirring for 2 h, which gave

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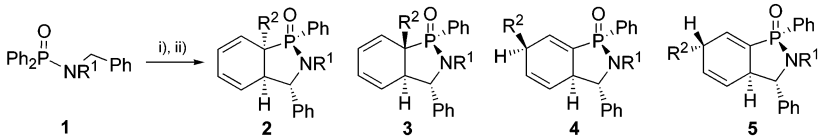
(34) Throughout the text, the reaction times are labeled t_1 and t_2 for the metalation and trapping steps, respectively.

(35) Ratio was determined from the inverse-gated proton-decoupled ^{31}P NMR spectrum of the crude reaction using a pulse width of 15°, a relaxation delay of 10 s, and an accumulation of 128 scans.

SCHEME 2[a]



R^1	R^2							
	Me	Bn	Allyl	CH_2CO_2Me	PhCHOH	*p*-Cl-C_6H_4CHOH	*p*-MeO-C_6H_4CHOH	^{i}PrCHOH
Me	**a**	**b**	**c**	**d**	**e**	**f**	**g**	**h**
Bn	**i**	**j**		**k**	**l**	**m**	**n**	
Bu^t	**o**				**p**			

[a] Conditions: (i) $LiBu^s$ (2.5 equiv), THF −90 °C, cosolvent (6 equiv), t_1 (h); (ii) E^+ = RX or RCHO (2.5 equiv), t_2 (h).

TABLE 1. Distribution of Products and Yields in the Alkylation of Lithiated 1a (R^1 = Me) under the Reactions Conditions Specified[a]

entry	R^2	cosolvent	t_1 (h)	t_2 (h)	**2**	**3**	**4**	**5**	yield (%)	α:γ
1	**a**		0.5	5	12	42	46		26[b]	54:46
2	**a**		10	12	9	28	63		77[c]	47:63
3	**a**	HMPA	0.5	2	11	15	74		53[d]	26:74
4	**a**	HMPA	10	12	9	28	63		75	37:63
5	**a**	DMPU	0.25	0.25	7	19	74		57[e]	26:74
6	**a**	DMPU	12	2	6	16	78		89	22:78
7	**a**[f]	DMPU	12	2	19	36	45		83	55:45
8	**b**	DMPU	12	2			>98		86	>1:99
9	**c**	DMPU	12	2			56	44	85	>1:99
10	**d**	DMPU	12	2			85	15	93	>1:99

[a] General reaction conditions unless otherwise stated: (i) $LiBu^s$ (2.5 equiv), THF −90 °C; (ii) E^+ (2.5 equiv). [b] Compounds **8** (5%) and **11a** (15%) were also isolated. [c] Also obtained were **8** (4%), **9a** (3%), and **9b** (4%). [d] Also obtained were **8** (9%), **9a** (15%), **9b** (10%), and **12** (8%). [e] Other products: **8** (4%), **9a** (6%), **9b** (6%), and **11a** (3%). [f] Methylation with methyl trifluoromethanesulfonate.

the azaphospholes **2a**:**3a**:**4a** in a ratio of 6:16:78, in 89% total yield (Scheme 2, Table 1). Purification through column chromatography (eluent: ethyl acetate) afforded 1,4-cyclohexadiene **4a** in an overall isolated yield of 66%.

The optimized procedure described in Scheme 2 was applied to other alkylating reagents (Table 1, entries 7−10). Of particular interest was the fact that the methylation with methyl trifluoromethanesulfonate, a stronger electrophile than MeI,[36] was less stereoselective. In fact, α-alkylation with respect to phosphorus was slightly preferred over the γ-position, giving rise to dienes **2a**:**3a**:**4a** in a ratio of 19:36:45, with a combined yield of 83%. Changing the alkylating reagent to benzyl bromide gave excellent results, with the γ-adduct **4b** (R^1 = Me, R^2 = $PhCH_2$) being the only dearomatized product formed (86% yield).[37] Allyl bromide and methyl 2-bromoacetate also gave, exclusively, the products derived from γ-alkylation (**4**−**5c** (85%) and **4**−**5d** (93%), respectively). However, the discrimination between both faces of the lithium cyclohexadiene system was less efficient, resulting in mixtures of epimers. Allyl bromide yielded an almost 1:1 mixture of **4c**:**5c**, whereas the use of methyl bromoacetate provided **4d** with a good dr (85:15 for **4d**:**5d**).

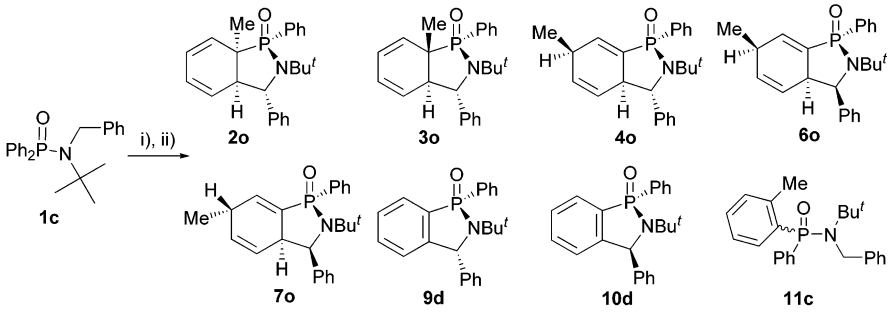
A coarse inspection of the ^{1}H and ^{13}C NMR spectra allowed us to establish the position of alkylation. α-Alkylation-derived products (**2** and **3**) produce a 1,3-cyclohexadiene system, with vinyl proton signals at δ 6.21−5.35 ppm. In addition, the protons of the methyl substituent adjacent to the carbon bridgehead show a vicinal ^{31}P, ^{1}H coupling constant larger than 10 Hz (see Experimental Section). In the ^{13}C NMR spectra, the quaternary sp^3-hybridized carbon linked to the phosphorus appears at δ < 43.86 ppm as a doublet with $^1J_{PC}$ > 87.7 Hz. The 1,4-cyclohexadiene moiety of compounds **4** and **5** is characterized, either in the ^{1}H or ^{13}C NMR spectra, by the large deshielding of the CH group β to the phosphorus due to the conjugation of the carbon−carbon double bond with the PO (δ_H > 6.56 ppm, $^3J_{PH}$ > 16.5 Hz; δ_C, > 132.34 ppm, $^2J_{PC}$ > 118.9 Hz). The ^{31}P NMR data also proved to be a valuable tool for structural diagnostics: α-substituted products **2** and **3** showed δ_P values around 50 ppm, while the magnitude was close to 30 ppm for γ-derivatives **4** and **5**. The relative configuration of all stereogenic centers could be unequivocally established through one- and two-dimensional NOESY experiments (see Supporting Information). Additionally, it has been observed that the ^{31}P signal of compounds **2a** with the alkyl substituent cis to the *P*-phenyl ring was deshielded by ca. 8 ppm (**2a**: δ 57.77 ppm) with respect to the trans isomer (**3a**: 48.86 ppm). On the other hand, the cis and trans γ-alkylated isomers (**4** and **5**, respectively) show similar ^{31}P chemical shifts ($\Delta\delta \approx 1$ ppm).

The NMR spectra of the aromatized byproducts **9a**,**b** and **11a** are much simpler. The characteristic features of **9a** and **9b** are, respectively, the singlet at δ 5.51 ppm for the methine proton of the azaphosphol ring and the methyl group linked to that carbon (δ_H 2.02 ppm, δ_C 24.34 ppm, $^3J_{PC}$ 3.7 Hz). The stereochemistry of both compounds was determined through the analysis of the two-dimensional gNOESY spectra. The *ortho*-methylation of **11a** was deduced by the signals observed in the ^{1}H and ^{13}C NMR spectra for the new methyl substituent: δ_H 2.59 ppm; δ_C 21.61 ppm, $^3J_{PC}$ 4.2 Hz. Moreover, this methylation renders the benzylic protons diastereotopic (δ 4.19, dd, 1H, $^3J_{HH}$ 14.7, $^3J_{PH}$ 5.9 Hz; 4.26, dd, 1H, $^3J_{HH}$ 14.7, $^3J_{PH}$ 6.2 Hz).

The dearomatizing−alkylation process of phosphinamide **1b** (R^1 = CH_2Ph) showed the same trends observed for **1a**: (i) improvement of regioselectivity and yield with the use of DMPU as a cosolvent, (ii) formation of mixtures of α- and γ-adducts when the reaction was quenched with MeI and CF_3SO_3Me, and (iii) exclusive γ-addition to phosphorus in all other cases (Table 2). In an attempt to increase the α-methylation selectivity, a reaction was

(36) Woodward, S. *Tetrahedron* **2002**, *58*, 1017.
(37) $Ph_2P(O)Bu^s$ (5%) arising from the nucleophilic attack of $LiBu^s$ on **1a** was also formed.

SCHEME 3[a]



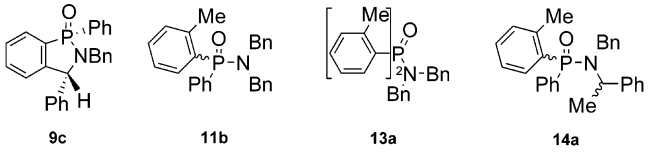
[a] Conditions: (i) LiBu^s (2.5 equiv), THF −90 °C, HMPA or DMPU (6 equiv); (ii) R^2X (2.5 equiv), 2 h.

TABLE 2. Distribution of Products and Yields in the Alkylation of Lithiated 1b ($R^1 = CH_2Ph$) under the Reactions Conditions Specified[a]

entry	R^2	cosolvent	t_1 (h)	t_2 (h)	**2**	**3**	**4**	**5**	yield (%)	α:γ
1	**i**	HMPA	0.5	0.5	7	41	52		47[b]	48:52
2	**i**	HMPA	12	0.5	12	37	51		52[c]	49:51
3	**i**	HMPA	24	0.5	11	38	51		54[d]	49:51
4	**i**	DMPU	12	2	9	31	60		88	40:60
5	**i**[e]	DMPU	12	2	20	42	38		89	62:38
6	**i**[f]	DMPU	12	2	22	16	62		32[g]	38:62
7	**j**	DMPU	12	2			>98		84	>1:99
8	**k**	DMPU	12	2			78	22	84	>1:99

[a] General reaction conditions: (i) LiBu^s (2.5 equiv), THF −90 °C; (ii) RX (2.5 equiv). [b] Also obtained were **11b** (29%), **13a** (3%), and **14a** (3%). [c] Also formed were yields of 3% of **11b**, 2% of **13a**, and 5% of **14a**. [d] Also formed were yields 1% of **13a** and 5% of **14a**. [e] Using methyl trifluoromethanesulfonate as a methylating agent. [f] Treatment with $Me_3O^+BF_4^-$ in the quenching step. [g] Also obtained was a 55% yield of **9c**.

CHART 1



carried out using $Me_3O^+BF_4^-$ as the electrophile. The major product was the rearomatized product **9c** (55%, Chart 1), which lacks the methyl substituent, while α-(**2i**, **3i**) and γ-methylated compounds (**4i**) were obtained in 12 and 20% yields, respectively.

Aromatization reactions have been observed in the alkylation of the anionic cycloadduct of *N*-methyl-*N*-benzyl(diaryl)phosphinamides (aryl = phenyl, naphthyl)[26,32] and explained by assuming a competing C- vs O-alkylation of the phosphorus-stabilized anion. The O-alkylated derivative is unstable[38] and rearomatizes either under the reaction conditions used or during workup. The fact that trimethyloxonium tetrafluoroborate is a good O-methylating reagent of enolates[39] supports this theory and explains the predominance of rearomatized products in its reactions with **Li$^+$1b$^-$**.

In the reaction with methyl iodide using HMPA as a cosolvent or in the absence of additives (Supporting Information), three byproducts (**11b**, **13a**, and **14a**) were also isolated (Chart 1, Table 2, entries 1−3) that are relevant for understanding the mechanism of the dearomatizing process.[40] The structural assignments were straightforward on the basis of the analysis of their NMR spectra. They can be identified by the signals of the methyl groups. In the proton spectrum, they appeared as a singlet for **11b** (δ 2.62 ppm, 3H) and **13a** (δ 2.65 ppm, 6H), whereas **14a** shows a singlet (δ 2.59 ppm, 3H) and a doublet (δ 1.36 ppm, $^3J_{HH}$ = 7.3 Hz, 3H). The characterization of compounds derived from the alkylation in the *ortho* and benzylic positions of the starting phosphinamide is consistent with a sequence of steps leading to the dearomatized compounds analogous to that proposed for the anionic cyclization of *N*-benzylbenzamides: (1) *ortho*-lithiation of a phenyl ring directed by the phosphinamide linkage, (2) translocation to a benzylic anion, and (3) dearomatization through intramolecular attack to the *ortho* position of a *P*-phenyl ring.[41]

TABLE 3. Distribution of Products and Yields in the Methylation of Lithiated 1c (R^1 = *t*-Bu) under the Reactions Conditions Specified[a]

entry	cosolvent	t_1 (h)	**2o**	**3o**	**4o**	**6o**	**7o**	yield (%)	α:γ	**9d** (%)	**10d** (%)
1	HMPA	0.5	16	14	44	14	12	37[b]	30:70	25	31
2	HMPA	12	13	19	51	9	7	79[b]	32:68	6	5
3	DMPU	12	13	15	47	18	7	86	28:72	5	5
4	DMPU[c]	12	26	52	11	7	3	71[d]	78:22	15	5

[a] General reaction conditions unless otherwise stated: (i) LiBu^s (2.5 equiv), THF −90 °C; (ii) MeI (2.5 equiv), 2 h. [b] Also obtained were **11c** (<4%) and recovered **1c** (<4%). [c] Using methyl trifluoromethanesulfonate as a methylating agent. [d] Recovered **1c** (8%).

As expected from the protonation studies,[29] the use of phosphinamide **1c** (R^1 = *t*-Bu) with a bulky *tert*-butyl group linked to the nitrogen was detrimental for the regio- and diastereselectivity of the dearomatizing−alkylation process (Scheme 4). The reaction of **1c** in the presence of HMPA, under the initial conditions (30 min of lithiation and 2 h of methylation), produced a mixture of dearomatized (37%), rearomatized **9d** (56%) and *ortho*-methylated **11c** (2%) species (Scheme 3, first entry of Table 3).

The ^{1}H NMR spectra of the purified material, tetrahydrobenzo-[1,2]-azaphospholes **6o** and **7o**, showed a pat-

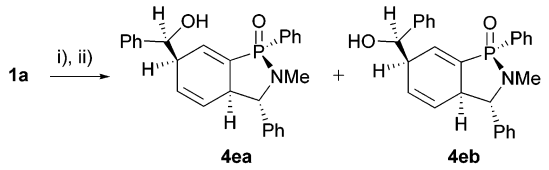
(38) (a) Mann, F. G.; Watson, J. *J. Org. Chem.* **1948**, *13*, 502. (b) Imamoto, T.; Kikuchi, S.-I.; Miura, T.; Wada, Y. *Org. Lett.* **2001**, *3*, 87.

(39) Heiszwolf, G. J.; Kloosterziel, H. *J. Chem. Soc., Chem. Commun.* **1966**, 51.

(40) Byproduct present in all reactions of **1b** was the phosphinamide $Ph_2P(O)NHCH(Ph)CH_2Ph$ formed by the rearrangement of metalated **1b**. At the low temperatures used, this rearrangement is minimized, causing only a slight decrease (2−6%) in the overall yield. See ref 31.

(41) (a) Ahmed, A.; Clayden, J.; Rowley, M. *Tetrahedron Lett.* **1998**, *39*, 6103. (b) Bragg, R. A.; Clayden, J. *Tetrahedron Lett.* **1999**, *40*, 8323. Bragg, R. A.; Clayden, J. *Tetrahedron Lett.* **1999**, *40*, 8327.

SCHEME 4[a]



[a] Conditions: (i) LiBu^s (1.5 equiv), THF −90 °C, HMPA (6 equiv), 30 min.; (ii) PhCHO (2.5 equiv), 2 h.

tern of olefinic protons typical of the [1,4] cyclohexadiene systems already discussed. NOE measurements led to the assignment of their stereochemistry, thus revealing that in both compounds the configuration of the methine proton linked to the nitrogen atom is inverted relative to that in isomer **4o**, and that **6o** and **7o** are epimers at the carbon bearing the methyl group due to the addition of the electrophile to both faces of the dearomatized ring. The reduced stereocontrol on the CH α to the nitrogen in the anionic cyclization of *N*-benzyl-*N*-(*tert*-butyl)-diphenylphosphinamide **1c** has been previously noted and attributed to the steric effects involving this position.[29] More importantly, the inversion of this CH is evidenced in the ^{1}H NMR spectra by a change in the multiplicity of the methine proton: in **6o** and **7o**, it is characterized by a double doublet arising from the coupling with the vicinal proton and the phosphorus atoms, whereas for **4o**, no coupling to the phosphorus is observed. The same rule applies to the rearomatized heterocycles **9d** and **10d**. In this case, homonuclear vicinal coupling is not possible, resulting in the C**H**N signal appearing as a singlet for **9d** and a doublet of $^3J_{PH}$ = 11 Hz for **10d**.

Better results are obtained when the time of the metalation step is increased to 12 h. In the presence of HMPA, the yield increases to 79%, the amount of rearomatization products is significantly reduced (11%); also, *ortho*-alkylation remains negligible (4%) (second entry, Table 3). Again, the use of DMPU as a cosolvent represents the best choice. Compared to HMPA, the distribution of products was similar. However, the reaction yield increases to 86% (third entry, Table 3). As in the case of **1a**, the methylation with CF_3SO_3Me favored the formation of products of attack α to the phosphorus. For **1c**, the effect is more pronounced and the ratio of α:γ alkylation raises to 78:22.

Reactions with Aldehydes. In our previous report,[26] we showed that the reaction of benzaldehyde with the dearomatized anion derived from the cyclization of lithiated **1a** was excellent, yielding quantitatively the two epimers **4ea** and **4eb**[42] in a ratio of 80:20 (Scheme 4). They are the result of the exclusive addition of the nucleophile through the γ-position with respect to the phosphorus to the two faces of the carbonyl group, which means that only 2 out of 16 possible diastereomers were formed. They could be separated by column chromatography (ethyl acetate/hexane 2:1) and identified by a combination of NMR and X-ray diffraction studies. According to the X-ray data, the major product corresponds to the attack of *like* topicity.[26]

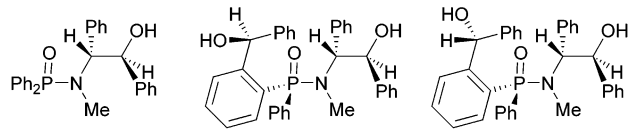
(42) In this case, the first letter refers as always to the electrophile used and the second to the relative configuration of the hydroxylated carbon atom: **a** = (*S**); **b** = (*R**).

TABLE 4. Distribution of Products and Yields in the Reaction of Lithiated 1A (R^1 = Me) with Benzaldehyde[a]

entry	cosolvent	t_1 (min)[b]	t_2 (min)[b]	**4ea**,**eb** (%)	**14ba** (%)	**14bb** (%)	**15a** (%)
1	HMPA	5	5	45	13	21	3
2	HMPA	5[c]	5	75	3	6	3
3	HMPA	5	15	55	14	19	4
4	HMPA	15	15	68	9	11	
5	HMPA	15	60	71	7	8	
6	HMPA	30[c]	60	>98 (80:20)			
7	HMPA	10 h	12 h	85 (64:36)			
8	DMPU	5	5	91 (82:18)[d]			
9	DMPU	15	15	93 (82:18)[d]			
10	DMPU	30[c]	60	86 (80:20)[d,e]			
11	DMPU	30	60	84 (80:20)[d,e]			
12	DMPU	10 h	12 h	85 (64:36)[d,e]			

[a] General reaction conditions: (i) LiBu^s (2.5 equiv), THF −90 °C; (ii) PhCHO (2.5 equiv). [b] See ref 34. [c] Employed 1.5 equiv LiBu^s. [d] Recovered $Ph_2P(O)Bu^s$ (6%). [e] See ref 44 (<5%).

CHART 2



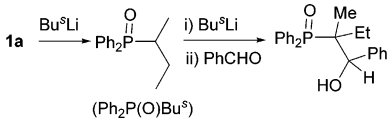
The synthesis of **4ea** and **4eb** in high yield and regio- and diastereoselectivity was the result of the optimization of several reaction parameters: (i) the time of metalation, t_1, (ii) the concentration of base, (iii) cosolvents, and (iv) the time of contact with the electrophile, t_2.

The initial reactions, which were performed in the presence of 6 equiv of HMPA, with short metalation and quench times ($t_1 = t_2 = 5$ min, Table 4), resulted in the formation of only 45% yield of dearomatized compounds **4ea** and **4eb**, plus 37% yield of three new products, which were identified as **15a** (3%), **14ba** (13%), and **14bb** (21%) (Chart 2).[43,44]

The *N*-phosphinoyl-1,2-amino alcohol **15a** is the product of addition of the benzylic anion of **1a** to the aldehyde. The configuration was deduced from the magnitude of $^3J_{XY}$ (X = ^{31}P, ^{1}H; Y = ^{13}C, ^{1}H) of the 1,2-amino alcohol moiety: $^3J_{HH}$ = 7.5, $^3J_{PH}$ = 7.7, and $^3J_{PCipso}$ = 5.5 Hz (see below).[45] Compounds **14ba** and **14bb** were recrystallized from dichloromethane−hexane and their structures determined by NMR spectroscopy and X-ray diffraction analysis.[46] Their crystal structures and molecular parameters are given in Supporting Information. The lattice in **14ba** is formed by a repetition of monomers, intercon-

(43) First letter refers to the electrophile used (PhCHO) and the second to the relative configuration of the hydroxylated carbon atom at the *P-ortho* position: **a** = (*S**); **b** = (*R**).

(44) Two byproducts were also isolated corresponding to the diastereomers derived from the nucleophilic attack of LiBu^s to **1a** followed by metalation and subsequent addition of benzaldehyde (see below). Davidson, A. H.; Earnshaw, C.; Grayson, J. I.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1452.



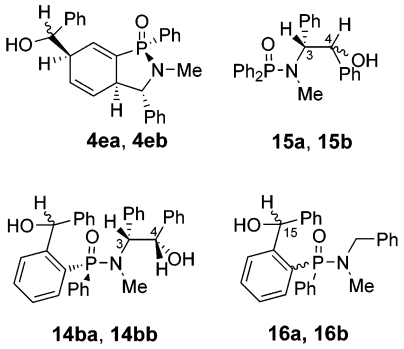
(45) Assigned on the basis of the values of $^3J_{HH}$ of diastereomeric 1,2-diphenyl-2-formamidoethanol and 1,2-diphenyl-2-(*N*-methyl)aminoethanol. Lou, R.; Mi, A.; Jiang, Y.; Qin, Y.; Li, Z.; Fu, F.; Chan, A. S. C. *Tetrahedron* **2000**, *56*, 5857.

nected through intermolecular hydrogen bonding. **14bb** crystallizes as a dimer, where the monomers are held in contact by intermolecular hydrogen bonding between the OH of the amino alcohol substructure of a monomer with the PO group and the OH of the *ortho* substituent of the other molecule. Both compounds show intramolecular hydrogen bonding between the PO linkage and the OH group of the *ortho* substituent (**14ba** (O(3A)−H(2)···O(2A)), 2.344 Å, 138°; **14bb** (O(3)−H(53)···O(2)), 2.032 Å, 141°). Although the synthesis of **14ba** and **14bb** gives rise to four new stereogenic centers, the compounds differ exclusively in the configuration of the carbon *ortho* to the phosphorus atom. Moreover, the configurations of the 1,2-amino alcohol fragments are again *unlike* (C(1)*S**,C(2)-*R**), as in phosphinamide **15a**. It is stabilized in a staggered conformation with an anti arrangement of the heteroatoms (torsion angle N(1)−C(2)−C(1)−O(1) is 174.99° for **14ba** and −173.75 and −174.35° for both monomers in **14bb**).

Apparently, **14ba** and **14bb** proceed from the reaction of benzaldehyde with a *P*-*ortho*, *N*-benzylic dianion of phosphinamide **1a**. Furthermore, this reaction is highly stereoselective. As deduced from the X-ray data, the benzylic anion attacks exclusively at the *Re* face of the benzaldehyde, whereas the ability of the *ortho* anion to discriminate between both faces of the aldehyde is lower, with the *Si* face being now favored (dr 38:62 for **14ba**:**14bb**). On the basis of the stoichiometry of the process (**1a**:LiBu^s = 1:2.5), a double metalation is, in principle, possible. However, the isolation of low quantities of **15a** indicates that the formation of **14ba**,**bb** is best explained through a stepwise process. First, the benzylic anion of **1a** reacts with total stereoselectivity with benzaldeyde, leading to the lithium alkoholate of **15a**, which then drives the metalation at the *ortho* position of a *P*-phenyl ring. Addition of this new anion to both faces of PhCHO would give rise to the epimers **14ba** and **14bb**. This analysis gives additional support to the stereochemical assignment[47] of **15a**. It also implies that in 5 min, the metalation of **1a** is practically quantitative; however, the anionic cyclization is incomplete, and the intermediate lithiated species can be trapped by the addition of excess electrophile. Accordingly, increasing t_2 to 15 min has only a marginal effect on the product distribution (entry 3, Table 4). On the contrary, the increase of t_1 to 15 min promotes a clear reduction of the amount of open chain compounds **15a** and **14ba**,**bb** obtained in favor of the dearomatized heterocycles **4ea**,**eb** (entries 4 and 5, Table 4).

The decrease of the base concentration used to 1.5 equiv has three beneficial effects. Besides the increased efficiency of the reaction and the anticipated large decrease in the yields of **15a**, **14ba**, and **14bb**, a remarkable and unexpected increase in the yield of **4ea**,**eb** (75%) was observed. This result is consistent with the existence of a competing process between the *N*-benzyl anion of **1a**

CHART 3



and the excess of LiBu^s for complexing HMPA, which would slow the rate of the cyclization step.[48] Accordingly, the optimal results were obtained by performing the metalation with 1.5 equiv of LiBu^s over 30 min and allowing the dearomatized anion to react with benzaldehyde for 2 h at a constant temperature of −90 °C (entry 6 Table 4). Increasing the two reaction periods t_1 and t_2 to ca. 12 h has a negligible effect on the yield. However, the diastereoselectivity decreases to a ratio of ∼60:40 for **4ea**:**4eb** (entry 7, Table 4), i.e., **4ea** and **4eb** are the products of kinetic and thermodynamic control, respectively.

Next, the optimization procedure was repeated replacing HMPA with the noncarcinogenic DMPU as a coordinating additive. Similar to the dearomatization−alkylation reactions previously discussed, the use of DMPU represented a valuable improvement of the performance of the process (Table 4). Even for t_1 and t_2 as short as 5 min, the only products formed are **4ea** and **4eb** (ratio = 82:18) in 91% yield. Increasing both times to 15 min affords a slight increase in the yield (93%) without modifying the dr (entry 9, Table 4). Again, under thermodynamic conditions both epimers equilibrate, reaching a ratio 64:36 for **4ea**:**4eb (**entry 12, Table 4). The reaction was rather insensitive to the excess of base used (entries 10 and 11), additional data that support the fact that DMPU exerts a more pronounced effect than HMPA in these anionic cyclizations.

As already noted in the dearomatization−alkylation process, in the absence of coordinating additives, all steps of the transformation of **1a** in dearomatized compounds are slowed, allowing for the electrophilic benzaldehyde to become trapped by the different lithiated species present in the reaction. At the shortest reaction times used, $t_1 = t_2 = 5$ min, the major compounds of the crude mixture are **16a** (29%) and **16b** (23%), the two diastereomers derived from the addition of benzaldehyde to the *ortho* lithiated anion of **1a** (Chart 3, Table 5). A flowchart showing the anions generated in the metalation of phosphinamide **1a** and their trapping with benzaldehyde is given in Scheme 5.

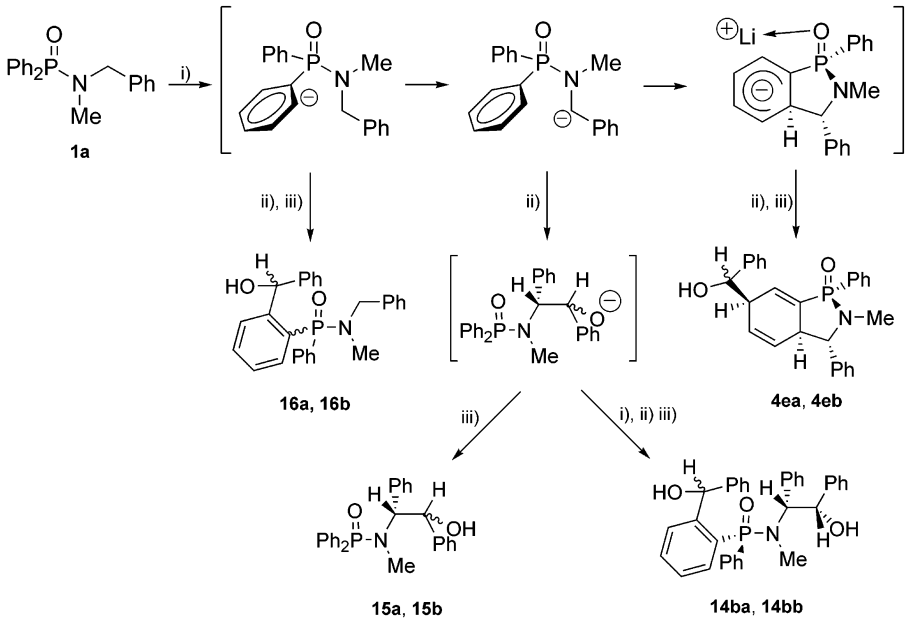
The incorporation of the *ortho* phenylhydroxymethyl substituent to **1a** is evidenced in the ^{13}C NMR spectrum

(46) Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 204302 and CCDC 204303 for **14ab** and **14bb**, respectively. Copies of the data can be obtained free of charge upon application to CCDC, 12 Union Road, Cambridge CB2 1 EZ, UK [fax, +44(0)-1223-336033; e-mail, deposit@ccdc.cam.ac.uk].

(47) $^3J_{HH}$ value for the NCH−CHO moiety is 8.4 Hz for **14ba** and 5.8 Hz for **14bb**.

(48) Formation of a mixed aggregate between the excess LiBu^s and the *N*-benzyl anion of **1a** seems less reasonable due to the presence of the strongly deaggregating agent HMPA. (a) Reich, H. J.; Sikorski, W. H. *J. Org. Chem.* **1999**, *64*, 14. (b) Sikorski, W. H.; Reich, H. J. *J. Am. Chem. Soc.* **2001**, *123*, 6527. (c) Juaristi, E.; Hernández-Rodríguez, M.; López-Ruiz, H.; Aviña, J.; Muñoz-Muñiz, O.; Hayakawa, M.; Seebach, D. *Helv. Chim. Acta* **2002**, *85*, 1999.

SCHEME 5. Anions Generated in the Lithiation of 1a and Subsequent Reaction with Benzaldehyde, Followed by Hydrolysis[a]



[a] See text for the specific reaction conditions used. (i) 1.5 equiv of LiBu^s, −90 °C, cosolvent, t_1 h; (ii) PhCHO; (iii) H_2O.

TABLE 5. Distribution of Products (%) in the Addition of Benzaldehyde to the Dearomatized Lithiated 1a in the Absence of Cosolvents[a,b]

t_1/t_2 (min)[c]	4ea,eb	4ba,bb	15a	15b	16a	16b
5/5	18		9	5	29	23
5/15	29	4	19	4		
30 min/2 h	55	4			8	5
10 h/12 h	77				3	4

[a] General reaction conditions: (i) LiBu^s (2.5 equiv), THF −90 °C; (ii) PhCHO (2.5 equiv). [b] Recovered $Ph_2P(O)Bu^s$ (<5%). See ref 42 (<5%). [c] See ref 34.

by the doublet of the CHOH carbon (**16a**, δ 72.52, d, $^3J_{PC}$ = 4.6 Hz; **16b**, δ 74.58, d, $^3J_{PC}$ = 4.2 Hz). The ^{1}H NMR spectra of these compounds show the diastereotopic methylene protons as double doublets by virtue of the ^{1}H,^{1}H geminal and ^{31}P,^{1}H vicinal coupling constants (Experimental Section). Addition to the benzylic anion of **1a** is also observed, although in much less extension (14%) and without the stereocontrol previously noted in the presence of HMPA. Both stereoisomers are obtained in a ratio 64:36 for **15a**:**15b**. Once the relative configuration of **15a** is established, the stereochemical assignment of **15b** is straightforward. The key coupling constants involving the 1,2-amino alcohol moiety are $^3J_{HH}$ = 10.3, $^3J_{PH}$ = 9.5, and $^3J_{PCipso} \approx 0$ Hz. The yield of dearomatized compounds is only 18% (ratio of **4ea**:**4eb** = 73:27). It increases to 77% by increasing t_1 and t_2 to ca. 12 h (entry 4, Table 5). Again, under thermodynamic reaction conditions, the ratio of stereoisomers almost equalizes: **4ea**:**4eb** = 53:47. Products of double addition **14ba**,**bb** were only observed at intermediate reaction times and in very low yield (4%).

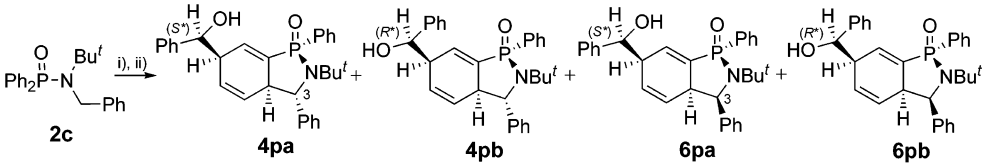
In consideration of the high regio- and stereoselectivity of the optimized reaction with benzaldehyde as a trapping reagent of dearomatized **1a**, the process was extended to other aldehydes and phosphinamides. The reaction conditions used were 30 min of metalation with 2.5 equiv of LiBu^s in the presence of 6 equiv of DMPU at −90 °C, followed by reaction with the aldehyde for 2 h. The selected aldehydes include aromatic (PhCHO, 4-Cl−C_6H_4-CHO, 4-MeO−C_6H_4CHO) and aliphatic ones ($(CH_3CH_2$-CH_2CHO, $(CH_3)_2CHCHO$). The results obtained are given in Table 6. For phosphinamides **1a** and **1b**, the performance was excellent for all aldehydes assayed except for butyraldehyde. In this case, no addition was observed. The easier accessibility of the α-hydrogen to the carbonyl group compared with *iso*-butyraldehyde probably drives the reaction through the alternative transmetalation−aldol condensation process. Yields were on the order of 90%, and the dr ranged between 85:15 and 70:30. It was assumed that attack to the aldehyde occurred preferentially through the *Re* face, by analogy with the reaction of benzaldehyde. In the reaction of lithiated **1a** with *iso*-butyraldehyde, a 3% yield of a new dearomatized product **17** was isolated, having the substituent on the carbon β to the phosphorus. The formation of this byproduct could be avoided by decreasing the amount of base used to 1.5 equiv.[49] In this way, the reaction yield was increased slightly (93%) without affecting to the diastereoselectivity (entry 5, Table 6).

TABLE 6. Distribution of Products (%) in theAddition of Aldehydes to Dearomatized 1a,b[a]

	relation (%)		
4	**a** (*S**)	**b** (*R**)	yield (%)
f	78	22	88
g	84	16	89
h	79	21	91[b]
h	80	20	93
l	74	26	90
m	70	30	90
n	85	15	90

[a] General reaction conditions: (i) LiBu^s (2.5 equiv), THF −90 °C, DMPU (6 equiv), 30 min.; (ii) ArCHO (2.5 equiv) 2 h. [b] Recovered **17** (3%).

SCHEME 6[a]



[a] Conditions: (i) LiBu^s (2.5 equiv), THF −90 °C, DMPU (6 equiv), 30 min.; (ii) PhCHO (2.5 equiv).

TABLE 7. Distribution of Products (%) in the Addition of Benzaldehyde to the Dearomatized Lithiated 1c[a,b]

t_2 (h)	**4pa**	**4pb**	**6pa**	**6pb**	yield (%)	**4pa**,**pb**:**6pa**,**pb**
0.5	37	12	44	7	65	49:51
1	55	16	26	3	75	71:29
4	70	13	14	3	57[c]	83:17

[a] General reaction conditions: (i) LiBu^s (2.5 equiv), THF −90 °C, DMPU (6 equiv), 30 min.; (ii) PhCHO (2.5 equiv). [b] Recovered **1c** (<6%). [c] Also obtained **18** (29%).

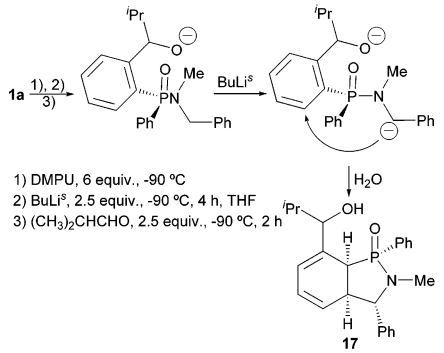
Phosphinamide **1c** showed the expected particular behavior associated with the effect of the bulkiness of the *tert*-butyl group linked to the nitrogen. The reaction with benzaldehyde afforded a 1:1 mixture of γ-substituted compounds **4pa**,**pb** and **6pa**,**pb**, epimers at the carbon adjacent to the nitrogen in 65% overall yield (Scheme 6, Table 7), considerably lower than that with the analogous reactions of **1a** and **1b**. More importantly, the relative proportion of isomers **4pa**,**pb** increased progressively with the increase of the metalation time t_1, reaching a ratio 83:17 for **4pa**,**pb**:**6pa**,**pb** when $t_1 = 4$ h (Table 7). The counterpart to the improved dr was a slight decrease of the reaction yield, and a considerable degradation (29%) of the starting phosphinamide, which gave rise to the phosphine oxide $Ph_2P(O)CH(OH)Ph$ **18**.[50] The equilibration between isomers **4pa**,**pb** and **6pa**,**pb** with the increase in the metalation time indicates that the dearomatized anion precursors of **4p** and **4pa** with a relative configuration (R_P*,3*S**,3a*R**) are thermodynamically more stable than their epimers (R_P*,3*R**,3a*R**) (see Experimental Section for the numbering scheme used), which lead to **6pa**,**pb**. This interconversion also implies that the anionic dearomatizing reaction must be reversible, a well-known characteristic of the addition of a nucleophile to electrophilic aromatic rings in S_NAr processes.[51] The fact that high yields of dearomatized compounds can be isolated in the reactions studied here may be interpreted as the result of the higher reactivity of the dearomatized anion compared to that of the open chain anions toward the electrophiles assayed.

All compounds were separated by column chromatography and identified through the same set of NMR spectra mentioned for the compounds described above. As in previous cases, inversion at the carbon α to the nitrogen was deduced from the multiplicity shown by its proton in the ^{1}H NMR spectra: a doublet for **4pa** ($^3J_{HH}$ = 8.9 Hz) and a double doublet for **6pa** ($^3J_{HH}$ = 7.4, $^3J_{PH}$ = 17.2 Hz). This assignment was supported by the NOEs observed in the respective gNOESY spectra.

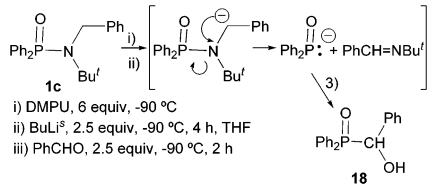
Conclusions

The tandem intramolecular nucleophilic dearomatization−electrophilic alkylation reactions of *N*-alkyl-*N*-benzyldiphenylphosphinamides have been generalized and optimized. In the absence of coordinating additives, the dearomatization takes place slowly. For metalation times shorter than 30 min, intermediate species having the anionic charge localized in an aromatic carbon *ortho* to the phosphorus and/or in the benzylic position could be trapped, thus revealing their participation in the reaction mechanism. Acceptable yields of dearomatized substituted bicycles having a 1,4-cyclohexadiene system fused to an [1,2]-1λ^5-azaphosphol ring were obtained only for reaction times (lithiation and electrophilic alkylation) longer than 10 h. The use of 6 equiv of HMPA sped up both reaction steps, improving the regio- and stereoselectivity, as well as the reaction yields. These improvements were even more pronounced when the noncarcinogenic DMPU was used as an additive. The dearomatization−alkylation process is best achieved by treating the phosphinamide with 2.5 equiv of LiBu^s at −90 °C in THF in the presence of 6 equiv of DMPU for 12 h and then reaction with the alkyl halide for an additional 2 h. When the electrophile was an aldehyde, the reaction time was

(49) Bridgehead carbons appeared at δ 37.88 ($^1J_{PC}$ = 83.5 Hz) and 43.75 ppm in the ^{13}C NMR spectrum, and the coupling constant of 12.4 Hz of the corresponding protons fixed the cis junction of the bicycle. The position of the hydroxyalkyl substituent was confirmed by the correlations observed in the gHMBC spectrum between the methine proton of the CHOH group with the carbon atoms β and γ to the phosphorus. A plausible mechanism for the formation of **16** is shown below.



(50) Degradation of lithiated **1c** leading to **18** may be explained through a pathway similar to the fragmentation of HMPA promoted by the action of organolithium bases: (i) metalation at the benzylic position, followed by β-elimination and subsequent addition of the phosphorus anion to benzaldehyde. (a) Abatjoglou, A. G.; Eliel, E. L. *J. Org. Chem.* **1974**, *39*, 3042. (b) Magnus, P.; Roy, G. *Synthesis* **1980**, 575.



(51) (a) Terrier, F. *Chem. Rev.* **1982**, *82*, 77. (b) Artamkina, G. A.; Egorov, M. P.; Beletskaya, I. P. *Chem. Rev.* **1982**, *82*, 427.

reduced (15 min), resulting in the formation of only two diastereoisomers containing five stereogenic centers. They are formed from the addition of the dearomatized anion to both faces of the carbonyl group, showing a large preference for the *Re* one. The ratio of isomers almost equalized under thermodynamic conditions, proving the reversibility of the addition.

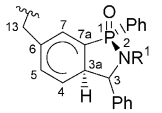
For *N*-(*tert*-butyl)phosphinamide, the effect of the bulkiness of the substituent on the nitrogen was reflected in a decrease of the reaction yields and in the stereocontrol of the anionic cyclization. Only in this case were dearomatized epimers at the carbon α to the nitrogen formed, a characteristic already noted in analogous protonation studies. The diastereoselectivity was improved by increasing the metalation time, which indicates that the epimers are in equilibrium, and consequently, that the anionic cyclization is reversible.

Experimental Section

For general experimental and X-ray data, see Supporting Information. Phosphinamides **1a**−**c** were prepared following literature procedures.[29] Azaphospholes **2**−**3a**, **4a**, **4ea**,**eb**, **9a**,**b**, **11a**, **15a**, and **16a**,**b** have been characterized previously.[26]

General Procedure for the Synthesis of Tetrahydrobenzo[*c*][1,2]-1λ^5-azaphospholes 2−7. To a solution of the appropriate phosphinamide (6.23×10^{-4} mol) and HMPA (3.72×10^{-3} mol) in THF (30 mL) was added a solution of Bu^{s}Li (1.2 mL of a 1.3 M solution in cyclohexane, 1.56×10^{-3} mol) at −90 °C. After the time of metalation t_1 (specified for each reaction in the main text) was added the corresponding electrophile (1.87×10^{-3} mol). The reaction mixture was stirred at −90 °C for t_2. Then, the reaction mixture was poured into ice water and extracted with ethyl acetate (3 × 15 mL). The organic layers were dried over Na_2SO_4 and concentrated in vacuo. ^{1}H, ^{1}H{^{31}P}, and ^{31}P NMR spectra of the crude reaction were measured in order to determine the stereoselectivity of the process. The reaction mixture was then purified by flash column chromatography using different mixtures of ethyl acetate/hexane as an eluent.

The same procedure was applied when the reaction was carried out either in the presence of DMPU (3.72×10^{-3} mol) or without cosolvent.

Scheme numbering used for the basic skeleton 

(1*R*$_P$*S*$_P$,3*SR*,3a*RS*,6*RS*)-2,3,3a,6-Tetrahydro-6-benzyl-2-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (4b). Yield after chromatography (ethyl acetate/hexane 1:1) was 82% (0.164 g). Mp: 131−133 °C dec. ^{1}H NMR: δ 2.35 (d, 3H, J_{PH} 9.2), 2.72 (dd, 2H, *J* 3.8 Hz), 2.77 (m, 1H), 3.29 (m, 1H), 3.98 (d, 1H, *J* 9.5 Hz), 5.59 (dddd, 1H, *J* 10.1, *J* 3.8, *J* 1.3, *J* 0.8 Hz), 5.76 (dddd, 1H, *J* 10.1, *J* 2.8, *J* 1.5, *J* 1.5 Hz), 6.72 (dddd, 1H, J_{PH} 16.7, *J* 4.9, *J* 1.5, *J* 2.9 Hz), 7.63−7.08 (m, 13H, ArH), 7.86 (m, 2H, ArH). ^{13}C NMR: δ 28.45 (d, CH_3, J_{PC} 2.8 Hz), 39.42 (d, CH, J_{PC} 12.5 Hz), 40.93 (d, CH_2, J_{PC} 1.9 Hz), 46.87 (d, CH, J_{PC} 13.9 Hz), 69.28 (d, CH, J_{PC} 11.6 Hz), 123.89 (d, HC═, J_{PC} 6.9 Hz), 129.45 (HC═), 131.81−127.68 (15CAr), 133.08 (d, C_{ipso}, J_{PC} 134.1 Hz), 134.16 (d, C═, J_{PC} 119.8 Hz), 137.88 (C_{ipso}), 138.94 (d, HC═, J_{PC} 8.8 Hz), 139.00 (d, C_{ipso}, J_{PC} 8.8 Hz). ^{31}P NMR: δ 31.03. MS (API-ES), *m*/*e*: 411 (M^+, 4), 320 (68), 201 (100), 118 (19), 91 (18), 77 (23), 40 (74). Anal. Calcd for $C_{27}H_{26}NOP$: C, 78.81; H, 6.37; N, 3.40. Found: C, 78.83; H, 6.27; N, 3.38.

(1*R*$_P$*S*$_P$,3*SR*,3a*RS*,6*RS*)-2,3,3a,6-Tetrahydro-6-allyl-2-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (4c). Yield after chromatography (ethyl acetate/hexane 2:1) was 37% (0.074 g). LC, HP Supersphere column, operation conditions: solvent flow = 0.8 mL/min, mobile phase = MeOH (A)/amonium formiate 50 mM: formic acid pH 3.5 (B), t = 0 min 60% B, t = 20 min 0% B, t = 21 min 0% B, t = 25 min 60% B. t_R = 17.40 min. Oil. ^{1}H NMR: δ 2.07 (dd, 1H, *J* 13.5, *J* 6.6 Hz), 2.13 (dd, 1H, *J* 13.5, *J* 5.5 Hz), 2.30 (d, 3H, J_{PH} 9.4 Hz), 3.05 (m, 1H), 3.16 (m, 1H, *J* 9.4, *J* 4.9, *J* 2.4 Hz), 3.97 (d, 1H, *J* 9.4 Hz), 4.91−4.80 (m, 2H), 5.75−5.50 (m, 3H), 6.64 (dddd, 1H, J_{PH} 16.5, *J* 4.8, *J* 2.9, *J* 1.5 Hz), 7.53−7.24 (m, 8H, ArH), 7.86 (m, 2H, ArH). ^{13}C NMR: δ 28.38 (d, CH_3, J_{PC} 2.4 Hz), 37.59 (d, CH, J_{PC} 12.6 Hz), 39.10 (d, CH_2, J_{PC} 2.4 Hz), 47.04 (d, CH, J_{PC} 13.8 Hz), 69.38 (d, CH, J_{PC} 11.4 Hz), 117.08 (H_2C═), 123.13 (d, HC═, J_{PC} 6.6 Hz), 128.79−127.59 (7CAr), 129.57 (d, HC═, J_{PC} 1.8 Hz), 131.61 (d, CAr, J_{PC} 10.2 Hz), 131.68 (d, CAr, J_{PC} 3.0 Hz), 133.06 (d, C_{ipso}, J_{PC} 134.0 Hz), 133.57 (d, C═, J_{PC} 119.6 Hz), 134.55 (HC═), 138.86 (d, C_{ipso}, J_{PC} 9.0 Hz), 139.25 (d, HC═, J_{PC} 8.4 Hz). ^{31}P NMR: δ 29.92. MS (API-ES), *m*/*e*: 363 (M + 2, 25), 362 (M + 1, 100), 120 (16). Anal. Calcd for $C_{23}H_{24}NOP$: C, 76.43; H, 6.69; N, 3.87. Found: C, 76.33; H, 6.70; N, 3.92.

(1*R*$_P$*S*$_P$,3*SR*,3a*RS*,6*SR*)-2,3,3a,6-Tetrahydro-6-allyl-2-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (5c). Yield after chromatography (ethyl acetate/hexane 2:1) was 48% (0.092 g). Oil. ^{1}H NMR: δ 2.31 (t, 1H, *J* 9.1 Hz), 2.40 (d, 3H, J_{PH} 9.1 Hz), 2.87 (m, 1H), 3.21 (dddd, 1H, *J* 11.9, *J* 9.5, *J* 5.1, *J* 2.6 Hz), 4.08 (d, 1H, *J* 9.5 Hz), 5.17−5.10 (m, 2H), 5.62 (dddd, 1H, J_{PH} 3.8, *J* 10.1, *J* 2.4, *J* 2.4 Hz), 5.70 (m, 1H, *J* 10.1, *J* 4.0, *J* 2.0 Hz), 5.81 (ddt, 1H, *J* 17.0, *J* 10.3, *J* 7.0 Hz), 6.64 (dddd, 1H, J_{PH} 16.9, *J* 2.8, *J* 1.8, *J* 1.8 Hz), 7.63−7.31 (m, 8H, ArH), 7.98 (m, 2H, ArH). ^{13}C NMR: δ 28.55 (d, CH_3, J_{PC} 3.0 Hz), 36.58 (d, CH, J_{PC} 12.6 Hz), 39.12 (CH_2), 47.30 (d, CH, J_{PC} 13.8 Hz), 69.23 (d, CH, J_{PC} 11.4 Hz), 117.43 (H_2C═), 122.54 (d, HC═, J_{PC} 6.6 Hz), 128.88−127.73 (7CAr), 129.90 (d, HC═, J_{PC} 1.8 Hz), 131.79 (d, CAr, J_{PC} 3.0 Hz), 131.87 (d, CAr, J_{PC} 10.8 Hz), 133.22 (d, C_{ipso}, J_{PC} 134.0 Hz), 133.30 (d, C═, J_{PC} 120.1 Hz), 135.36 (HC═), 139.02 (d, C_{ipso}, J_{PC} 9.0 Hz), 139.03 (d, HC═, J_{PC} 9.5 Hz). ^{31}P NMR: δ 29.33. MS (API-ES), *m*/*e*: 363 (M + 2, 31), 362 (M + 1, 100), 361 (M^+, 22), 360 (M − 1, 45), 320 (10). Anal. Calcd for $C_{23}H_{24}NOP$: C, 76.43; H, 6.69; N, 3.87. Found: C, 76.33; H, 6.70; N, 3.92.

(1*R*$_P$*S*$_P$,3*SR*,3a*RS*,6*RS*)-2,3,3a,6-Tetrahydro-6-(methoxycarbonylmethyl)-2-methyl-1,3-diphenylbenzo[*c*][1,2]-azaphosphole 1-Oxide (4d). Yield after chromatography (ethyl acetate) was 77% (0.154 g). LC, HP Supersphere column, operation conditions: solvent flow = 0.8 mL/min, mobile phase = MeOH (A)/amonium formiate 50 mM: formic acid pH 3.5 (B), t = 0 min 60% B, t = 20 min 0% B, t = 21 min 0% B, t = 25 min 60% B. t_R = 14.83 min. Oil. Identified from a 79:21 mixture of **4d** and **5d**. ^{1}H NMR: δ 2.30 (dd, 1H, *J* 15.8, *J* 7.0 Hz), 2.36 (dd, 1H, *J* 15.8, *J* 6.6 Hz), 2.38 (d, 3H, J_{PH} 9.3 Hz), 3.20 (m, 1H, *J* 9.5, *J* 8.8 Hz), 3.40 (m, 1H, *J* 7.0, *J* 4.4 Hz), 3.56 (s, 3H), 4.05 (d, 1H, *J* 9.5 Hz), 5.64 (dd, 1H, *J* 10.6, *J* 3.3 Hz), 5.79 (ddd, 1H, *J* 10.6, *J* 3.3, *J* 3.3 Hz), 6.75 (d, 1H, J_{PH} 16.5 Hz), 7.58−7.28 (m, 8H, ArH), 7.94 (m, 2H, ArH). ^{13}C NMR: δ 28.46 (d, CH_3, J_{PC} 2.2 Hz), 34.18 (d, CH, J_{PC} 12.5 Hz), 39.19 (d, CH_2, J_{PC} 2.4 Hz), 46.74 (d, CH, J_{PC} 13.2 Hz), 51.66 (CH_3), 69.24 (d, CH, J_{PC} 11.4 Hz), 124.00 (d, HC═, J_{PC} 6.6 Hz), 128.92−127.68 (7CAr), 128.56 (d, HC═, J_{PC} 1.8 Hz), 131.86 (d, CAr, J_{PC} 3.0 Hz), 131.88 (d, CAr, J_{PC} 10.2 Hz), 132.86 (d, C_{ipso}, J_{PC} 133.1 Hz), 134.63 (d, C═, J_{PC} 118.9 Hz), 137.77 (d, HC═, J_{PC} 9.0 Hz), 138.71 (d, C_{ipso}, J_{PC} 9.0 Hz), 171.39 (C═O). ^{31}P NMR: δ 29.64. MS (API-ES), *m*/*e*: 395 (M + 2, 100), 393 (M + 1, 45). Anal. Calcd for $C_{23}H_{24}NO_3P$: C, 70.22; H, 6.15; N, 3.56. Found: C, 70.19; H, 6.10; N, 3.66.

(1*R*$_P$*S*$_P$,3*SR*,3a*RS*,6*SR*)-2,3,3a,6-Tetrahydro-6-(methoxycarbonylmethyl)-2-methyl-1,3-diphenylbenzo[*c*][1,2]-azaphosphole 1-Oxide (5d). Yield after chromatography (ethyl acetate) was 14% (0.028 g). LC, HP Supersphere column, operation conditions: solvent flow = 0.8 mL/min, mobile phase = MeOH (A)/amonium formiate 50 mM: formic acid pH 3.5 (B), t = 0 min 60% B, t = 20 min 0% B, t = 21 min 0% B, t = 25 min 60% B. t_R = 15.58 min. Oil. Identified from a 21:79

mixture of **5d** and **4d**. ^{1}H NMR: δ 2.39 (d, 3H, J_{PH} 9.3 Hz), 2.47 (dd, 1H, *J* 16.5, *J* 6.6 Hz), 2.55 (dd, 1H, *J* 16.5, *J* 6.6 Hz), 3.20 (m, 1H, *J* 12.8, *J* 8.8 Hz), 3.29 (m, 1H), 3.67 (s, 3H), 4.05 (d, 1H, *J* 8.8 Hz), 5.64 (m, 2H, 6.56 (d, 1H, J_{PH} 16.9 Hz), 7.58−7.28 (m, 8H, ArH), 7.94 (m, 2H, ArH). ^{13}C NMR: δ 28.53 (d, CH_3, J_{PC} 2.4 Hz), 33.67 (d, CH, J_{PC} 12.5 Hz), 38.99 (CH_2), 46.93 (d, CH, J_{PC} 15.6 Hz), 51.75 (CH_3), 69.08 (d, CH, J_{PC} 10.8 Hz), 123.17 (d, HC═, J_{PC} 7.2 Hz), 128.92−127.68 (7CAr), 128.40 (d, HC═, J_{PC} 6.2 Hz), 131.86 (d, CAr, J_{PC} 3.0 Hz), 131.88 (d, CAr, J_{PC} 10.2 Hz), 132.81 (d, C_{ipso}, J_{PC} 131.3 Hz), 133.88 (d, C═, J_{PC} 120.1 Hz), 137.89 (d, HC═, J_{PC} 9.6 Hz), 138.77 (d, C_{ipso}, J_{PC} 9.6 Hz), 172.03 (C═O). ^{31}P NMR: δ 29.33. MS (API-ES), *m/e*: 395 (M + 2, 22), 394 (M + 1, 100). Anal. Calcd for $C_{23}H_{24}NO_3P$: C, 70.22; H, 6.15; N, 3.56. Found: C, 70.19; H, 6.10; N, 3.66.

(1*R*$_P$*S*$_P$,3*SR*,3a*RS*,6*RS*,13*SR*)-2,3,3a,6-Tetrahydro-6-(1-hydroxy-*para*-chlorophenylmethyl)-2-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (4fa). Yield after chromatography (ethyl acetate/hexane 1:1) was 69% (0.027 g). Mp: 195−197 °C dec. ^{1}H NMR: δ 2.35 (d, 3H, J_{PH} 9.2 Hz), 3.21 (m, 2H), 3.93 (bs, OH), 3.98 (d, 1H, J_{HH} 9.1 Hz), 4.97 (s, 1H), 5.69 (m, 2H), 6.68 (d, 1H, J_{PH} 17.2 Hz), 7.62−7.34 (m, 12H, ArH), 7.94 (m, 2H, ArH). ^{13}C NMR: δ 28.48 (d, CH_3, J_{PC} 2.9 Hz), 44.95 (d, CH, J_{PC} 12.0 Hz), 47.40 (d, CH, J_{PC} 13.6 Hz), 69.16 (d, CH, J_{PC} 11.2 Hz), 74.54 (CH), 124.36 (d, HC═, J_{PC} 6.6 Hz), 125.25 (HC═), 128.92−127.69 (11CAr), 131.93 (d, CAr, J_{PC} 10.7 Hz), 132.05 (d, CAr, J_{PC} 2.9 Hz), 132.38 (d, C_{ipso}, J_{PC} 136.0 Hz), 133.04 (C_{ipso}), 135.43 (d, C═, J_{PC} 119.1 Hz), 137.31 (d, HC═, J_{PC} 9.9 Hz), 138.68 (d, C_{ipso}, J_{PC} 9.1 Hz), 140.50 (C_{ipso}). ^{31}P NMR: δ 30.84. MS (API-ES), *m/e*: 462 (M + 1, 100), 444 (8). Anal. Calcd for $C_{27}H_{25}NO_2PCl$: C, 70.21; H, 5.67; N, 3.03. Found: C, 70.29; H, 5.65; N, 3.02.

(1*R*$_P$*S*$_P$,3*SR*,3a*RS*,6*RS*,13*RS*)-2,3,3a,6-Tetrahydro-6-(1-hydroxy-*para*-chlorophenylmethyl)-2-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (4fb). Yield after chromatography (ethyl acetate/hexane 1:1) was 88% (0.176 g). Identified from a 52:48 mixture of **4fa** and **4fb**. ^{1}H NMR: δ 2.21 (d, 3H, J_{PH} 9.2 Hz), 3.21 (m, 2H), 3.80 (d, 1H, J_{HH} 8.8 Hz), 4.83 (d, 1H, J_{HH} 5.5 Hz), 5.69 (m, 1H), 5.82 (d, 1H, J_{HH} 10.3 Hz), 6.89 (d, 1H, J_{PH} 16.9 Hz), 7.27−7.57 (m, 12H, ArH), 7.82 (m, 2H, ArH). ^{13}C NMR: δ 28.43 (d, CH_3, J_{PC} 2.3 Hz), 45.00 (d, CH, J_{PC} 12.5 Hz), 47.44 (d, CH, J_{PC} 4.1 Hz), 68.85 (d, CH, J_{PC} 11.1 Hz), 75.17 (CH), 124.19 (d, HC═, J_{PC} 6.5 Hz), 127.90 (HC═), 131.98−127.68 (14CAr), 132.33 (d, C_{ipso}, J_{PC} 135.5 Hz, C), 132.92 (C_{ipso}), 134.21 (d, C═, J_{PC} 120.2 Hz), 136.48 (d, HC═, J_{PC} 10.2 Hz), 138.84 (d, C_{ipso}, J_{PC} 9.3 Hz), 141.57 (C_{ipso}). ^{31}P NMR: δ 30.84. MS (API-ES), *m/e*: 462 (M + 1, 100).

(1*R*$_P$*S*$_P$,3*SR*,3a*RS*,6*RS*,13*SR*)-2,3,3a,6-Tetrahydro-6-(1-hydroxy-*para*-methoxyphenylmethyl)-2-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (4ga). Yield after chromatography (ethyl acetate) was 75% (0.148 g). Oil. ^{1}H NMR: δ 2.35 (d, 3H, J_{PH} 9.2 Hz), 3.26−3.12 (m, 2H), 3.35 (d, OH, J_{HH} 4.2 Hz), 3.83 (s, 3H), 3.98 (d, 1H, J_{HH} 8.8 Hz), 4.71 (dd, 1H, J_{HH} 5.5, J_{HH} 4.2 Hz), 5.56 (m, 1H, J_{HH} 9.9, J_{HH} 3.3, J_{HH} 1.8 Hz), 5.66 (m, 1H, J_{PH} 3.7, J_{HH} 9.9, J_{PH} 2.2 Hz), 6.92 (d, 1H, J_{HH} 8.8 Hz), 6.95 (d, J_{PH} 17.2 Hz), 7.59−7.33 (m, 10H, ArH), 7.95 (m, 2H, ArH). ^{13}C NMR: δ 28.53 (d, CH_3, J_{PC} 2.5 Hz), 45.02 (d, CH, J_{PC} 12.0 Hz), 47.44 (d, CH, J_{PC} 14.1 Hz), 55.23 (CH_3), 69.13 (d, CH, J_{PC} 10.7 Hz), 75.64 (CH), 113.77 (CAr), 124.34 (d, HC═, J_{PC} 6.6 Hz), 127.58 (CAr), 127.66 (HC═), 131.99−127.63 (10CAr), 132.76 (d, C_{ipso}, J_{PC} 131.1 Hz), 134.44 (C_{ipso}), 134.48 (d, C═, J_{PC} 119.9 Hz), 136.49 (d, HC═, J_{PC} 9.9 Hz), 138.93 (d, C_{ipso}, J_{PC} 9.1 Hz), 159.02 (C_{ipso}). ^{31}P NMR: δ 30.93. MS (API-ES), *m/e*: 480 (M + Na, 25), 458 (M + 1, 100), 440 (95), 321 (35), 287 (30). Anal. Calcd for $C_{28}H_{28}NO_3P$: C, 73.51; H, 6.17; N, 3.06. Found: C, 73.49; H, 6.17; N, 3.11.

(1*R*$_P$*S*$_P$,3*SR*,3a*RS*,6*RS*,13*SR*)-2,3,3a,6-Tetrahydro-6-(1-hydroxy-2-methylpropyl)-2-methyl-1,3-diphenylbenzo[*c*]-[1,2]azaphosphole 1-Oxide (4ha). Yield after chromatography (ethyl acetate and then ethyl acetate/methanol 20:1) was 88% (0.176 g). Oil Identified from a 78:22 mixture of **4ha** and **4hb**. ^{1}H NMR: δ 0.91 (d, 3H, *J* 7.0 Hz), 1.01 (d, 3H, *J* 6.6 Hz), 1.90 (m, 1H), 2.35 (d, 3H, J_{PH} 9.2 Hz), 3.04 (m, 1H), 3.20 (m, 3H, *J* 11.0, *J* 10.6 Hz), 3.42 (dd, 1H, *J* 7.7, *J* 4.0 Hz), 4.05 (d, 1H, *J* 9.2 Hz), 5.67 (m, 1H, *J* 10.3 Hz), 5.89 (d, 1H, *J* 10.3 Hz), 6.65 (d, 1H, J_{PH} 17.2 Hz), 7.58−7.30 (m, 8H, ArH), 7.95 (m, 2H, ArH). ^{13}C NMR: δ 18.77 (CH_3), 19.59 (CH_3), 28.50 (d, CH_3, J_{PC} 2.4 Hz), 30.52 (CH), 40.98 (d, CH, J_{PC} 12.0 Hz), 47.39 (d, CH, J_{PC} 13.8 Hz), 69.36 (d, CH, J_{PC} 11.4 Hz), 78.50 (CH), 123.71 (d, HC═, J_{PC} 6.6 Hz), 126.40 (d, HC═, J_{PC} 1.8 Hz), 128.86−127.69 (7CAr), 131.91 (d, CAr, J_{PC} 10.5 Hz), 131.92 (d, CAr, J_{PC} 2.7 Hz), 132.66 (d, C_{ipso}, J_{PC} 135.5 Hz), 134.05 (d, C═, J_{PC} 120.1 Hz), 138.89 (d, C_{ipso}, J_{PC} 9.6 Hz), 139.23 (d, HC═, J_{PC} 9.6 Hz). ^{31}P NMR: δ 29.99. MS (API-ES), *m/e*: 417 (M + 1 + Na^+, 27), 416 (M + Na^+, 100), 395 (M + 2, 25), 394 (M + 1, 8). Anal. Calcd for $C_{24}H_{28}NO_2P$: C, 73.26; H, 7.17; N, 3.60. Found: C, 73.20; H, 7.11; N, 3.63.

(1*R*$_P$*S*$_P$,3*SR*,3a*RS*,6*RS*,13*RS*)-2,3,3a,6-Tetrahydro-6-(1-hydroxy-2-methylpropyl)-2-methyl-1,3-diphenylbenzo[*c*]-[1,2]azaphosphole 1-Oxide (4hb). Yield after chromatography (ethyl acetate and then ethyl acetate/methanol 20:1) was 26% (0.052 g). Oil. Identified from a 22:78 mixture of **4ha** and **4hb**. ^{1}H NMR: δ 0.92 (d, 3H, *J* 6.6 Hz), 1.00 (d, 3H, *J* 6.2 Hz), 1.95 (m, 1H), 2.35 (d, 3H, J_{PH} 9.2 Hz), 3.03 (m, 1H, *J* 9.5 Hz), 3.19 (m, 3H, *J* 11.0, *J* 10.6 Hz), 3.36 (dd, 1H, *J* 6.6, *J* 5.5 Hz), 4.05 (d, 1H, *J* 9.2 Hz), 5.66 (m, 1H, *J* 10.3 Hz), 5.79 (d, 1H, *J* 10.3 Hz), 6.82 (d, 1H, J_{PH} 17.2 Hz), 7.58−7.30 (m, 8H, ArH), 7.95 (m, 2H, ArH). ^{13}C NMR: δ 18.12 (CH_3), 19.90 (CH_3), 28.50 (d, CH_3, J_{PC} 2.4 Hz), 30.74 (CH), 41.29 (d, CH, J_{PC} 11.4 Hz), 47.45 (d, CH, J_{PC} 13.8 Hz), 69.27 (d, CH, J_{PC} 11.4 Hz), 78.65 (CH), 123.46 (d, HC═, J_{PC} 6.6 Hz), 128.86−127.69 (7CAr), 128.82 (d, HC═, J_{PC} 2.1 Hz), 131.92 (d, CAr, J_{PC} 2.7 Hz), 131.94 (d, CAr, J_{PC} 10.5 Hz), 132.74 (d, C_{ipso}, J_{PC} 135.2 Hz), 134.14 (d, C═, J_{PC} 120.7 Hz), 137.04 (d, C_{ipso}, J_{PC} 9.6 Hz), 138.92 (d, HC═, J_{PC} 9.0 Hz). ^{31}P NMR: δ 29.97.

(1*S*$_P$*R*$_P$,3*SR*,3a*RS*,7a*SR*,13*SR*)-2,3,3a,7a-Tetrahydro-7-(1-hydroxy-2-methylpropyl)-2-methyl-1,3-diphenylbenzo-[*c*][1,2]azaphosphole 1-Oxide (17). Yield after chromatography (ethyl acetate, and then AcOEt/MeOH 20:1.) 3% (0.006 g). Oil. ^{1}H NMR: δ 0.90 (d, 3H, *J* 6.6 Hz), 0.95 (d, 3H, *J* 6.6 Hz), 1.79 (dsp, 1H, *J* 7.0, *J* 6.6 Hz), 2.34 (d, 3H, J_{PH} 8.7 Hz), 2.48 (sa, OH), 2.90 (m, 1H), 3.14 (m, 1H, *J* 12.4, *J* 4.4 Hz), 3.86 (d, 1H, *J* 7.0 Hz), 4.17 (d, 1H, *J* 9.1 Hz), 5.47 (dd, 1H, *J* 9.8, *J* 6.6 Hz), 5.82 (dd, 1H, J_{PH} 9.2, *J* 2.9 Hz), 6.11 (d, 1H, *J* 9.2 Hz), 7.58−7.26 (m, 8H, ArH), 7.91 (m, 2H, ArH). ^{13}C NMR: δ 18.06 (CH_3), 19.26 (CH_3), 28.49 (d, CH_3, J_{PC} 2.4 Hz), 32.24 (CH), 37.88 (d, CH, J_{PC} 83.5 Hz), 43.75 (CH), 70.48 (d, CH, J_{PC} 20.4 Hz), 79.24 (CH), 114.90 (d, HC═, J_{PC} 8.4 Hz), 124.03 (d, HC═, J_{PC} 10.8 Hz), 124.45 (d, HC═, J_{PC} 3.0 Hz), 128.73−127.34 (7CAr), 131.67 (d, HCAr, J_{PC} 10.2 Hz), 131.93 (d, HCAr, J_{PC} 3.0 Hz), 133.17 (d, C_{ipso}, J_{PC} 126.8 Hz), 138.27 (d, C_{ipso}, J_{PC} 10.2 Hz), 139.58 (d, C, $^2J_{PC}$ 10.8 Hz). ^{31}P NMR: δ 50.82. MS (API-ES), *m/e*: 396 (M + 3, 10), 395 (M + 2, 23), 394 (M + 1, 100), 375 (42), 321 (15). Anal. Calcd for $C_{24}H_{28}NO_2P$: C, 73.26; H, 7.17; N, 3.56. Found: C, 73.24; H, 7.19; N, 3.51.

(1*RS*,3*SR*,3a*RS*,7a*RS*)-2,3,3a,7a-Tetrahydro-2-benzyl-7a-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (2i). Yield after chromatography (ethyl acetate/hexane 1:1) was 18% (0.036 g), methylation with CF_3SO_3Me. Mp: 72−74 °C. ^{1}H NMR: δ 0.85 (d, 3H, J_{PH} 16.8 Hz), 2.65 (ddd, 1H, *J* 9.9, ^3J 6.1, *J* 1.0 Hz), 3.73 (dd, 1H, J_{PH} 13.4, *J* 14.3 Hz), 4.02 (dd, 1H, J_{PH} 1.0, *J* 9.9 Hz), 4.26 (dd, 1H, J_{PH} 8.4, *J* 14.3 Hz), 5.30 (m, 1H, *J* 8.8, *J* 6.1, *J* 1.0 Hz), 6.00 (dd, 1H, *J* 8.8, *J* 5.2 Hz), 6.13 (ddt, 1H, J_{PH} 0.9, *J* 9.8, *J* 5.2, *J* 1.0 Hz), 6.27 (ddd, 1H, J_{PH} 11.8, *J* 9.8, *J* 1.0 Hz), 7.63−7.08 (m, 13H, ArH), 8.03 (m, 2H, ArH). ^{13}C NMR: δ 19.90 (CH_3), 39.57 (d, C, J_{PC} 88.3 Hz), 46.17 (d, CH_2, J_{PC} 1.8 Hz), 50.04 (d, CH, J_{PC} 4.1 Hz), 65.58 (d, CH, J_{PC} 19.4 Hz), 122.08 (d, HC═, J_{PC} 11.6 Hz), 123.06 (d, HC═, J_{PC} 8.8 Hz), 124.13 (d, HC═, J_{PC} 2.3 Hz), 131.89−126.90 (13CAr), 127.08 (d, HC═, J_{PC} 6.0 Hz), 132.16 (d, C_{ipso}, J_{PC} 124.4 Hz), 133.18 (d, CAr, J_{PC} 9.2 Hz), 136.13 (C_{ipso}), 139.12 (d, C_{ipso}, J_{PC} 8.8 Hz). ^{31}P NMR: δ 56.56. MS (API-ES), *m/e*: 412 (M +

1, 80), 229 (12), 196 (100), 91 (43). Anal. Calcd for $C_{27}H_{26}NPO$: C, 78.81; H, 6.37; N, 3.40. Found: C, 78.64; H, 6.39; N, 3.40.

(1*RS*,3*SR*,3a*RS*,7a*SR*)-2,3,3a,7a-Tetrahydro-2-benzyl-7a-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (3i). Yield after chromatography (ethyl acetate/hexane 1:1) was 37% (0.074 g), methylation with CF_3SO_3Me. Mp: 70−71 °C. ^{1}H NMR: δ 1.29 (d, 3H, J_{PH} 13.1 Hz), 3.22 (m, 1H), 3.69 (dd, 1H, J_{PH} 12.5, J 14.3 Hz), 3.98 (d, 1H, J 11.3 Hz), 4.42 (dd, 1H, J_{PH} 8.0, J 14.3 Hz), 5.43 (m, 1H), 5.82 (m, 1H), 5.87 (m, 1H), 6.03 (m, 1H, J_{PH} 8.4, J 8.7 Hz), 7.59−7.26 (m, 13H, ArH), 8.09 (m, 2H, ArH). ^{13}C NMR: δ 10.35 (CH_3), 38.82 (d, C, J_{PC} 94.1 Hz), 45.68 (d, CH_2, J_{PC} 2.2 Hz), 48.56 (CH), 60.77 (d, CH, J_{PC} 9.5 Hz), 123.30 (d, HC=, J_{PC} 12.7 Hz), 125.28 (d, HC=, J_{PC} 2.2 Hz), 125.56 (d, HC=, J_{PC} 10.2 Hz), 132.65−127.26 (13CAr), 130.80 (HC=), 132.37 (d, CAr, J_{PC} 9.4 Hz), 133.46 (d, C_{ipso}, J_{PC} 121.0 Hz), 136.76 (C_{ipso}), 137.63 (d, C_{ipso}, J_{PC} 5.4 Hz). ^{31}P NMR: δ 48.29. MS (API-ES), *m*/*e*: 412 (M + 1, 100), 196 (10). Anal. Calcd for $C_{27}H_{26}NPO$: C, 78.81; H, 6.37; N, 3.40. Found: C, 78.83; H, 6.37; N, 3.38.

(1*RS*,3*SR*,3a*RS*,6*RS*)-2,3,3a,6-Tetrahydro-2-benzyl-6-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (4i). Yield after chromatography (ethyl acetate/hexane 1:1) was 52% (0.104 g), methylation with MeI. Mp: 96−97 °C. ^{1}H NMR: δ 1.06 (d, 3H, J 7.3 Hz), 2.99 (m, 1H), 3.29 (m, 1H), 3.65 (dd, 1H, J_{PH} 13.8, J 14.7 Hz), 3.93 (d, 1H, J 9.5 Hz), 4.29 (dd, 1H, J_{PH} 8.8, J 14.7 Hz), 5.46 (m, 1H, J 10.1 Hz), 5.73 (m, 1H, J 10.1 Hz), 6.78 (m, 1H, J_{PH} 16.7 Hz), 7.59−7.08 (m, 13H, ArH), 7.99 (m, 2H, ArH). ^{13}C NMR: δ 20.36 (d, CH_3, J_{PC} 1.5 Hz), 32.54 (d, CH, J_{PC} 12.5 Hz), 45.97 (CH_2), 46.46 (d, CH, J_{PC} 14.5 Hz), 66.25 (d, CH, J_{PC} 12.5 Hz), 121.78 (d, HC=, J_{PC} 6.5 Hz), 131.84−127.01 (15CAr), 131.63 (HC=), 131.84 (d, C=, J_{PC} 120.7 Hz), 133.93 (d, C_{ipso}, J_{PC} 134.8 Hz), 136.15 (C_{ipso}), 138.50 (d, C_{ipso}, J_{PC} 8.0 Hz), 141.19 (d, HC=, J_{PC} 8.1 Hz). ^{31}P NMR: δ 29.96. MS (API-ES), *m*/*e*: 411 (M^+, 5), 396 (M − 15, 62), 149 (73), 91 (100), 69 (79), 44 (55). Anal. Calcd for $C_{27}H_{26}NPO$: C, 78.81; H, 6.37; N, 3.40. Found: C, 78.74; H, 6.39; N, 3.41.

(1*RPSP*,3*SR*,3a*RS*,6*RS*)-2,3,3a,6-Tetrahydro-2-benzyl-6-benzyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (4j). Yield after chromatography (ethyl acetate) was 81% (0.162 g). Oil. ^{1}H NMR: δ 2.70 (dd, 1H, J 13.4, J 6.9 Hz), 2.75 (dd, 1H, J 13.4, J 6.3 Hz), 2.84 (m, 1H, J 6.3, J 2.7 Hz), 3.29 (m, 1H), 3.58 (dd, 1H, J_{PH} 13.7, J 14.7 Hz), 3.86 (d, 1H, J 9.3 Hz), 4.27 (dd, 1H, J_{PH} 8.9, J 14.7 Hz), 5.51 (m, 1H, J 9.6 Hz), 5.71 (dd, 1H, J 9.6, J 1.3 Hz), 6.77 (dd, 1H, J_{PH} 16.8, J 1.3 Hz), 7.64−6.92 (m, 18H, ArH), 7.87 (m, 2H, ArH). ^{13}C NMR: δ 39.32 (d, CH, J_{PC} 12.0 Hz), 40.83 (d, CH_2, J_{PC} 1.8 Hz), 45.87 (d, CH_2, J_{PC} 3.0 Hz), 46.72 (d, CH, J_{PC} 13.8 Hz), 65.97 (d, CH, J_{PC} 12.6 Hz), 123.95 (d, HC=, J_{PC} 6.6 Hz), 126.01 (HC=), 129.49−127.04 (17 CAr), 131.60 (d, CAr, J_{PC} 10.2 Hz), 131.63 (d, CAr, J_{PC} 3.0 Hz), 133.68 (d, C=, J_{PC} 120.8 Hz), 133.81 (d, C_{ipso}, J_{PC} 134.0 Hz), 136.12 (C_{ipso}), 137.85 (C_{ipso}), 138.41 (d, C_{ipso}, J_{PC} 9.4 Hz), 139.09 (d, HC=, J_{PC} 8.4 Hz). ^{31}P NMR: δ 28.82. MS (API-ES), *m*/*e*: 490 (M + 3, 7), 489 (M + 2, 40), 488 (M + 1, 100), 396 (16). Anal. Calcd for $C_{33}H_{30}NOP$: C, 81.29; H, 6.20; N, 2.87. Found: C, 81.19; H, 6.20; N, 2.92.

(1*RPSP*,3*SR*,3a*RS*,6*RS*)-2,3,3a,6-Tetrahydro-2-benzyl-6-(methoxycarbonylmethyl)-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (4k). Yield after chromatography (ethyl acetate/hexane 2:1) was 66% (0.132 g). Oil. ^{1}H NMR: δ 2.33 (dd, 1H, J 15.8, J 7.5 Hz), 2.40 (dd, 1H, J 15.8, J 7.2 Hz), 3.29 (m, 1H, J 9.5 Hz), 3.42 (m, 1H, J 7.0, J 4.4 Hz), 3.61 (s, 3H), 3.68 (dd, 1H, J_{PH} 13.9, J 14.7 Hz), 3.92 (d, 1H, J 9.5 Hz), 4.28 (dd, 1H, J_{PH} 9.2, J 14.7 Hz), 5.57 (m, 1H, J 12.5, J 3.7, J 2.9 Hz), 5.76 (d, 1H, J 12.5 Hz), 6.81 (ddd, 1H, J_{PH} 16.5, J 6.2, J 3.3 Hz), 7.59−7.17 (m, 13H, ArH), 7.97 (m, 2H, ArH). ^{13}C NMR: δ 34.11 (d, CH, J_{PC} 12.0 Hz), 39.21 (d, CH_2, J_{PC} 2.4 Hz), 45.94 (d, CH_2, J_{PC} 3.0 Hz), 46.60 (d, CH, J_{PC} 13.8 Hz), 51.68 (CH_3), 66.00 (d, CH, J_{PC} 12.6 Hz), 124.03 (d, HC=, J_{PC} 7.2 Hz), 129.51−127.06 (12CAr), 127.96 (HC=), 131.75 (d, CAr, J_{PC} 3.0 Hz), 131.80 (d, CAr, J_{PC} 10.8 Hz), 133.62 (d, C_{ipso}, J_{PC} 134.0 Hz), 134.14 (d, C=, J_{PC} 120.1 Hz), 136.00 (C_{ipso}), 137.88 (d, HC=, J_{PC} 9.0 Hz), 138.23 (d, C_{ipso}, J_{PC} 7.8 Hz), 171.41 (C=O). ^{31}P NMR: δ 28.53. MS (API-ES), *m*/*e*: 493 (M + 1 + Na^+, 27), 492 (M + Na^+, 100), 471 (M + 2, 22), 470 (M + 1, 80), 398 (10). Anal. Calcd for $C_{29}H_{28}NO_3P$: C, 74.19; H, 6.01; N, 2.98. Found: C, 74.19; H, 6.00; N, 2.96.

(1*RPSP*,3*SR*,3a*RS*,6*SR*)-2,3,3a,6-Tetrahydro-2-benzyl-6-(methoxycarbonylmethyl)-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (5k). Yield after chromatography (ethyl acetate/hexane 2:1) was 18% (0.036 g). Oil. Identified from a 34:66 mixture of **4k** and **5k**. ^{1}H NMR: δ 2.50 (dd, 1H, J 16.5, J 6.2 Hz), 2.60 (dd, 1H, J 16.5, J 7.3 Hz), 3.27 (m, 1H), 3.42 (m, 1H), 3.62 (dd, 1H, J_{PH} 14.5, J 14.7 Hz), 3.68 (s, 3H), 3.92 (d, 1H, J 9.5 Hz), 4.28 (dd, 1H, J_{PH} 9.2, J 14.7 Hz), 5.53 (dd, 1H, J 10.2, J 3.3 Hz), 5.61 (d, 1H, J 10.2 Hz), 6.60 (d, 1H, J_{PH} 16.5 Hz), 7.65−7.06 (m, 13H, ArH), 7.98 (m, 2H, ArH). ^{13}C NMR: δ 33.62 (d, CH, J_{PC} 13.2 Hz), 38.95 (CH_2), 46.03 (d, CH_2, J_{PC} 3.0 Hz), 46.78 (d, CH, J_{PC} 15.6 Hz), 51.73 (CH_3), 65.90 (d, CH, J_{PC} 12.6 Hz), 123.20 (d, HC=, J_{PC} 6.6 Hz), 129.49−127.06 (12 CAr), 128.43 (d, HC=, J_{PC} 1.8 Hz), 131.75 (d, CAr, J_{PC} 3.0 Hz), 131.77 (d, CAr, J_{PC} 9.0 Hz), 133.40 (d, C=, J_{PC} 121.3 Hz), 133.62 (d, C_{ipso}, J_{PC} 134.0 Hz), 136.04 (C_{ipso}), 137.84 (d, HC=, J_{PC} 9.6 Hz), 138.25 (d, C_{ipso}, J_{PC} 7.8 Hz), 172.10 (C=O). ^{31}P NMR: δ 28.23. MS (API-ES), *m*/*e*: 493 (M + 1 + Na^+, 25), 492 (M + Na^+, 100), 470 (M + 1, 61). Anal. Calcd for $C_{29}H_{28}NO_3P$: C, 74.19; H, 6.01; N, 2.98. Found: C, 74.19; H, 6.00; N, 2.96.

(1*RPSP*,3*SR*,3a*RS*,6*RS*,13*SR*)-2,3,3a,6-Tetrahydro-2-benzyl-6-(1-hydroxyphenylmethyl)-1,3-diphenylbenzo[*c*][1,2]-azaphosphole 1-Oxide (4la). Precipitated from Et_2O. Yield: 67% (0.134 g). Mp: 77−79 °C. ^{1}H NMR: δ 3.26 (m, 2H), 3.61 (dd, 1H, J_{PH} 13.9, J 14.5 Hz), 3.86 (d, 1H, J 8.4 Hz), 4.16 (dd, 1H, J_{PH} 9.5, J 14.5 Hz), 4.96 (dd, 1H, J 4.0 Hz), 5.57 (dd, 1H, J 9.9, J 4.0 Hz), 5.81 (d, 1H, J 9.9 Hz), 6.73 (d, 1H, J_{PH} 17.2 Hz), 7.59−7.02 (m, 18H, ArH), 7.92 (m, 2H, ArH). ^{13}C NMR: δ 44.97 (d, CH, J_{PC} 12.0 Hz), 46.08 (d, CH_2, J_{PC} 1.7 Hz), 47.41 (d, CH, J_{PC} 14.1 Hz), 66.08 (d, CH, J_{PC} 12.0 Hz), 75.06 (CH), 123.86 (d, HC=, J_{PC} 7.0 Hz), 126.07 (HC=), 131.92−126.51 (18 CAr), 131.84 (d, CAr, J_{PC} 10.3 Hz), 133.46 (d, C_{ipso}, J_{PC} 134.0 Hz), 134.28 (d, C=, J_{PC} 121.2 Hz), 136.06 (C_{ipso}), 138.04 (d, HC=, J_{PC} 9.1 Hz), 138.43 (d, C_{ipso}, J_{PC} 9.1 Hz), 142.21 (C_{ipso}). ^{31}P NMR: δ 29.06. MS (API-ES), *m*/*e*: 505 (M + 2, 35), 504 (M + 1, 100), 486(14). Anal. Calcd for $C_{33}H_{30}NO_2P$: C, 78.71; H, 6.00; N, 2.78. Found: C, 78.69; H, 6.10; N, 2.72.

(1*RPSP*,3*SR*,3a*RS*,6*RS*,13*SR*)-2,3,3a,6-Tetrahydro-2-benzyl-6-(1-hydroxy-*para*-chlorophenylmethyl)-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (4ma). Precipitated from Et_2O. Yield: 63% (0.126 g). Mp: 212−213 °C. ^{1}H NMR: δ 3.25 (m, 2H), 3.60 (dd, 1H, J_{PH} 14.1, J 14.3 Hz), 3.80 (d, 1H, J 8.5 Hz), 4.18 (dd, 1H, J_{PH} 9.1, J 14.3 Hz), 4.98 (m, 1H), 5.56 (dd, 1H, J 9.9, J 3.7 Hz), 5.70 (d, 1H, J 9.9 Hz), 6.77 (d, 1H, J_{PH} 16.5 Hz), 7.59−7.02 (m, 18H, ArH), 7.93 (m, 2H, ArH). ^{13}C NMR: δ 44.80 (d, CH, J_{PC} 12.0 Hz), 46.06 (d, CH_2, J_{PC} 2.5 Hz), 47.29 (d, CH, J_{PC} 13.6 Hz), 66.08 (d, CH, J_{PC} 12.4 Hz), 74.50 (CH), 124.25 (d, HC=, J_{PC} 7.0 Hz), 125.37 (HC=), 131.88−127.10 (18 CAr), 131.83 (d, CAr, J_{PC} 10.3 Hz), 132.95 (C_{ipso}), 133.15 (d, C_{ipso}, J_{PC} 136.5 Hz), 134.94 (d, C=, J_{PC} 120.8 Hz), 135.93 (C_{ipso}), 137.49 (d, HC=, J_{PC} 9.9 Hz), 138.23 (d, C_{ipso}, J_{PC} 8.3 Hz), 140.58 (C_{ipso}). ^{31}P NMR: δ 28.45. MS (API-ES), *m*/*e*: 541 (M + 2, 18), 540 (M + 1, 48), 539 (M^+, 42), 538 (M − 1, 100). Anal. Calcd for $C_{33}H_{29}NO_2PCl$: C, 73.53; H, 5.42; N, 2.60. Found: C, 73.49; H, 5.37; N, 2.62.

(1*RPSP*,3*SR*,3a*RS*,6*RS*,13*SR*)-2,3,3a,6-Tetrahydro-2-benzyl-6-(1-hydroxy-*para*-chlorophenylmethyl)-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (4na). Yield after chromatography (ethyl acetate/hexane 2:1) was 76% (0.152 g). Mp: 183−185 °C. ^{1}H NMR: δ 3.18 (m, 1H), 3.29 (m, 1H, J 11.7, J 2.2 Hz), 3.62 (dd, 1H, J_{PH} 13.9, J 14.5 Hz), 3.79 (s, 3H), 3.90 (d, 1H, J 8.8 Hz), 4.16 (dd, 1H, J_{PH} 9.5, J 14.5 Hz), 4.59 (bs, OH), 4.91 (d, 1H, J 4.4 Hz), 5.55 (m, 1H, J 10.3 Hz), 5.77 (d, 1H, J 10.3 Hz), 6.69 (d, 1H, J_{PH} 17.2 Hz), 7.60−6.83 (m, 18H, ArH), 7.92 (m, 2H, ArH). ^{13}C NMR: δ 45.12 (d, CH, J_{PC} 12.4 Hz), 46.08 (d, CH_2, J_{PC} 2.0 Hz), 47.41 (d, CH,

J_{PC} 13.8 Hz), 55.19 (CH_3), 66.09 (d, CH, J_{PC} 12.0 Hz), 74.58 (CH), 113.60 (CAr), 123.82 (d, HC═, J_{PC} 6.6 Hz), 125.97 (HC═), 129.45−126.79 (14 CAr), 131.84 (d, CAr, J_{PC} 3.0 Hz), 131.85 (d, CAr, J_{PC} 10.2 Hz), 134.05 (d, C═, J_{PC} 120.7 Hz), 134.30 (C_{ipso}), 135.08 (d, C_{ipso}, J_{PC} 134.0 Hz), 138.35 (d, C_{ipso}, J_{PC} 10.2 Hz), 138.39 (d, HC═, J_{PC} 7.8 Hz), 158.70 (C_{ipso}). ^{31}P NMR: δ 29.04. MS (API-ES), *m/e*: 535 (M + 2, 35), 534 (M + 1, 100), 516 (18). Anal. Calcd for $C_{34}H_{32}NO_3P$: C, 76.53; H, 6.05; N, 2.63. Found: C, 76.49; H, 6.10; N, 2.62.

(1*RS*,3*SR*,3a*RS*,7a*RS*)-2,3,3a,7a-Tetrahydro-2-(*tert*-butyl)-7a-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (2o). Yield after chromatography (ethyl acetate/hexane 1:1) was 18% (0.018 g), methylation with CF_3SO_3Me. Mp: 102−105 °C dec. ^{1}H NMR: δ 0.71 (d, 3H, J_{PH} 16.5 Hz), 1.12 (s, 9H), 2.56 (ddd, 1H, *J* 9.9, *J* 6.2, *J* 1.1 Hz), 4.41 (dd, 1H, J_{PH} 1.5, *J* 9.9 Hz), 5.17 (dddt, 1H, J_{PH} 2.9, *J* 9.5, *J* 6.2, *J* 1.1 Hz), 6.02 (dd, 1H, *J* 9.5, *J* 5.4 Hz), 6.15 (ddd, 1H, *J* 9.9, *J* 5.4, *J* 1.1 Hz), 6.22 (ddd, 1H, J_{PH} 9.2, *J* 9.9, *J* 1.1), 7.66−7.01 (m, 8H, ArH), 8.15 (m, 2H, ArH). ^{13}C NMR: δ 19.80 (d, CH_3, J_{PC} 1.8 Hz), 30.74 (d, CH_3, J_{PC} 3.2 Hz), 39.48 (d, C, J_{PC} 87.4 Hz), 49.44 (d, CH, J_{PC} 5.1 Hz), 57.13 (d, C, J_{PC} 0.9 Hz), 66.27 (d, CH, J_{PC} 18.0 Hz), 122.41 (d, HC═, J_{PC} 12.0 Hz), 122.84 (d, HC═, J_{PC} 8.3 Hz), 123.90 (d, HC═, J_{PC} 2.8 Hz), 127.89 (d, HC═, J_{PC} 6.5 Hz), 132.61−126.27 (10CAr), 135.64 (d, C_{ipso}, J_{PC} 123.46 Hz), 144.98 (d, C_{ipso}, J_{PC} 10.2 Hz). ^{31}P NMR: δ 58.74. MS (API-ES), *m/e*: 378 (M + 1, 100), 322 (6). Anal. Calcd for $C_{24}H_{28}NOP$: C, 76.37; H, 7.48; N, 3.71. Found: C, 76.34; H, 7.45; N, 3.80.

(1*RS*,3*SR*,3a*RS*,7a*SR*)-2,3,3a,7a-Tetrahydro-2-(*tert*-butyl)-7a-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (3o). Yield after chromatography (ethyl acetate/hexane 1:1) 35% (0.071 g), methylation with CF_3SO_3Me. Mp: 85−86 °C dec. ^{1}H NMR: δ 1.24 (s, 9H), 1.34 (d, 3H, J_{PH} 13.2 Hz), 3.00 (m, 1H), 4.46 (dd, 1H, J_{PH} 0.7, *J* 11.4 Hz), 5.33 (m, 1H), 5.79 (m, 2H), 5.91 (m, 1H), 7.57−7.21 (m, 8H, ArH), 8.16 (m, 2H, ArH). ^{13}C NMR: δ 10.40 (d, CH_3, J_{PC} 3.2 Hz), 30.89 (d, CH_3, J_{PC} 2.8 Hz), 39.19 (d, C, J_{PC} 93.1 Hz), 48.35 (d, CH, J_{PC} 6.7 Hz), 56.75 (C), 61.76 (d, CH, J_{PC} 8.8 Hz), 123.23 (d, HC═, J_{PC} 13.7 Hz), 125.28 (d, HC═, J_{PC} 2.5 Hz), 125.37 (d, HC═, J_{PC} 10.2 Hz), 131.27 (d, HC═, J_{PC} 2.8 Hz), 132.59−127.06 (10CAr), 135.65 (d, C_{ipso}, J_{PC} 122.1 Hz), 143.53 (d, C_{ipso}, J_{PC} 7.4 Hz). ^{31}P NMR: δ 50.71. MS (API-ES), *m/e*: 378 (M + 1, 100), 362 (5), 320 (8). Anal. Calcd for $C_{24}H_{28}NOP$: C, 76.37; H, 7.48; N, 3.71. Found: C, 76.40; H, 7.48; N, 3.70.

(1*RS*,3*SR*,3a*RS*,6*RS*)-2,3,3a,6-Tetrahydro-2-(*tert*-butyl)-6-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (4o). Yield after chromatography (ethyl acetate/hexane 1:1) was 41% (0.082 g), methylation with MeI. Mp: 74−77 °C. ^{1}H NMR: δ 1.00 (d, 3H, *J* 7.3 Hz), 1.16 (s, 9H), 2.95 (m, 1H), 3.20 (m, 1H), 4.29 (d, 1H, *J* 9.5 Hz), 5.40 (dddd, 1H, J_{PH} 1.1, *J* 9.9, *J* 2.2, *J* 1.1 Hz), 5.72 (m, 1H), 6.63 (dddd, 1H, J_{PH} 16.1 *J* 4.8, *J* 2.9, *J* 1.5 Hz), 7.51−7.15 (m, 8H, ArH), 8.08 (m, 2H, ArH). ^{13}C NMR: δ 20.34 (d, CH_3, J_{PC} 2.8 Hz), 30.85 (d, CH_3, J_{PC} 3.2 Hz), 32.40 (d, CH, J_{PC} 12.0 Hz), 45.69 (d, CH, J_{PC} 15.3 Hz), 57.15 (d, C, J_{PC} 1.4 Hz), 67.09 (d, CH, J_{PC} 11.6 Hz), 121.50 (d, HC═, J_{PC} 6.9 Hz), 131.60 (d, HC═, J_{PC} 1.4 Hz), 132.79 (d, C═, J_{PC} 119.3 Hz) 133.59−127.81 (10CAr), 137.44 (d, C_{ipso}, J_{PC} 132.2 Hz), 138.78 (d, HC═, J_{PC} 8.3 Hz), 144.00 (d, C_{ipso}, J_{PC} 9.7 Hz). ^{31}P NMR: δ 32.30. MS (API-ES), *m/e*: 377 (M^+, 15), 306 (100), 201 (75), 39 (33). Anal. Calcd for $C_{24}H_{28}NOP$: C, 76.37; H, 7.48; N, 3.71. Found: C, 76.30; H, 7.47; N, 3.76.

(1*RS*,3*RS*,3a*RS*,6*RS*)-2,3,3a,6-Tetrahydro-2-(*tert*-butyl)-6-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (6o). Yield after chromatography (ethyl acetate/hexane 1:1) 16% (0.032 g), methylation with MeI. Oil. Identified from a 62:48 mixture of **7o** and **6o**. ^{1}H NMR: δ 0.86 (d, 3H, *J* 7.3 Hz), 1.13 (s, 9H), 2.64 (m, 1H), 3.83 (m, 1H), 4.87 (dd, 1H, J_{PH} 18.0, *J* 7.7 Hz), 5.39−5.25 (m, 2H), 6.43 (d, 1H, J_{PH} 16.5 Hz), 7.58−7.11 (m, 8H, ArH), 7.95 (m, 2H, ArH). ^{13}C NMR: δ 20.98 (s, CH_3), 30.56 (d, CH_3, J_{PC} 2.4 Hz), 31.19 (d, CH, J_{PC} 12.3 Hz), 42.78 (d, CH, J_{PC} 16.1 Hz), 55.40 (d, C, J_{PC} 2.8 Hz), 63.84 (d, CH, J_{PC} 11.2 Hz), 121.83 (d, HC═, J_{PC} 7.0 Hz), 127.60−131.78 (10CAr), 130.66 (d, HC═, J_{PC} 1.8 Hz), 131.87 (d, C═, J_{PC} 121.8 Hz), 137.09 (d, C_{ipso}, J_{PC} 128.8 Hz), 139.92 (d, HC═, J_{PC} 9.5 Hz), 141.99 (d, C_{ipso}, J_{PC} 0.7 Hz). ^{31}P NMR: δ 26.04.

(1*RS*,3*RS*,3a*RS*,6*SR*)-2,3,3a,6-Tetrahydro-2-(*tert*-butyl)-6-methyl-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (7o). Yield after chromatography (ethyl acetate/hexane 1:1) was 6% (0.012 g), methylation with MeI. Oil. Identified from a 62:48 mixture of **7o** and **6o**. ^{1}H NMR: δ 0.91 (d, 3H, *J* 7.3 Hz), 1.11 (s, 9H), 2.64 (m, 1H), 3.83 (m, 1H, 4.86 (dd, 1H, J_{PH} 17.6, *J* 7.3 Hz), 5.39−5.25 (m, 2H), 6.56 (d, 1H, J_{PH} 16.1 Hz), 7.58−7.11 (m, 8H, ArH), 7.97 (m, 2H, ArH). ^{13}C NMR: δ 20.63 (d, CH_3, J_{PC} 2.5 Hz), 30.55 (d, CH_3, J_{PC} 2.5 Hz), 31.62 (d, CH, J_{PC} 12.3 Hz), 42.73 (d, CH, J_{PC} 16.1 Hz), 55.39 (d, C, J_{PC} 2.8 Hz), 64.04 (d, CH, J_{PC} 11.6 Hz), 122.36 (d, HC═, J_{PC} 7.0 Hz), 127.60−131.78 (10CAr), 130.88 (d, HC═, J_{PC} 1.8 Hz) 131.90 (d, C═, J_{PC} 121.8 Hz), 137.04 (d, C_{ipso}, J_{PC} 128.8 Hz), 140.28 (d, HC═, J_{PC} 9.1 Hz), 142.14 (d, C_{ipso}, J_{PC} 0.7 Hz). ^{31}P NMR: δ 26.42. MS (API-ES), *m/e*: 377 (M^+, 100). Anal. Calcd for $C_{24}H_{28}NOP$: C, 76.37; H, 7.48; N, 3.71. Found: C, 76.45; H, 7.27; N, 3.70.

(1R_PS_P,3*SR*,3a*RS*,6*RS*,13*SR*)-2,3,3a,6-Tetrahydro-2-(*tert*-butyl)-6-(1-hydroxyphenylmethyl)-1,3-diphenylbenzo[*c*]-[1,2]azaphosphole 1-Oxide (4pa). Yield after chromatography (ethyl acetate/hexane 2:1) 42% (0.084 g). Oil. ^{1}H NMR: δ 1.10 (s, 9H), 3.19 (m, 2H), 4.23 (d, 1H, *J* 8.9 Hz), 4.99 (d, 1H, *J* 3.2 Hz), 5.52 (m, 1H), 5.70 (d, 1H, *J* 9.7 Hz), 6.56 (d, 1H, J_{PH} 17.0 Hz), 7.53−7.12 (m, 13H, ArH), 8.12 (m, 2H, ArH). ^{13}C NMR: δ 30.78 (d, CH_3, J_{PC} 3.2 Hz), 45.04 (d, CH, J_{PC} 11.6 Hz), 46.55 (d, CH, J_{PC} 14.8 Hz), 57.24 (C), 66.82 (d, CH, J_{PC} 11.6 Hz), 74.73 (CH), 123.83 (d, HC═, J_{PC} 7.4 Hz), 125.35 (HC═), 132.33−126.09 (13 CAr), 130.53 (d, C═, J_{PC} 124.3 Hz), 131.45 (d, CAr, J_{PC} 10.2 Hz), 133.47 (d, C_{ipso}, J_{PC} 136.4 Hz), 136.33 (d, HC═, J_{PC} 9.7 Hz), 142.12 (C_{ipso}), 143.43 (d, C_{ipso}, J_{PC} 10.2 Hz). ^{31}P NMR: δ 32.29. MS (API-ES), *m/e*: 470 (M + 1, 45), 469 (M^+, 28), 413 (25), 337 (30), 309 (100 Anal. Calcd for $C_{30}H_{32}NO_2P$: C, 76.74; H, 6.87; N, 2.98. Found: C, 76.70; H, 6.81; N, 3.00.

(1R_PS_P,3*RS*,3a*RS*,6*RS*,13*SR*)-2,3,3a,6-Tetrahydro-2-(*tert*-butyl)-6-(1-hydroxyphenylmethyl)-1,3-diphenylbenzo[*c*]-[1,2]azaphosphole 1-Oxide (6pa). Yield after chromatography (ethyl acetate/hexane 2:1, and then ethyl acetate/hexane 1:1) was 28% (0.011 g). Oil. ^{1}H NMR: δ 1.15 (s, 9H), 2.98 (m, 1H, *J* 5.2, *J* 2.2 Hz), 3.90 (m, 1H, *J* 9.9, *J* 5.2, *J* 2.6 Hz), 4.26 (d, 1H, *J* 6.2 Hz), 4.94 (dd, 1H, J_{PH} 17.2, *J* 7.3 Hz), 5.14 (m, 1H, *J* 10.3 Hz), 5.46 (dddd, 1H, *J* 10.3, *J* 4.4, *J* 2.6, *J* 2.6 Hz), 6.66 (ddd, 1H, J_{PH} 16.5, *J* 4.0, *J* 2.2 Hz), 7.57−7.16 (m, 13H, ArH), 7.93 (m, 2H, ArH). ^{13}C NMR: δ 30.49 (d, CH_3, J_{PC} 3.0 Hz), 43.61 (d, CH, J_{PC} 16.8 Hz), 44.32 (d, CH, J_{PC} 12.0 Hz), 55.60 (d, C, J_{PC} 2.4 Hz), 63.68 (d, CH, J_{PC} 10.8 Hz), 76.18 (CH), 125.57 (d, HC═, J_{PC} 7.2 Hz), 128.43−126.20 (12 CAr), 126.92 (d, HC═, J_{PC} 1.2 Hz), 131.32 (d, CAr, J_{PC} 2.4 Hz), 131.62 (d, CAr, J_{PC} 10.8 Hz), 134.31 (d, C═, J_{PC} 125.0 Hz), 135.27 (d, HC═, J_{PC} 10.2 Hz), 136.29 (d, C_{ipso}, J_{PC} 129.8 Hz), 141.65 (d, C_{ipso}, J_{PC} 0.9 Hz), 141.72 (C_{ipso}). ^{31}P NMR: δ 24.84. MS (API-ES), *m/e*: 471 (M + 2, 23), 470 (M + 1, 100), 396 (10), 306 (7). Anal. Calcd for $C_{30}H_{32}NO_2P$: C, 76.74; H, 6.87; N, 2.98. Found: C, 76.69; H, 6.87; N, 3.02.

(1R_PS_P,3*RS*)-2,3-Dihydro-2-benzyl-1,3-diphenylbenzo-[*c*][1,2]azaphosphole 1-Oxide (9c). Yield after chromatography (ethyl acetate) was 53% (0.106 g). Oil. ^{1}H NMR: δ 3.66 (dd, 1H, J_{PH} 13.0, *J* 15.1 Hz), 4.45 (dd, 1H, J_{PH} 8.4, *J* 15.1 Hz), 5.38 (s, 1H), 7.71−6.98 (m, 13H, ArH), 7.92 (m, 2H, ArH). ^{13}C NMR: δ 45.51 (d, CH_2, J_{PC} 4.2 Hz), 65.27 (d, CH, J_{PC} 12.6 Hz), 124.84 (d, CAr, J_{PC} 9.6 Hz), 128.94−127.37 (16CAr), 129.66 (d, C_{ipso}, J_{PC} 126.8 Hz), 131.92 (d, CAr, J_{PC} 2.4 Hz), 132.50 (d, C_{ipso}, J_{PC} 134.0 Hz), 132.54 (d, CAr, J_{PC} 10.8 Hz), 136.82 (C_{ipso}), 138.95 (d, C_{ipso}, J_{PC} 6.0 Hz), 147.36 (d, C_{ipso}, J_{PC} 15.6 Hz). ^{31}P NMR: δ 36.35. MS (API-ES), *m/e*: 419 (M + 1 + Na^+, 25), 418 (M + Na^+, 100), 396 (M + 1, 47). Anal. Calcd for $C_{26}H_{22}NPO$: C, 78.97; H, 5.61; N, 3.54. Found: C, 78.94; H, 5.69; N, 3.51.

(1*R*$_P$*S*$_P$,3*RS*)-2,3-Dihydro-2-(*tert*-butyl)-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (9d). Yield after chromatography (ethyl acetate/hexane 1:1) was 22% (0.044 g). Oil. ^{1}H NMR: δ 1.32 (s, 9H), 5.85 (s, 1H), 7.53−6.98 (m, 12H, ArH), 7.99 (m, 2H, ArH). ^{13}C NMR: δ 30.75 (d, CH3, J_{PC} 3.3 Hz), 56.84 (d, C, J_{PC} 2.1 Hz), 66.23 (d, CH, J_{PC} 11.6 Hz), 124.46 (d, CAr, J_{PC} 10.3 Hz), 129.66 (d, C_{ipso}, J_{PC} 125.7 Hz), 132.63−127.21 (14CAr), 135.93 (d, C_{ipso}, J_{PC} 133.6 Hz), 144.86 (d, C_{ipso}, J_{PC} 7.0 Hz), 147.31 (d, C_{ipso}, J_{PC} 17.8 Hz). ^{31}P NMR: δ 40.59. MS (API-ES), *m*/*e*: 362 (M + 1, 100). Anal. Calcd for $C_{23}H_{24}$NOP: C, 76.43; H, 6.69; N, 3.87. Found: C, 76.34; H, 6.65; N, 3.88.

(1*R*$_P$*S*$_P$,3*SR*)-2,3-Dihydro-2-(*tert*-butyl)-1,3-diphenylbenzo[*c*][1,2]azaphosphole 1-Oxide (10a). Yield after chromatography (ethyl acetate/hexane 1:1) was 27% (0.054 g). Mp: 195−197 °C. ^{1}H NMR: δ 1.15 (s, 9H), 5.72 (d, 1H, J_{PH} 11.0 Hz), 7.54−6.99 (m, 12H, ArH), 7.70 (m, 2H, ArH). ^{13}C NMR: δ 30.86 (d, CH3, J_{PC} 2.5 Hz), 55.61 (d, C, J_{PC} 3.7 Hz), 66.66 (d, CH, J_{PC} 12.8 Hz), 124.16 (d, CAr, J_{PC} 9.5 Hz), 130.13 (d, C_{ipso}, J_{PC} 122.0 Hz), 132.61−126.15 (14CAr), 136.55 (d, C_{ipso}, J_{PC} 127.4 Hz), 144.41 (C_{ipso}), 147.40 (d, C_{ipso}, J_{PC} 16.5 Hz). ^{31}P NMR: δ 34.31. MS (API-ES), *m*/*e*: 362 (M + 1, 100), 306 (22). Anal. Calcd for $C_{23}H_{24}$NOP: C, 76.43; H, 6.69; N, 3.87. Found: C, 76.44; H, 6.69; N, 3.85.

***N*,*N*-Dibenzyl(*o*-methylphenyl)phenylphosphinamide (11b).** Yield after chromatography (ethyl acetate/hexane 1:1) was 25% (0.050). Oil. ^{1}H NMR: δ 2.63 (s, 3H), 4.12 (ddd, 4H, J_{PH} 9.8, J 16.6 Hz), 7.59−7.13 (m, 17H, ArH), 7.78 (m, 2H, ArH). ^{13}C NMR: δ 21.78 (d, CH_3, J_{PC} 3.5 Hz), 48.58 (d, CH_2, J_{PC} 4.0 Hz), 132.43−125.07 (18CAr), 130.35 (d, C_{ipso}, J_{PC} 124.7 Hz), 133.16 (d, CAr, J_{PC} 12.0 Hz), 137.01 (d, C_{ipso}, J_{PC} 3.0 Hz), 143.49 (d, C_{ipso}, J_{PC} 9.5 Hz). ^{31}P NMR: δ 37.09. MS (API-ES), *m*/*e*: 412 (M + 1, 100), 347 (7). Anal. Calcd for $C_{27}H_{26}$NPO: C, 78.81; H, 6.37; N, 3.40. Found: C, 78.74; H, 6.35; N, 3.42.

***N*-Benzyl-*N*-(*tert*-butyl)(*o*-methylphenyl)phenylphosphinamide (11c).** Yield after chromatography (ethyl acetate/hexane 1:1) was 3% (0.006 g). Oil. ^{1}H NMR: δ 1.50 (s, 9H), 2.52 (s, 3H), 4.31 (d, 2H, J_{PH} 14.3 Hz), 7.63−7.01 (m, 12H, ArH), 8.08 (m, 2H, ArH). ^{13}C NMR: δ 21.83 (d, CH_3, J_{PC} 3.2 Hz), 31.28 (d, CH_3, J_{PC} 2.8 Hz), 49.67 (d, CH_2, J_{PC} 6.6 Hz), 58.40 (d, C, J_{PC} 1.8 Hz), 133.05−121.23 (14CAr), 135.17 (d, C_{ipso}, J_{PC} 123.0 Hz), 140.99 (d, C_{ipso}, J_{PC} 1.9 Hz), 143.07 (d, C_{ipso}, J_{PC} 9.7 Hz). ^{31}P NMR: δ 37.35. MS (API-ES), *m*/*e*: 378 (M + 1, 100). Anal. Calcd for $C_{24}H_{28}$NPO: C, 76.37; H, 7.48; N, 3.71. Found: C, 76.24; H, 7.39; N, 3.81.

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Supporting Information Available: Figure S1, distribution of product for the alkylation of **1b** in the presence of HMPA and DMPU; Figure S2, distribution of products for the alkylation of **1b** without cosolvents; Figure S3, one-dimensional gTOCSY spectra of **4ha** and **17**; Figure S4, one-dimensional gNOESY spectra of **4b**; Figure S5, two-dimensional gNOESY of **4fa**; Figure S6, two-dimensional gNOESY of **4ga**; and X-ray data of **14ba** (Figure S7) and **14bb** (Figure S8). This material is available free of charge via the Internet at http://pubs.acs.org.

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