The isomeric structure of pentacoordinate chiral spirophosphoranes in solution by the combined use of NMR experiments and GIAO DFT calculations of NMR parameters†

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The interplay of NMR experiments and DFT calculations of NMR parameters is a reliable method for determining the relative configurations of pentacoordinate chiral spirophosphoranes bearing two six- or five-membered rings at the phosphorus atom in solution. The major product of the Betti based derivatives corresponds to the isomers with both substituents at chiral carbons being opposite to the P–H proton. The next populated product corresponds to the isomer with different chiralities at carbons. The least populated isomer is one with both substituents being at the same side of the heterocycle as the P–H bond.

Introduction

Chiral phosphorus compounds are widely used in stereo-selective synthesis. For example, chiral phosphorus ligands are of importance in the design of catalysts for asymmetric homogeneous catalysis. Pentacoordinate phosphorus compounds have drawn special attention for their role as intermediates in some biological processes (e.g. enzymatic phosphoryl transfer reactions, hydrolysis/formation of DNA, RNA, cyclic AMP). Their structural and dynamic properties strongly correlate with the reactivity/selectivity of the processes they are involved in. Although the knowledge about the stereochemistry (the absolute and relative configurations) of these compounds is important in understanding these processes, very few structural studies of pentacoordinate phosphorus systems have been published so far.

Pentacoordinate phosphoranes with an asymmetric phosphorus atom and with several additional chiral chelate ligands are especially difficult to analyze, since these chiral centers may generate a variety of stereoisomers and the determination of their fine structure is not straightforward. To this end X-ray single crystal investigations could be helpful, but obtaining good single crystals is often time consuming and sometimes impossible. This point, coupled with the fact that most chemical reactions and biological processes occur in solution, makes it highly desirable to find an alternative, reliable, and easy way to determine the relative configurations of such hypervalent chiral phosphorus compounds directly in solution.

Progress in NMR correlation techniques and the state-of-the-art density functional theory (DFT) calculations of NMR parameters has emerged in recent years as a very powerful tool for fine structural analysis of organic compounds and biomolecules. There are a number of examples when DFT calculations of 1H, 13C and 15N parameters in the frame of the GIAO method allowed the establishment of tautomeric, isomeric and conformational structures as well. However applications of similar approaches to analyze phosphorus compounds by DFT calculations of 31P NMR parameters are very rare.

The study here shows that the interplay of the NMR experiment and theory is a powerful method for determining the relative configurations of pentacoordinate chiral spirophosphoranes. For the illustration several pentacoordinate spirophosphoranes bearing two six-membered (Betti based derivatives) and five-membered (α-aminocarboxylic acid derivatives) rings at the phosphorus atom were used.

Results

Synthesis

Three chiral elements (two centres and one axis) lead to the four possible combinations. In order to obtain the full set of
stereoisomers we used racemic Betti bases. The synthesis of P-H-spirophosphoranes was carried out by substituting the amino groups in the hexaethyltriamidophosphite by 1-(α-aminobenzyl)-2-naphthols (Scheme 1). For example, in the $^{31}$P{$^1$H} NMR spectra of the reaction mixture of 4 there are two signals with the chemical shifts (CS) characteristic of phosphoranes ($-75.4$ (65%) and $-76.7$ (35%) ppm) that may be attributed to the formation of two isomers.

In contrast to the dominant product ($\delta^{31}$P = $-75.4$ ppm), the $^1$H spectra of which correspond to the high symmetry structure, the second component apparently has no symmetry, and two spiro halves of phosphorane 4 differ in the $^1$H NMR spectrum. When diethylamine hydrochloride is used as the catalyst, these two isomers could be obtained in an about 1:1 ratio and their isolation in individual form becomes possible via crystallization. It is interesting that after about 4-6 hours in the NMR spectrum of the individual product that was major in the initial reaction mixture ($\delta^{31}$P = $-75.4$ ppm), additional signals appeared which can also be attributed to the structure of high symmetry ($\delta^{31}$P = $-80.7$ ppm) with two spiro-connected six-membered heterocycles being equivalent in the $^1$H NMR spectra.

In a similar manner for 5 the formation of two isomers was observed which were separated and analyzed (Fig. 1a and b). In this case the $^{19}$F NMR is particularly useful and allows distinguishing symmetrical (one singlet, $\delta^{19}$F = $-116$ ppm) and non-symmetrical (two singlet’s of equal intensity, $\delta^{19}$F = $-115.8$ and $\delta^{19}$F = $-116.6$ ppm) isomers. The monitoring of the major isomer 5a via the $^1$H and $^{31}$P NMR showed that after some time an additional product appeared (10%) in solution ($\delta^{19}$F = $-115.5$ and $\delta^{31}$P = $-81.0$ ppm) which presumably corresponds to another symmetrical isomer (Fig. 1c).

For compound 6 very similar spectra and their evolution were observed (ESI†).

**Structure determination**

**Chemical structure and assignment.** A variety of NMR correlations allows one to prove the chemical structure of two main stereoisomers practically directly. For example, first, starting
most spectacular are the values of direct pseudorotation process, so its configuration was assigned as CSs and spin particularities diastereomers of the phosphoranes (be used in fine structural analysis. Meters, being related to local magnetic environments, could spectra, only some principal resonances can be identified with establish connectivities up to fluorine atoms. As to the third bond (Δ_pR_pR_Λ_pS_pS_c, I), with one aryl opposite to the P–H bond and another one being on the same side of the cycle with the P–H bond (Δ_pR_pS_pS/p_pS_pR_Λ_p, II), in the third isomer both aryls are at the same side of the cycle with the P–H bond (Δ_pR_pR_Λ_pS_pS_c, III) (Fig 2).

Qualitative consideration of these structures predicts some stereospecific features. There are different dihedral angles between H_4–C and N–P in isomers I and III, that may lead to different three bond SCSs. As to the II-nd isomer, the geometries of its two spiro-halves are very similar to the halves of the I-st and III-rd isomers, therefore two sets of signals are expected for its 1H (13C, 19F) spectra.

Thus, preliminary identification can be based on NOEs and symmetry considerations. Presumably, the “a” (major) products can be ascribed to the I isomer because there is no NOE between the ortho-aryl and P–H protons. Lack of symmetry in the second product (“b”) may be indicative of the II-isomer. As to the co-product (“c”) that appeared after some time in solution of the major isomer (“a”), there are no clear NOEs that can be used due to its low population and the signal overlapping with the main product.

To develop a well-argued relationship between the NMR parameters and the fine isomeric structure, DFT calculations of the NMR parameters were carried out for these structural hypotheses. It is well demonstrated that modern GIAO CS calculations on 13C, 15N and 1H nuclei achieved experimental accuracy and can be used as an additional tool for chemical structure elucidation. There are a number of examples of application of such calculations on these nuclei to obtain fine information on the isomeric, tautomeric and conformational structure.39–53,57–60 At the same time the examples of

Table 1  Some experimental and calculated NMR parameters\(^a\) for compounds 4–6

| Comp. | X at C_{11} | R at C_{4} | Isomer | Δ_p \(^b\) | δ_{13}P | δ_H6 | δ_H16,20 | δ_H17,19 | δ_H4 | δ_H5 | 1J_{P11} | 1J_{P14} |
|-------|-------------|------------|---------|----------|--------|------|--------|--------|------|------|--------|--------|
| 4     | H           | Ph         | I       | Exp (a)  | −75.4  | 7.08 | 7.32  | 7.19  | 5.95 | 4.18 | 788.5  | 34.1   |
|       |             |            | II      | Exp (b)  | −75.2  | 7.66 | 7.64  | 7.41  | 5.98 | 3.77 | 715.6  | 36.1   |
|       |             |            | II      | 0.53     | −76.4  | 7.80 | 7.42  | 7.21  | 5.81 | 3.46 | 742.6  | 35.2   |
|       |             |            | III     | Exp (c)  | −80.7  | 7.54 | nd\(^d\) | nd    | 5.74 | 3.58 | 848.6  | 25.6   |
| 5     | H           | FcH_{4}    | I       | Exp (a)  | −75.2  | 7.09 | 7.26  | 6.88  | 5.91 | 4.17 | 792.1  | 34.1   |
|       |             |            | II      | Exp (b)  | −76.6  | 7.32 | 6.91  | 6.58  | 6.95 | 3.77 | 824.0  | 27.7, 33.6 |
|       |             |            | III     | Exp (a)  | −80.5  | 7.52 | nd\(^d\) | nd    | 5.70 | 3.56 | 849.0  | 25.0   |
| 6     | Br          | Ph         | I       | Exp (a)  | −76.4  | 7.08 | 7.27  | 7.19  | 5.89 | 4.17 | 790.4  | 34.1   |
|       |             |            | II      | Exp (b)  | −75.6  | 7.62 | 7.58  | 7.41  | 5.92 | 3.74 | 718.3  | 36.0   |
|       |             |            | III     | Exp (c)  | −81.4  | 7.54 | nd\(^d\) | nd    | 5.71 | 3.58 | 852.3  | 25.1   |

\(^a\) Chemical shifts in ppm, spin–spin couplings in Hz. \(^b\) Relative energy, in kcal mol\(^{-1}\). \(^c\) Experimental data. \(^d\) No data.

\(^\dagger\) The isomer III might be produced from isomer Δ_pR_pR_ (Δ_pS_pS_c) by the Berry pseudorotation process, so its configuration was assigned as Δ_pR_pR_ (Δ_pS_pS_c).

from \(^1\)H–\(^15\)N HSQC connectivities the NH protons were revealed, then the vicinal H_4 protons were assigned based on COSY data. Next, the \(^1\)H–\(^31\)P HMBC connectivities from the NH and H_4 to phosphorus allowed the determination of the structure of this central moiety (Fig. 1d). Further on, the \(^3\)H–\(^13\)C HSQC/HMBC and \(^3\)H–\(^1\)H COSY correlations allow establishing the structures of two aromatic fragments (ESI†). In addition, for 5 the \(^1\)H–\(^19\)F HETCOR correlations help to establish connectivities up to fluorine atoms. As to the third (minor) isomer due to its low population and extensive overlapping with the signals of the first isomer in the \(^1\)H NMR spectra, only some principal resonances can be identified with confidence (e.g. Fig. 1c). However, the 2D \(^1\)H–\(^31\)P HMBC experiments (ESI†) allow one to unambiguously reveal its signal in the \(^31\)P spectra and also the PH, NH and H_4 proton resonances (e.g. for 5c Fig. 1c).

Isomeric structure. The analysis of the NMR parameters of diastereomers of the phosphoranes 4–6 reveals some general particularities – namely, there are notable differences in some CSs and spin–spin couplings (SSCs) of the isomers (ESI†). The most spectacular are the values of direct \(^1\)J_{HP} SSCs, that vary from ~790 (a-product) up to ~850 (c-product) Hz (Table 1), and also the difference in \(^1\)J_{P14} SSCs. The \(^1\)H CSs of PH, H_4 and aryl protons and \(^31\)P CSs are diastereomer dependent in these products as well. Thus, it is likely that NMR parameters, being related to local magnetic environments, could be used in fine structural analysis.

In general, three chiral centers (at P, C_4 and C_{4c}) may generate four diastereomers: Δ_pR_pR_Λ_pS_pS_c, Δ_pR_pR_Λ_pS_pS_c, Δ_pR_pR_Δ_pS_pS_c and Δ_pS_pR_Δ_pR_pS_c. However, when both aryls in chiral centers are the same the last two isomers become equivalent in terms of NMR. Thus three main isomers were considered in details: with both aryl substituents being opposite to the P–H bond (Δ_pR_pR_Λ_pS_pS_c, I), with one aryl opposite to the P–H bond and another one being on the same side of the cycle with the P–H bond (Δ_pR_pS_pS/p_pS_pR_Λ_p, II), in the third isomer both aryls are at the same side of the cycle with the P–H bond (Δ_pR_pR_Λ_pS_pS_c, III) (Fig 2).
application of these approaches on phosphorus are rather sparse.\textsuperscript{54–56}

We used a combination (PBE1PBE/6-311G(2d,2p)/PBE1PBE/6-31+G(d)) that proved to be reliable and effective for \(^{31}\text{P}\) NMR CS calculations. First, the geometry optimization in the frames of the DFT (PBE1PBE/6-31+G(d)) method predicts that these three main isomers are close in energy (Table 1). Additional calculations with the inclusion of solvent effects (in the frames of the PCM model, Table S1) do not change notably the energy distribution. In general, these results are in qualitative agreement with experimental findings that all three isomers are present in the reaction mixture after some time.

The results of the CS and SSC calculations (GIAO PBE1PBE/6-311G(2d,2p)) for optimized structures are also in agreement with preliminary conclusions (some essential data are summarized in Table 1). According to the calculations, the PH, H\(_4\) and NH protons and \(^{31}\text{P}\) CSs should be notably different, particularly, for the I-st and the III-rd isomers. Namely, for the I-isomer, the PH proton should resonate at a higher field than for the III-isomer, while for the H\(_4\) and the NH protons the reverse should be observed. Likewise the \(^{31}\text{P}\) resonance signal of the I-isomer should be at a lower field than in the III-isomer. For the II-isomer, intermediate values are expected (Table 1). Thus, according to the CS data the major (“a”) product should be assigned to the I-isomer for all title compounds. The second non-symmetrical product corresponds to the II-diastereomer while the minor product may be assigned to the III-isomer.

Some SSCs also demonstrate spectacular distinctions for three isomers (Table 1) that correlate well with experimental data. As can be seen the \(J_{\text{HP}}\) constants are characteristic of these isomers and can be used to assign the isomeric structure. The smallest values (715.4 Hz) are predicted for the I-st isomers while for the III-rd forms these values are notably larger (762.7 Hz). For the II-isomers the PH direct SSCs are expected to have intermediate values (742.6 Hz). The calculations slightly underestimate (by ca. 1.1) the experimental data although the correlation is quite good. Thus, the comparison of the calculated versus experimental SSCs allows the assignment of the major product to the I-st isomer, the second product to the II-rd isomer and the least populated product to the III-rd isomer.

The \(J_{\text{HP}}\) between P and H\(_4\) is also very stereospecific (Table 1). First, the calculations predict SSCs to have large absolute values and be essentially different, at least, for the I-st and III-rd isomers. For the II-rd isomers there are two different values for each half but these SSC are close to the corresponding SSCs of the I-st and III-rd isomers, respectively. In spite of the fact that theory slightly underestimates these SSCs, the calculated values and tendencies are in good agreement with the experimentally observed data (Table 1). Thus, the comparison of the experimental versus calculated data also allows the assignment that is in accordance with the above conclusion.

These conclusions were supported by solid-state data in some cases. Namely, good crystals suitable for X-ray analysis were grown for the second isomer of racemic 4, which is crystallized as a conglomerate, and for the major product of racemic 5. The results of X-ray single crystal diffraction turned out to be in full agreement with the NMR data. In crystals the major product of 5 is realized in the I form (see Fig. 3) with both aryls directed opposite to the P-H bond. In general, the solid-state geometry is close to the DFT optimized one.

It is interesting that the crystallized product of 4 corresponded to the asymmetrical II-form that is also in agreement with the conclusion based on the NMR data. Thus for the title chiral pentacoordinate spirophosphoranes there are several NMR parameters that can be used to establish the isomeric structure. These relationships are summarized in Fig. 4.

**Correlation of NMR parameters with the isomeric structure for other chiral pentacoordinate spirophosphoranes**

The interplay of the NMR experiment and theory can be safely used to determine the isomeric structure of chiral pentacoordinate spirophosphoranes with six-membered heterocycles. To this end it is of interest to see if this approach could also be applied to determine the isomeric structure of other similar chiral pentacoordinate spirophosphoranes, e.g. with five-membered heterocycles. For example, there are experimental data for a series of chiral pentacoordinate spirophosphoranes obtained from \(\alpha\)-amino carboxic acids (Scheme 2).\textsuperscript{33–37} These
compounds were extensively analyzed by CD and X-ray single
diffraction. When enantiomerically pure reagents were being
used, the reactions produced only two diastereomers.

A brief survey of available NMR data demonstrates that
there are also some specific features of experimental CSs and
SSCs characteristic of two diastereomers although somewhat
distinct from those observed for the title compounds. First, for
five-membered spirophosphoranes the reverse $^{31}$P CS distri-
bution is observed, i.e. the “I” isomers resonate at a higher
field than “III” isomers (some data are included in Table 2).

Second, the $^{1}J_{PH}$ values are smaller for the “I” isomers than for
the “III”-forms. As to the $^{3}J_{PH}$ constants they are notably
smaller (<13 Hz). Third, there are substantial long range $^{3}J_{HPH}$
SSCs (2.4 Hz) in the “III” forms that were not seen in the
“I” isomers presumably due to their small values.

These differences are reproduced by theory. According to
our calculations performed for the simplest compounds from
this series with i-Pr (7) or Bz (8) groups at chiral carbons
(Table 2), indeed, the “I” isomer has to resonate at a higher
field in the $^{31}$P NMR spectra than the “III” form.

The calculated SSCs are also qualitatively consistent with
the experimental values, although some underestimation is
also seen. First, a larger one bond SSC is predicted for the
“III”-isomers (Table 2) than for the “I” form. According to the
calculations, the $^{3}J_{PH}$ SSCs should be notably smaller than for
the title compounds. Moreover, for the “III”-isomers one
may expect a long range four bond SSC between HP and H4
(2.0 versus 0.5 Hz) larger than for the “I” isomer. Thus, several
NMR parameters can also be used to determine the relative
configuration at chiral carbons in these pentacoordinate
spirophosphoranes.

Discussion

Let us consider why some relationships are different in these
two series of spirophosphoranes. There are two essential NMR
features that distinguish 5-membered spirophosphoranes from
6-membered compounds: (a) $^{3}J_{PH}$ – small absolute value for
the 5-cycle and large for the 6-cycle; (b) $\delta^{31}P_{I} > \delta^{31}P_{III}$ for
6-membered and $\delta^{31}P_{I} < \delta^{31}P_{III}$ for 5-membered.

To reveal key factors that determine these differences we
analyzed the influence of substituents at carbon chiral centers
and the nature of the fused aromatic fragments theoretically.

Unfortunately, $^{1}H$ CS’s data cannot be analyzed in this case as different sol-
vents were used in experiments for different diastereomers.

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\[\begin{array}{ccc}
\delta^{31}P_{I} & > & \delta^{31}P_{II} > \delta^{31}P_{III} \\
^{1}J_{PH} & < & ^{1}J_{PH} < ^{1}J_{PH} \\
^{3}J_{PH} & > & ^{3}J_{PH} > ^{3}J_{PH}
\end{array}\]
with small (Me, 10) and large (t-Bu, 11) alkyl groups, as well as aromatic (Ph, 9) fragments at chiral centers (Fig. 5c and d). According to calculations (Table 3), the main tendencies are also the same as for the title compounds. That is there is no specific influence of the R at the chiral carbon atoms on the $\delta^{31}P$ and $^3J_{PH}$ difference in the main isomers.

In order to reveal the impact of the fused aromatic unit on NMR parameters, the benzo fragment was replaced by a double bond (12, Fig. 4e) in the next step. In this case the reverse distribution of $^{31}P$ CSs for the two main isomers and notably smaller $^3J_{PH}$ SSCs are expected. This is very similar to the trends found in 5-membered compounds.

### Table 2
Some experimental and calculated NMR parameters$^a$ for compounds 7 and 8

| Comp. | R at C$_4$ | Isomer | $\Delta^b$ | $\delta^{31}P$ | $\delta$H$_6$ | $\delta$H$_4$ | $\delta$H$_5$ | $^1J_{PH}$ | $^3J_{PH}$ | $^3J_{PH4}$ |
|-------|------------|---------|-------------|----------------|-------------|-------------|-------------|------------|------------|-------------|
| 7     | i-Pr       | I       | Exp (a)$^{37}$ | -65.0          | 7.18        | 3.71        | 5.76        | 798.5      | 13.0       | n/d$^d$     |
|       |            | III     | Exp (b)$^{37}$ | -63.7          | 7.43        | 3.80        | 3.47        | 824.4      | n/d        | 2.4         |
| 8     | Bz         | I       | Exp (a)$^{36}$ | -63.0          | 7.09        | n/d         | n/d         | 804.9      | n/d        | 2.4         |
|       |            | III     | Exp (b)$^{36}$ | -60.0          | 5.64        | n/d         | n/d         | 810.2      | n/d        | 2.4         |

$^{a}$ Chemical shifts in ppm, spin–spin couplings in Hz. $^b$ Relative energy, in kcal mol$^{-1}$. $^c$ Experimental data. $^d$ No data.

### Table 3
Calculated$^a$ NMR parameters for models 9–12

| Comp. | R at C$_4$ | Isomer | $\Delta^b$ | $\delta^{31}P$ | $\delta$H$_6$ | $\delta$H$_4$ | $\delta$H$_5$ | $^1J_{PH}$ | $^3J_{PH}$ | $^3J_{PH4}$ |
|-------|------------|---------|-------------|----------------|-------------|-------------|-------------|------------|------------|-------------|
| 9     | Ph         | I       | 0           | -72.7          | 7.41        | 5.11        | 3.56        | 717.5      | 35.4       |
|       |            | III     | 0.92        | -80.6          | 7.90        | 4.87        | 3.24        | 770.5      | 20.8       |
| 10    | Me         | I       | 0           | -72.8          | 7.19        | 4.04        | 3.41        | 707.9      | 34.5       |
|       |            | III     | 1.02        | -78.5          | 7.67        | 3.84        | 2.78        | 782.2      | 25.3       |
| 11    | t-Bu       | I       | 0           | -73.5          | 7.17        | 3.77        | 3.30        | 687.4      | 30.1       |
|       |            | III     | 0.84        | -76.7          | 7.67        | 3.44        | 2.74        | 771.5      | 21.1       |
| 12    | Ph         | I       | 0           | -93.8          | 7.71        | 4.86        | 3.45        | 729.1      | 21.2       |
|       |            | III     | 0.30        | -88.1          | 7.30        | 5.28        | 2.60        | 826.4      | 0.6        |

$^{a}$ Chemical shifts in ppm, spin–spin couplings in Hz. $^b$ Relative energy, in kcal mol$^{-1}$. 

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Fig. 5 Step-by-step simplification of the title pentacoordinate spirophosphoranes.

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Thus, in both series the nature of the substituent at the chiral center is not principal. The nature of the fused aromatic fragment is also not crucial. But NMR parameters are considerably different for compounds with the aromatic system and those without the aromatic system. In this case, it is the geometry of the heterocycle which plays the crucial role: while in 6-membered spirophosphoranes with the fused aromatic system the heterocycle adopts boat conformation, in 5- and 6-membered compounds without the aromatic fragment the heterocycle is essentially flat (or envelope) (Fig. 6). Therefore, in the first case the $H_4^c-C_4^c-N-P$ dihedral angle is about $156^\circ$ and results in a large $J_{PH}$ value, in the latter cases these angles are ca. $126^\circ$ and $107^\circ$, thus small $J_{PH}$ should be observed. The same difference in the conformation leads to a different distribution of $^{31}P$ CSs in the two main isomers.

**Conclusions**

The major product of the Betti based derivatives corresponds to the isomers with both substituents at chiral carbons being opposite to the P–H proton. The next populated product corresponds to the isomer with different chiralities at carbons. The least populated isomer is one with both substituents at the same side of the heterocycle as the P–H bond.

For such pentacoordinate chiral spirophosphoranes bearing two six-membered rings at the phosphorus atom the distinct NMR features, which allow establishing the isomeric bearing two six-membered rings at the phosphorus atom the NMR indicators are slightly different, in full agreement with the theory.

This study shows that the interplay of NMR experiments and DFT calculations of NMR parameters is a powerful and reliable method for determining the relative configurations of the pentacoordinate P–H-spirophosphoranes in solution.

**Experimental section**

**NMR spectroscopy**

All NMR experiments were performed with 600, 500 and 400 MHz (600.1, 500.1 and 400.1 MHz for $^1H$ NMR; 150.9, 125.8 and 100.6 MHz for $^{13}C$ NMR; 242.9, 202.5 and 162.0 MHz for $^{31}P$ NMR, 60.81 MHz for $^{15}N$ NMR; 376.5 for $^{19}F$ respectively) spectrometers equipped with a 5 mm diameter probehead and a pulsed gradient unit capable of producing magnetic field pulse gradients in the $z$-direction of 53.5 G cm$^{-1}$. For $^1H$–$^{13}C$ correlations the HSQC experiment is optimized for $J = 145$ Hz. For $^1H$–$^{15}N$ long range correlations the HMBC experiment is optimized for $J = 8$ Hz. For $^1H$–$^{31}P$ long range correlations the HMBC experiment is optimized for $J = 6$ Hz. For $^{19}F$–$^1H$ long range correlations the HETCOR experiment is optimized for $J = 3$ Hz. DOSY experiments were performed with ledsbgp2s, using a stimulated echo sequence and two spoil gradients, and 1D DPFGNOE techniques. CSs ($\delta$ in ppm) were referenced to the solvent CDCl$_3$ ($\delta = 7.27$ ppm for $^1H$ and 77.0 ppm for $^{13}C$ NMR) and to external H$_2$PO$_4$ (0.0 ppm) for $^{31}P$ NMR spectra, to external CH$_3$CN (235.5 ppm) for $^{15}N$ NMR spectra, to external C$_6$F$_6$ (~164.9 ppm) for $^{19}F$ NMR spectra.

**Calculations**

The quantum chemical calculations were performed using the Gaussian 03 software package. Full geometry optimizations have been carried out within the framework of the DFT (PBE1PBE) method using 6-31+G(d) basis sets. $^{31}P$ CSs were
calculated at the PBE1PBE/6-311G(2d,2p) level of theory.\textsuperscript{56} \textsuperscript{31}P CSSs were referred to H$_3$PO$_4$ calculated at the same level of theory. The linear scaling procedure was applied.\textsuperscript{56} \textsuperscript{1}H CSSs were referred to TMS.

**Synthesis of 1-(α-aminobenzyl)-2-naphthols (1–3)**

Compounds 1–3 were synthesized in several steps. First, the corresponding 1,3-diaryl-2,3-dihydro-1H-naphth[1,2-c][1,3]oxazines were obtained.\textsuperscript{62–64} which were then hydrolyzed by trifluoroacetic acid in the presence of water.\textsuperscript{65} The free bases were isolated by treating the resulting trifluoroacetates with sodium carbonate.\textsuperscript{66}

**Synthesis of P–H-spirophosphoranes (4–6)**

Spirophosphoranes (4–6) were synthesized by the reaction of the Betti bases and hexaethyltrimidophosphate: (1) without the addition of the catalyst (method A, only 4) resulting in the predominant formation of the (Δ$_1$R$_1$R$_1$/Δ$_1$S$_1$S$_1$)-isomer; (2) with the addition of diethylhydrochloride (5 mol%) as the catalyst (method B), which allows obtaining (Δ$_1$R$_1$R$_1$/Δ$_1$S$_1$S$_1$)- and (Δ$_1$R$_1$S$_1$/Δ$_1$S$_1$R$_1$/Δ$_1$R$_1$S$_1$)-isomers in a ratio close to 1:1 by influencing the rate of P–Z bond cleavage (Z = O, N).\textsuperscript{67}

**Method A:** 1-(α-Aminobenzyl)-2-naphthol (1) (4 mmol) was dissolved in dry benzene (12 mL) under heating. Then the solution of hexaethyltrimidophosphate (2 mmol) in dry benzene (3 mL) was added and the reaction mixture was kept at reflux under argon for 8 hours. After that the solvent was removed and the residue was analyzed by \textsuperscript{1}H and \textsuperscript{31}P NMR spectroscopy for the diastereomers\textsuperscript{(a and b)} ratio determination [(Δ$_1$R$_1$R$_1$/Δ$_1$S$_1$S$_1$):(Δ$_1$R$_1$S$_1$/Δ$_1$S$_1$R$_1$/Δ$_1$R$_1$S$_1$) = 65:35]. Pure (Δ$_1$R$_1$R$_1$/Δ$_1$S$_1$S$_1$)-P–H-spirophosphorane (4a) was obtained by recrystallization from benzene.

**Method B:** 1-(α-Aminobenzyl)-2-naphthol (1–3) (4 mmol) were dissolved in dry benzene (12 mL) under heating. Then dry diethylhydrochloride (0.1 mmol, 5 mol%) was added followed by the addition of hexaethyltrimidophosphate solution (2 mmol) in dry benzene (3 mL). The resulting reaction mixture was kept at reflux under argon for 5 hours. After that the solvent was removed and the residue was analyzed by \textsuperscript{1}H and \textsuperscript{31}P NMR spectroscopy for the diastereomers\textsuperscript{(a and b)} ratio determination [(Δ$_1$R$_1$R$_1$/Δ$_1$S$_1$S$_1$):(Δ$_1$R$_1$S$_1$/Δ$_1$S$_1$R$_1$/Δ$_1$R$_1$S$_1$) = 1:1:1 for 4, 1:1 for 5, 0:0:1 for 6]. Pure (Δ$_1$R$_1$R$_1$/Δ$_1$S$_1$S$_1$)-4a–6a and (Δ$_1$R$_1$S$_1$/Δ$_1$S$_1$R$_1$/Δ$_1$R$_1$S$_1$)-4b–6b diastereomers of P–H-spirophosphoranes were obtained by fractional crystallization from benzene.

**Physical data**

1-[4-(4-fluorophenyl)ethyl]-2-naphthyl trifluoroacetate (2-C$_2$F$_4$COOH). Yield: 82.2% m.p. 150–151 °C. $\delta_H$ (400.1 MHz; DMSO-d$_6$; TMS) 6.30 (1 H, s, PhCHN), 7.19–8.06 (10 H, m, Ph), 8.80 (3 H, br, NH$_3^+$). IR (KBr): $\nu$ = 1516 (COO–), 1586, 1601 (C=C-naphth), 1665 (COO–), 3066, 3288 cm$^{-1}$ (NH$_3^+$); elemental analysis calcld (%) for C$_{14}$H$_{14}$F$_2$NO: C 59.83, H 3.96, N 6.67; found: C 59.68, H 3.77, N 3.55.

1-(α-Aminobenzyl)-6-bromo-2-naphthyl trifluoroacetate (3-C$_2$F$_4$COOH). Yield: 84.0%. m.p. 162–164 °C. $\delta_H$ (400.1 MHz; DMSO-d$_6$; TMS) 6.29 (1 H, s, PhCHN), 7.30–8.16 (10 H, m, Ph), 8.79 (3 H, br, NH$_3^+$). IR (KBr): $\nu$ = 1503 (COO–), 1582, 1598 (C=C-naphth), 1664 (COO–), 3066, 3254 cm$^{-1}$ (NH$_3^+$); elemental analysis calcld (%) for C$_{14}$H$_{14}$BrF$_2$NO$_3$: C 51.60, H 3.42, Br 18.07, N 3.17; found: C 51.78, H 3.57, Br 17.89, N 3.35.

1-(α-Aminobenzyl)-6-bromo-2-naphthol trifluoroacetate (3-C$_2$F$_4$COOH). Yield: 84.0%. m.p. 156–164 °C. $\delta_H$ (400.1 MHz; DMSO-d$_6$; TMS) 7.30–8.16 (10 H, m, Ph), 8.79 (3 H, br, NH$_3^+$). IR (KBr): $\nu$ = 1503 (COO–), 1582, 1598 (C=C-naphth), 1664 (COO–), 3066, 3254 cm$^{-1}$ (NH$_3^+$); elemental analysis calcld (%) for C$_{14}$H$_{14}$BrF$_2$NO$_3$: C 51.60, H 3.42, Br 18.07, N 3.17; found: C 51.78, H 3.57, Br 17.89, N 3.35.

**Electrochemical properties**

**Synthesis of 1-(α-aminobenzyl)-2-naphthols (1–3)**

Compounds 1–3 were synthesized in several steps. First, the corresponding 1,3-diaryl-2,3-dihydro-1H-naphth[1,2-c][1,3]oxazines were obtained.\textsuperscript{62–64} which were then hydrolyzed by trifluoroacetic acid in the presence of water.\textsuperscript{65} The free bases were isolated by treating the resulting trifluoroacetates with sodium carbonate.\textsuperscript{66}
(δ<sub>P</sub>S<sub>1</sub><sup>1</sup>/δ<sub>R</sub><sup>1</sup>)<sub>S,R</sub>-6a-Hydro-5,14-diphenyldinaphtho[2,1-b,2,1-h]-1,7,5,11,6-dioxadiazaphosphaspiro[5.5]undecadiene-7,16a (5b). 0.28 g, 24.8%, method B; m.p. 141–143 °C. δ<sub>HH</sub> (600.1 MHz; CDCl<sub>3</sub>; TMS) 7.89 (1 H, d, J<sub>HH</sub> 8.0, H<sub>10</sub>), 7.85 (1 H, d, J<sub>HH</sub> 8.0, H<sub>10</sub>), 7.84 (1 H, d, J<sub>HH</sub> 8.0, H<sub>10</sub>), 7.80 (1 H, d, J<sub>HH</sub> 7.7, H<sub>7</sub>), 7.78 (1 H, d, J<sub>HH</sub> 8.1, H<sub>11</sub>), 7.73 (1 H, d, J<sub>HH</sub> 8.5, H<sub>5</sub>), 7.54 (1 H, t, J<sub>HH</sub> 7.2, H<sub>12</sub>), 7.48 (1 H, t, J<sub>HH</sub> 7.5, H<sub>12</sub>), 7.43 (1 H, t, J<sub>HH</sub> 7.5, H<sub>11</sub>), 7.39 (3 H, m, H<sub>11</sub>, H<sub>16</sub>, H<sub>16</sub>), 7.32 (1 H, d, J<sub>PH</sub> 8.20, H<sub>8</sub>), 7.18 (1 H, d, J<sub>PH</sub> 8.9, H<sub>7</sub>), 7.16 (1 H, d, J<sub>PH</sub> 9.2, H<sub>6</sub>), 6.95 (2 H, d, J<sub>PH</sub> 9.2, H<sub>6</sub>, H<sub>7</sub>), 6.91 (2 H, d, J<sub>PH</sub> 8.8, J<sub>PH</sub> 6.5, H<sub>6</sub>), 6.68 (1 H, d, J<sub>PH</sub> 8.8, H<sub>8</sub>), 5.82 (1 H, dd, J<sub>PH</sub> 27.7, J<sub>PH</sub> 6.8, H<sub>4</sub>), 5.76 (1 H, dd, J<sub>PH</sub> 33.6, J<sub>PH</sub> 7.6, H<sub>5</sub>), 3.95 (1 H, dd, J<sub>PH</sub> 14.0, J<sub>PH</sub> 6.8, H<sub>4</sub>), 3.77 (1 H, dd, J<sub>PH</sub> 16.8, J<sub>PH</sub> 7.2, H<sub>3</sub>), δ<sub>C</sub> (150.9 MHz; CDCl<sub>3</sub>; TMS) 162.0 (d, J<sub>CF</sub> 247.3, C<sub>18</sub>), 161.6 (d, J<sub>CF</sub> 244.8, C<sub>19</sub>), 151.1 (d, J<sub>CF</sub> 9.9, C<sub>13</sub>), 151.0 (d, J<sub>CF</sub> 14.8, C<sub>12</sub>), 139.8 (d, J<sub>CF</sub> 3.0, C<sub>13</sub>), 139.1 (d, J<sub>CF</sub> 3.4, C<sub>12</sub>), 130.7 (s, C<sub>14</sub>), 130.6 (s, C<sub>14</sub>), 129.8 (d, J<sub>CF</sub> 10.0, C<sub>12</sub>), 129.4 (d, J<sub>CF</sub> 23.6, C<sub>16</sub>), 128.9 (s, C<sub>18</sub>), 128.3 (d, J<sub>CF</sub> 8.5, C<sub>16</sub>, C<sub>20</sub>), 128.0 (d, J<sub>CF</sub> 8.2, C<sub>16</sub>, C<sub>20</sub>), 127.1 (s, C<sub>16</sub>), 126.9 (s, C<sub>16</sub>), 124.8 (d, J<sub>CF</sub> 9.1, C<sub>12</sub>), 123.9 (s, C<sub>11</sub>), 123.7 (s, C<sub>11</sub>), 122.9 (d, J<sub>PH</sub> 10.9, C<sub>9</sub>), 121.6 (s, C<sub>13</sub>), 121.5 (s, C<sub>13</sub>), 121.4 (d, J<sub>CF</sub> 2.7, C<sub>11</sub>), 120.4 (d, J<sub>CF</sub> 1.3, C<sub>13</sub>), 115.4 (d, J<sub>CF</sub> 21.5, C<sub>17</sub>, C<sub>19</sub>), 114.7 (d, J<sub>CF</sub> 21.3, C<sub>17</sub>, C<sub>19</sub>), 53.3 (s, C<sub>9</sub>), 52.6 (s, C<sub>4</sub>), δ<sub>P</sub> (242.9 MHz; CDCl<sub>3</sub>; H<sub>3</sub>PO<sub>4</sub>) -76.6 (s, P<sub>9</sub>), δ<sub>N</sub> (60.8 MHz; CDCl<sub>3</sub>; NH<sub>2</sub>) 62.4 (d, J<sub>PN</sub> 30.0, N<sub>3</sub>), 60.2 (d, J<sub>PN</sub> 45.0, N<sub>3</sub>), δ<sub>F</sub> (376.5 MHz; CDCl<sub>3</sub>; CF<sub>3</sub>) -115.8 (s, F<sub>14</sub>), -116.6 (s, F<sub>18</sub>), IR (KBr): ν = 1191 (POC), 1586, 1624 (C=C=napth), 2358 (PH), 3422 cm<sup>-1</sup> (NH); elemental analysis calculated (% for C<sub>2</sub>H<sub>2</sub>Br<sub>2</sub>N<sub>2</sub>O<sub>2</sub>P): C 76.99, H 4.48, N 4.98, P 5.51; found: C 77.04, H 4.59, N 4.83, P 5.41.
54.5 (s, C4), 53.6 (s, C4). δp (242.94 MHz; CDCl3; H2PO4) −77.7 (s, P). δν (60.88 MHz; CDCl3; NH3) 61.9 (d, JPN 30.0, Nv), 59.9 (d, JPN 40.0, Nv). IR (KBr): v = 1191 (POC), 1586, 1617 (C=Csp2, phosphinate), 2370 (PH), 3422 cm−1 (NH); elemental analysis calcd (%) for C34H25Br2N2O2P: C 59.67, H 3.68, Br 23.35, N 4.27, P 4.65.

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