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"Through-space" nuclear spin−spin couplings in ferrocenyl polyphosphanes and diphosphino cavitands: A new way of gathering structural information in constrained P(III) ligands by NMR

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This article is dedicated to Prof. P.H. Dixneuf for his commitment in promoting research and organometallic chemistry in France and beyond.

Abstract

Nuclear magnetic resonance is an invaluable technique for investigating a variety of important issues ranging from the determination of molecular structure to therapeutic medical imaging. In this respect, the indirect nuclear spin−spin coupling involving common nuclei such as ^1H, ^{13}C or ^{31}P provides, via the J constant, conclusive data for compound characterization in solution. This electron-mediated nuclear spin coupling is usually regarded as being transmitted by covalently bonded magnetic atoms. However, several experimental and theoretical studies, first focused on constrained organofluorides, and more recently devoted to phosphane ligands highlighted the existence of very intense J-couplings operating "through-space". Herein, the intramolecular "through-space" $^{31}P^{31}P$ and $^{31}P^{13}C$ couplings are discussed in the light of recent examples found in constrained phosphorus-containing ligands such as *phosphinocalixarenes*, *phosphinocyclodextrins* and *ferrocenyl phosphanes*. The emphasis is put on the origin and transmitting mode of these nonbonded spin−spin couplings as well as on the relevant structural information they provide in solution. ***To cite this article: Jean-Cyrille Hierso et al., C. R. Chimie 12 (2009).***
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Résumé

La résonance magnétique nucléaire (RMN) occupe une place essentielle dans le domaine de l'analyse chimique. Elle s'applique à des domaines très variés, tels que par exemple l'élucidation de structures moléculaires, l'imagerie médicale, ou encore l'étude de systèmes biologiques complexes. L'étude RMN en solution du couplage de spin indirect entre des noyaux tels que le proton, le carbone, ou le phosphore (^1H, ^{13}C et ^{31}P) apporte, par le biais de la constante de couplage J, des indications structurales précieuses sur l'état des espèces étudiées. Ce couplage de spin nucléaire est habituellement considéré comme se transmettant à travers les liaisons covalentes; il est généralement peu ou non détectable au-delà de trois liaisons. Le mode de transmission de l'information de

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spin entre deux noyaux est cependant, en réalité, un processus plus complexe. Ainsi, un phénomène de RMN étonnamment méconnu est le mode de couplage de spin de noyaux dit «à longue distance» (quatre liaisons et au-delà). Cette terminologie peut sembler trompeuse pour un type de couplage qui s'opère «à travers l'espace» entre noyaux qui ne sont pas liés de manière covalente. Cette manifestation, détectée avec une intensité notable dans plusieurs types de ligands polyphosphorés contraints, s'est révélée très utile en termes de caractérisation. La présente mise au point revient sur les couplages intramoléculaires «à travers l'espace» $^{31}P^{31}P$ et $^{31}P^{13}C$ en s'appuyant sur des études récentes portant sur des *phosphinocalixarènes*, des *phosphinocyclodextrines* ainsi que des *poly-phosphines ferrocéniques*. L'origine et le mode de transmission de ces couplages sont discutés et leur rôle dans l'élucidation de structures est détaillé. ***Pour citer cet article : Jean-Cyrille Hierso et al., C. R. Chimie 12 (2009).***

1. Introduction

Nuclear magnetic resonance is recognized as one of the most useful and innovative techniques available to chemists and biologists for determining the structures of molecules. Indirect nuclear spin−spin coupling provides, via the *J* constant, key data for compound characterization, regardless of the nature (organic,
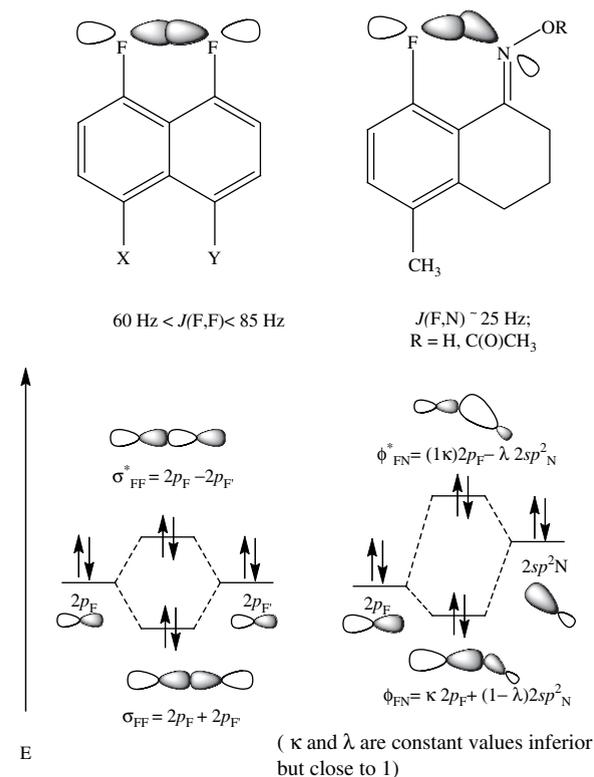

Fig. 1. Bonding and anti-bonding orbitals generated by the overlap of two lone-pair orbitals on intramolecularly crowded nitrogen- and fluorine-containing constrained molecules.

organometallic) or the size (small molecules, pharmaceuticals, biomolecules) of the observed systems. For many years, this electron-mediated *J*-coupling has been commonly thought as only transmitted by covalently bonded ''magnetic'' atoms. However, a significant number of experimental and theoretical reports now bring to the fore the existence of *J*-couplings operating ''through-space'' (TS). They range from small (*ca.* 4 Hz) to very large values (higher than 60 Hz). They are often called ''long-range'' couplings in the literature, the corresponding nuclei being separated by at least four covalent bonds. However, this term is somewhat misleading since with the exception of fully conjugated systems, spin−spin transmission does not occur through the many bonds that link the two remote, interacting atoms. The ''long-range'' coupling is in fact a consequence of a direct nuclear−nuclear nonbonded, electron-mediated interaction. The present account aims at highlighting the ''through-space'' contribution of indirect nuclear spin−spin in various polyphosphane ligands, notably ferrocenyl phosphanes and phosphino cavitands. The NMR data will be correlated to solid state and computer modelled structures.

2. Background of ''through-space'' NMR spin coupling

2.1. Origin and scope of ''through-space'' coupling

Since Roberts et al. reported in the sixties the observation of ''long-range'' spin−spin coupling constants apparently transmitted via spin polarization of nonbonded-electron pairs (named later ''through-space'' couplings, TS) many papers were published reporting a wide variety of magnetic coupling situations related to
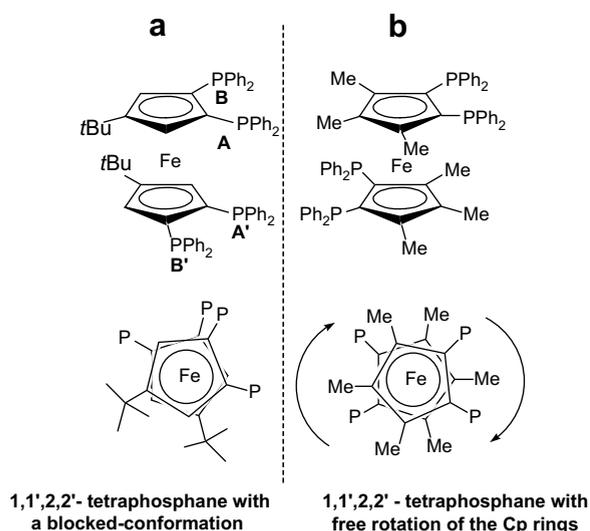
a

b

Fig. 2. Ferrocenyl tetraphosphanes with different conformational properties: blocked (left) or flexible (right) ligands.

this phenomenon [1]. It was clearly established that organic compounds containing two fluorine atoms separated by four or more bonds, but spatially close, exhibit large FF nuclear spin coupling constants J(F,F) [2]. This phenomenon, best designated as nuclear spin–spin coupling via nonbonded interactions, has been intensively studied for over thirty years by Mallory and co-workers, who produced a useful combination of experimental and theoretical works [3]. These "through-space" couplings first identified from FF J-constants in small organic molecules, were shown to be a general phenomenon encountered for nuclei as different as ^{14}N, ^{31}P [4], ^{77}Se, ^{13}C and even ^{1}H when involved in hydrogen

bonding. The studies reviewed by Contreras et al. provided a more theoretical and predictive background for the observed phenomenon. These are based on modelling and calculation approaches, which take into account the four terms contributing to J(X,X$'$), namely the Fermi contact (FC), spin dipolar (SD), paramagnetic spin–orbit (PSO) and diamagnetic spin–orbit (DSO) interactions [5,6].

2.2. Geometrical approach and simplified modelling

The studies conducted by Mallory showed that "through-space" couplings result from overlap interactions between lone-pair orbitals on the two crowded atoms. For instance, in the particular constrained geometry of the compounds sketched in Fig. 1 (top), the C–F/C–F, or C–F/C–N bonds, are coplanar and approximately parallel. As a consequence, the nonbonding distances d F⋯F, or d F⋯N, are short. In this orientation, the two lone-pair orbitals experience a σ-directed overlap. As displayed in Fig. 1 (bottom), the overlap between these lone-pair orbitals is expected to afford an in-phase and out-of-phase combination. As both orbitals are occupied (two-orbitals, four-electron interaction) no stabilization is observed. However, it provides an adequate pathway for transmitting spin–spin information between the coupled nuclei. The magnitude of J(F,F) depends on the extent in which the two lone-pair orbitals interact as a result of their overlap.

This model, which initially was mainly qualitative [2,3a,3b], eventually allowed the so-called overlap interaction to be quantitatively estimated for a number of 1,8-difluoronaphthalene derivatives.
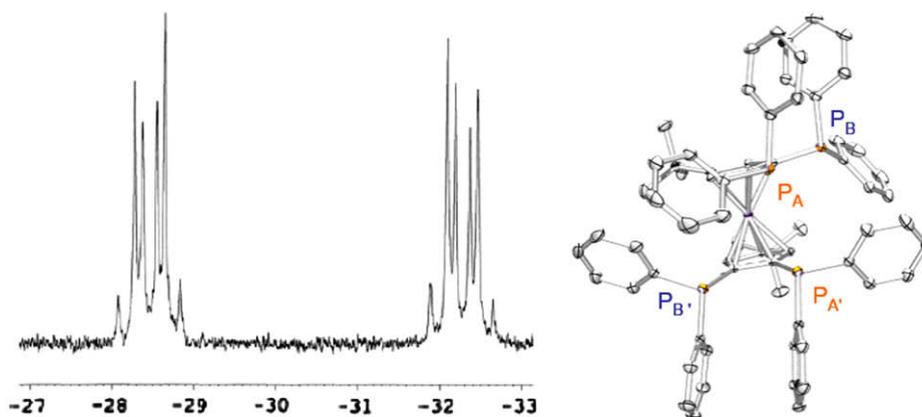

Fig. 3. ^{31}P NMR spectrum showing the AA'BB' system and X-ray structure (POV-Ray) of Fc(P)$_4$tBu. The phosphorus atoms A and A$'$ are eclipsed and their lone-pairs point towards each other. The large nonbonded J(P,P) coupling constant (60 Hz) originates from the overlapping P orbitals.

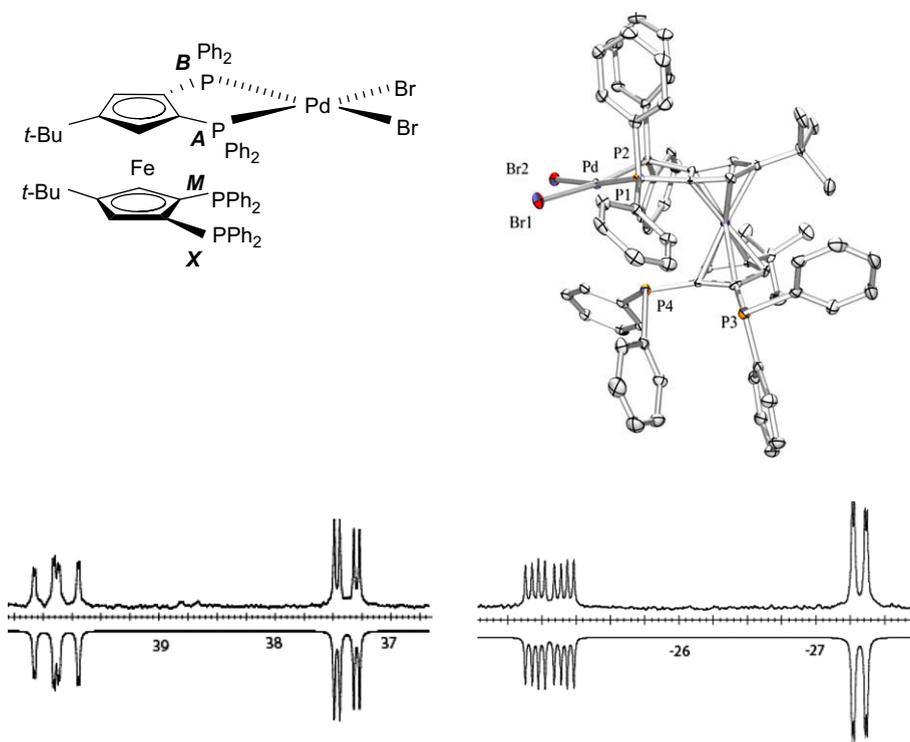Fig. 4. Example of a palladium dibromide tetraphosphane complex. X-ray structure (POV-Ray) and ^{31}P NMR spectrum showing multiple *J*(P,P) couplings between the four anisochronous P nuclei giving rise to an ABMX spin system (*G-NMR modelling of spectrum in mirror*).

This became possible once an exponential relationship between the *ab initio* calculated internuclear distances and the observed *J*(F,F) coupling was established. This work confirmed previous studies by Ernst and Ibrom, who came up with a similar valuable semi-quantitative relationship in a number of difluorocyclophanes [7].

2.3. General requirements for the occurrence of ''through-space'' nuclear spin−spin coupling

In the general approach, the nuclear spin−spin coupling constant *J*(X,X′) is expressed as the sum of three terms (Eq. (1)):

$$J(X,X') = {}^{TS}J(X,X') + {}^{TB(\pi)}J(X,X') + {}^{TB(\sigma)}J(X,X') \tag{1}$$

The $^{TS}J(X,X')$ term corresponds to ''through-space'' coupling. The other two arise from ''through-bond'' interactions (involving σ- and π-orbitals) [5]. The usual method for evaluating experimentally strong $^{TS}J(X,X')$ values consists in studying systems where the shortest ''through-bond'' pathway is long enough (at least four bonds) for ''through-bond'' contributions to nuclear coupling to be considered as negligible in magnitude. A better understanding of NMR *J*-coupling constants would much benefit from the development of quantitative models allowing clear discrimination between the different *J* terms. Computational efforts are currently undertaken to achieve this goal [5a,5b,8e].

Empiric requirements for the detection of ''through-space'' coupling constants were detailed in studies dealing with FF [3a,3e,3g], NF [3d,3f] HF or CF [3b,3c], and occasionally with PX spin−spin couplings [3g,8a−d] (with X = P, Se, F). They can be expressed as follows: (*i*) chemically identical nuclei in interaction need to be anisochronous. In other words, the molecule must be in some way dissymmetric as regards the environment of the observed nuclei; (*ii*) the nuclei must be in close proximity *in solution*, as in Mallory's fluoroaromatic compounds (Fig. 1) and in related phosphinonaphthalenes, which both contain rigid backbones [4,9]. The same is also true for the P-containing polymetallic catenates reported by Rheingold and Fountain [10] as well as for some bis(ferrocenyl)diphosphanes [11]; (*iii*) finally, each of the interacting nuclei should usually bear a lone-pair for mutual overlap. However, recent findings contradict this last assertion (see below).

Table 1

P···P distances (Å)/J (P,P) constants (Hz)	[PdCl$_2${Fc(P)$_4t$Bu}]	[PdBr$_2${Fc(P)$_4t$Bu}]
d P$_A$···P$_M$/J(A,M)	3.842(1)/*24.0*	3.6765(12)/*25.6*
d P$_A$···P$_X$/J(A,X)	4.698(2)/n.d.	5.3971(13)/*1.9*
d P$_B$···P$_M$/J(B,M)	4.440(1)/*6.4*	4.4879(13)/*5.8*
d P$_B$···P$_X$/J(B,X)	6.292(2)/n.d.	6.7628(13)/n.d.

Data for d P$_A$···P$_B$ and d P$_M$···P$_X$ are not suitable for TS correlation since "through-bond" ^3J(P,P) contributions cannot be neglected; n.d. = not detected.

3. "Through-space" ^{31}P^{31}P spin–spin couplings in constrained diphosphane and polyphosphane ligands

3.1. Ferrocenyl tri- and tetraphosphanes and their coordination complexes

A number of polyphosphanes with interesting structural and catalytic properties appear every year in the literature. Among them the ferrocenyl tetraphosphane (1,1′,2,2′-tetrakis(diphenylphosphino)-4,4′-di-*tert*-butylferrocene (Fc(P)$_4t$Bu, Fig. 2 left)) was recently shown to promote various palladium-catalysed C–C cross-coupling reactions [12,13]. This was attributed to a conformationally blocked ferrocene backbone, which allows this ligand to bind the metal centre by three instead of only two phosphorus atoms, incidentally increasing the electron density on the metal. This behaviour contrasts with that of related ferrocenyl tetraphosphanes in which the Cp rings rotate freely (Fig. 2) [14].

The conformational rigidity of Fc(P)$_4t$Bu was inferred from the corresponding ^{31}P NMR spectrum which shows an AA'BB' system (Fig. 3). The occurrence of nonbonded nuclear spin couplings between phosphorus atoms was clear from the intense J(P,P) coupling constant (60 Hz) found between the heteroannular P atoms corresponding to A and A′ (see Fig. 2). From X-ray structure analysis a *quasi* eclipsed conformation is observed for these nuclei, with lone-pairs orientated towards each other (Fig. 3, internuclear distance determined in the solid state from X-ray measurements was d P···P′ = 3.728(2) Å). In keeping with Mallory's model, the phosphorus lone-pairs of Fc(P)$_4t$Bu undergo a strong overlap which is responsible for the observed direct "through-space" spin–spin interaction.

In the course of NMR-mechanistic studies on transition metal complexes derived from the tetraphosphane ligand Fc(P)$_4t$Bu [15], unusual features that can only be explained by the presence of TS spin

couplings were detected in their ^{31}P NMR spectra (See Fig. 4). In order to gain more in depth information on the nuclear spin–spin interactions in these coordinated tetraphosphanes, the palladium complexes [PdX$_2${Fc(P)$_4t$Bu}], [Pd$_2$X$_4${Fc(P)$_4t$Bu}] (X = Cl or Br), as well as their nickel analogs [NiX$_2${Fc(P)$_4t$Bu}] and [Ni$_2$X$_4${Fc(P)$_4t$Bu}] were synthesized and characterized by X-ray crystallography in the solid state and ^{31}P NMR in solution [16]. The coordination complexes of Fc(P)$_4t$Bu keep the conformational rigidity of the free ligand in solution. As a result, the same type of spin–spin coupling seen in the ligand was detected in the complexes. Data presented in Table 1 clearly establish a correlation between the P···P′ separations between non-adjacent phosphorus atoms (determined from crystallographic data) and the corresponding coupling constants.

The collected data allowed to correlate geometric features found in the solid state with J(P,P) coupling constants (solution spectra), so that an expression of J(P,P) *vs*. d P···P′ in coordination complexes could be devised (see details in Section 5).

TS spin couplings were also observed for other members of this family of ligands and related to their structure in solution. The ^{31}P NMR pattern of 1,1′,2-tris(diphenylphosphino)-4-*tert*-butylferrocene (Fig. 5, right) displays a triplet at −19.3 ppm and a doublet at −23.0 ppm in CDCl$_3$, which were assigned to the 1′-PPh$_2$ and to the 1,2-PPh$_2$ groups, respectively (A$_2$B spin system). The observed spin–spin coupling constant was found to be larger in C$_6$D$_6$, J(P,P) = 5.0 Hz, than in CDCl$_3$ (J(P,P) = 2.8 Hz). The J(P,P) value of 5.0 Hz appears to be too high for a classical "through-bond" ^4J(P,P) coupling constant (usually in ferrocenyl polyphosphane ^4J(P,P) between anisochronous heteroannular phosphorus atoms is null); such a strong dependence on solvent is also unexpected for a "through-bond" coupling. Thus, only a "through-space" spin–spin coupling mediated by the ferrocenyl ring rotation and/or by changes in the relative orientation of the phosphino groups can explain such unusual values. To account for this TS
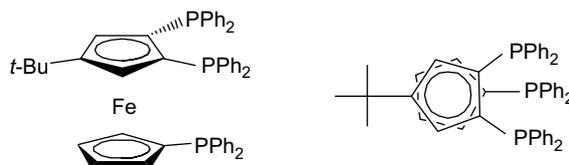

Fig. 5. Molecular conformation of highest symmetry (*Cs*). A conformation of this type would explain a "through-space" ^{31}P spin–spin coupling.
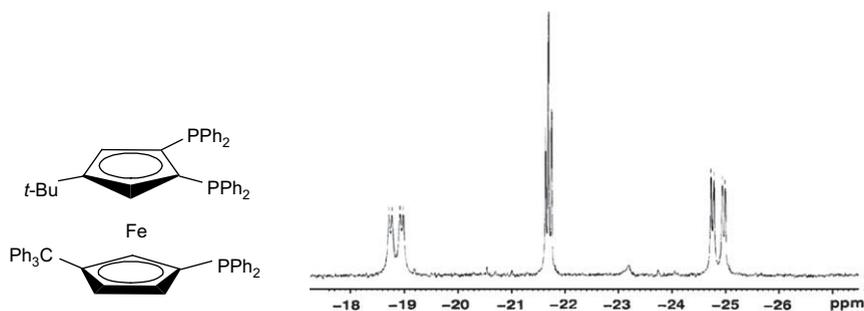
Fig. 6. The triphosphane ligand 1,1′,2-tris(diphenylphosphino)-3′-(tris-phenyl)methyl-4-*tert*-butyl ferrocene and its ABC NMR spin system.

coupling, the relative rotation of the cyclopentadienyl rings (which is not blocked in this case) has to be restricted to a certain degree around the conformation of higher symmetry (*C*s) pictured in Fig. 5 [17], and possibly occurs rapidly to facilitate via space−spin interaction of phosphorus nuclei.

The interpretation of the NMR spectrum of another ferrocene derivative, namely triphosphane 1,1′,2-tris(diphenylphosphino)-3′-(tris-phenyl)methyl-4-*tert*-butyl ferrocene [18], also required a nonbonded coupling to be considered (see Fig. 6). The signals corresponding to the phosphorus atoms of the chelating pair, 1-P and 2-P, are centred at −18.8 and −24.9 ppm. They appear as doublet of doublets, due to a strong, but classical coupling constant of $^3J(P,P) = 41$ Hz, as well as to another coupling constant with the 1′-P phosphorus atom (in the following P′ designates a P atom belonging to the other Cp ring). The signal of the third phosphorus atom is a pseudo-triplet, thus reflecting nearly identical $^{TS}J(P,P)$ coupling constants ($^{TS}J(P,P) = 11$ and 12 Hz, respectively). These intense spin−spin couplings between heteroannular

phosphorus atoms most probably operate "through-space" and therefore result from a spatial proximity of the spin-active nuclei. Consequently, in the absence of X-ray, we assigned to this triphosphane the conformation depicted in Fig. 6. This assumption was confirmed by the NMR spectrum of the coordination complex which readily formed with [Pd(allyl)Cl]$_2$. In this complex, all three phosphorus atoms are involved in binding, as deduced from the observed ^{31}P chemical shifts (Fig. 7) [18]. Very interestingly, one of the phosphorus atoms (presumably 1′-P) is less strongly bonded, its signal appearing at −10 ppm, instead of an expected value near 25−30 ppm.

This example is the first in which NMR analysis allowed both to identify the existence of "through-space" $J(P,P)$ coupling constants and, incidentally, to anticipate the tridentate coordination behaviour of a triphosphane [18]. In view of the $^{TS}J(P,P)$ coupling constants inferred from the spectral analysis (10−12 Hz), we can reasonably assume that for each pair of phosphorus atoms the d P···P′ distance in solution is smaller than 4.3 Å.

3.2. Calixarene P(III)-podands

The $^{TS}J(P,P)$ coupling constants observed in the aforementioned polyphosphanes and related to short spatial separations between phosphorus nuclei (d < 5.5 Å) are not restricted to ferrocene-derived P(III)-ligands. The successful preparation of a series of regioselectively phosphinated calix[4]arenes led Dieleman et al. to investigate the calixarenes **1−6** in which two proximal phenoxy rings are substituted by a −CH$_2$PPh$_2$ podand [19,20]. In these molecules the phosphorus atoms are separated by *ten* chemical bonds (Fig. 8). Calixarenes **2−6** are chiral, and were isolated either as optically pure compounds (**2−4**) or as a racemic mixture (**5 + 6**). Due to the difference between R^1 and R^2 groups the ^{31}P NMR spectra of the latter display two distinct phosphorus signals. However, while the spectra of **2−4** are each
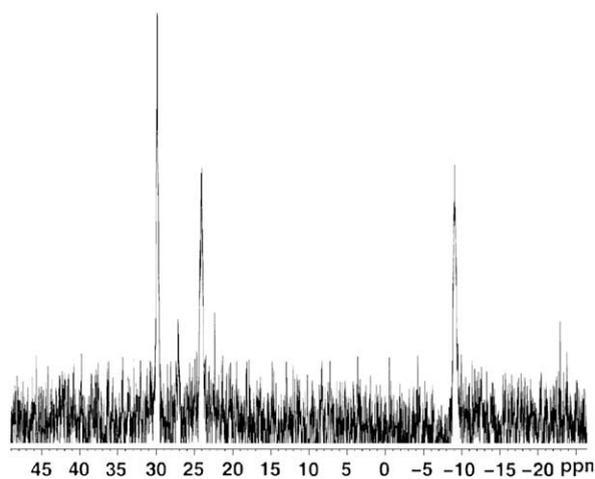

Fig. 7. ^{31}P NMR spectrum of the [Pd(allyl)Cl]/triphosphane complex in CD$_2$Cl$_2$.

1 $R^1 = R^2 = H$

2 $R^1 = CH_2C(O)NHCHPhMe$, $R^2 = H$

3 $R^1 = CH_2C(O)NHCHPhMe$, $R^2 = SiMe_3$

4 $R^1 = R^2 = CH_2C(O)NHCHPhMe$

5 $R^1 = C(O)Ph$, $R^2 = H$
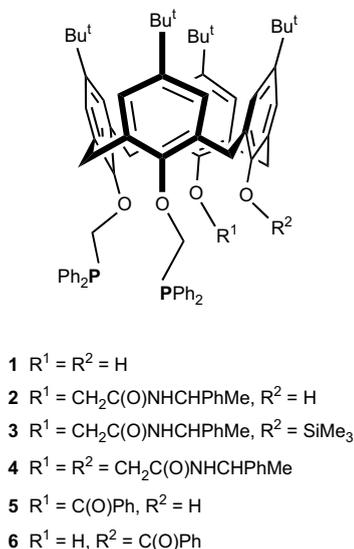
6 $R^1 = H$, $R^2 = C(O)Ph$

Fig. 8. Proximally-diphosphinated calixarenes **1**–**6**.

characterized by clear singlets (with no J(P,P) couplings detected), the ^{31}P NMR spectrum of the benzoyl-substituted enantiomers **5** and **6** displays a typical AB spin system with J(P,P) = 8 Hz, the corresponding doublets being centred at −20.1 ppm and −22.2 ppm, respectively [21].

The spin coupling existing between the two phosphorus atoms, separated by ten bonds, in **5/6** was evidenced by measuring the spectrum in CDCl$_3$ at different fields and also by carrying out a 2D homonuclear ^{31}P
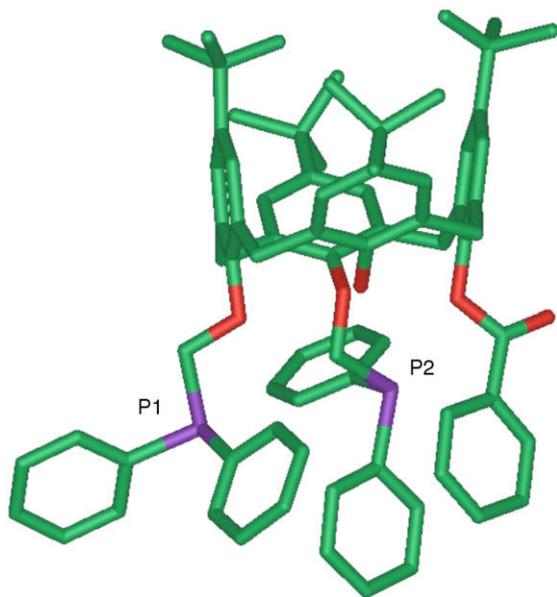

Fig. 9. Molecular structure of diphosphino-calixarene **6**.

COSY experiment. When the experiments were repeated in CD$_3$OD, the magnitude of the coupling did not significantly change. The observed coupling constant was intuitively assigned to a ''through-space'' interaction rather than to a ''through-bond'' coupling since the phosphorus atoms of **5/6** are linked through a non-conjugated bond system. It is worth noting, that in a highly conjugated naphthyl-derived diphosphane, a ^9J(P,P) of barely 4.0 Hz has been reported [22]. The solid state structure of the enantiomeric mixture (**5** + **6**) was determined by an X-ray diffraction study (Fig. 9).

In the solid state, the separation between the two phosphorus atoms was found to be of 5.333(1) Å, with an approximate alignment of the two phosphorus lone-pairs. It appears likely that in solution the P···P$'$ separation becomes even temporarily shorter. As revealed by a 2D ROESY experiments, the calixarene core of **6** displays a high flexibility, the unsubstituted phenolic ring flipping rapidly through the calixarene annulus. This fluxional behaviour combined with the mobility of the −OCH$_2$PPh$_2$ arms increases the probability of interaction of the phosphorus lone-pairs. The J(P,P) coupling constant value increases upon lowering the temperature (from 8.0 Hz at 283 K to 10.5 Hz at 183 K), an observation that is consistent with a statistically longer period of overlap of the lone-pairs as a result of slower molecular dynamics. The spatial proximity in solution of the phosphorus atoms of **6** was further substantiated by the easy formation of *cis*-chelate coordination complexes. Finally, the ''through-space'' J(P,P) coupling constant observed for the **5/6** couple was rather unexpected, and to date, there is no other example of chelating diphosphane with a ten bond P···P$'$ separation for which such an intense spin coupling is directly observable.

4. Rare ''through-space'' ^{31}P^{13}C spin couplings

Although virtually all spin-active nuclei are susceptible to display nonbonded nuclear spin couplings, nonbonded spin–spin nuclear couplings between phosphorus and carbon atoms are not very common. To the best of our knowledge, the first identification of such a coupling was made by Pascal et al.[23]. They observed J(P,C) couplings involving the phosphorus atom of a cyclophane phosphane and the six carbon atoms of an aromatic ring facing the P lone-pair. Despite the five-bond separation between each carbon atom and the P atom (see Fig. 10), J(P,C) coupling constants ranging from 3.5 to 7.5 Hz were observed, thus reflecting the spatial proximity of the coupling nuclei. As shown by an X-ray diffraction
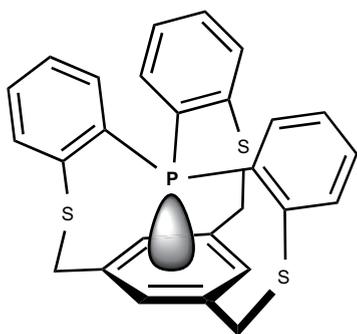
Fig. 10. Pascal's constrained cyclophane phosphane.

study, the corresponding P···C distances are of *ca.* 3.1 Å. More recent examples of such ''through-space'' couplings are outlined hereafter.

4.1. $^{31}P^{13}C$ spin couplings in ferrocenyl polyphosphanes

The proximity of the two cyclopentadienyl rings in the ferrocene unit, which is in part responsible for the PP ''through-space'' couplings discussed in Section 3, also gives rise to P···C spin couplings between atoms connected to distinct Cp rings. The ferrocenyl triphosphane shown in Fig. 11 provides a remarkable example of ligand in which such a coupling occurs [24].

The ^{13}C NMR spectroscopic data revealed a neat PC spin–spin nuclear coupling (J(P,C) = 5.5 Hz) between the methyl carbon atoms of the *t*Bu group (fast rotating methyl groups) and the P*i*Pr$_2$ phosphorus atom, as unambiguously demonstrated by selective ^{31}P decoupling experiments (see Fig. 12). This means that the corresponding phosphorus atom is located close to the *t*Bu group, and accordingly no J(P,P) coupling constant is observed from the A$_2$X ^{31}P NMR spectrum of this triphosphane (the lone-pair is involved in J(P,C)
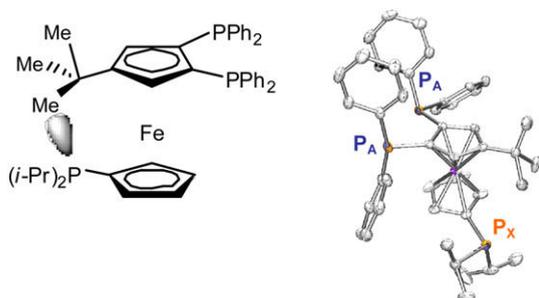

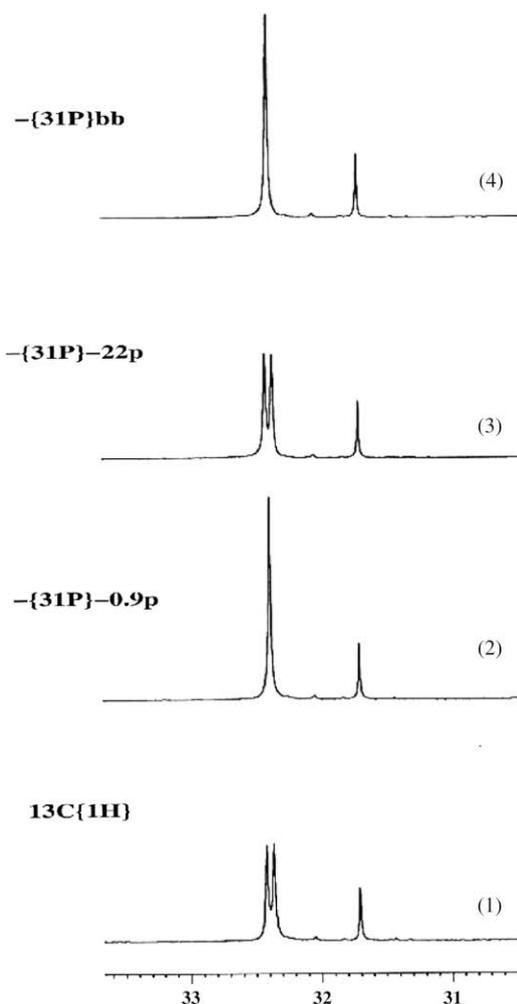
Fig. 11. Dissymmetric triphosphane and X-ray view.

Fig. 12. ^{13}C NMR spectra (C*C*H$_3$ region) of a ferrocenyl triphosphane with selective phosphorus decoupling: (1) δ = 32.4 ppm (d, 3C, Me of *t*Bu, J(C,P) = 5.5 Hz), no decoupling; (2) saturation of the P signal at -0.9 ppm ($-$P(*i*Pr)$_2$); (3) saturation of the signal at -22 ppm ($-$PPh$_2$); (4) phosphorus broad band decoupling.

coupling). The five-bond separation between the P and C nuclei of concern cannot lead to a detectable ^5J(P,C) if only ''through-bond'' spin coupling is operating. Further proof for a ''through-space'' coupling mechanism came from the absence of any other ^4J(P,C) or ^5J(P,C) coupling constant. A single crystal X-ray diffraction study confirmed the spatial proximity of the *t*Bu and P*i*Pr$_2$ groups (see Fig. 11 left; shortest P···C separation: 3.64 Å). The staggered conformation imposed by the ferrocene backbone favours the observed *P,C* interaction. The P lone-pair is directed towards the carbon atoms of the *t*Bu group, thus supporting the existence of an overlap between this orbital and a filled Csp$_3$ orbital (or with the C–C bond of *t*Bu group since no J(P,H) is observed).
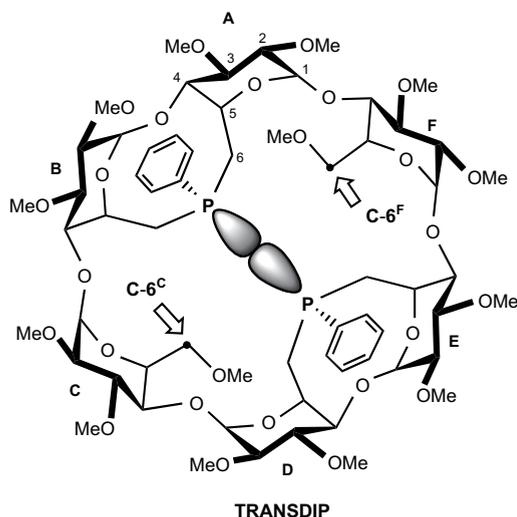
Fig. 13. Cyclodextrin-based diphosphane TRANSDIP.

4.2. A trans-spanning cyclodextrin-diphosphane

Nonbonded PC spin−spin couplings are naturally not limited to ferrocenyl phosphanes. Such a phenomenon was also revealed in the rigid, C_2-symmetrical cyclodextrin-derived TRANSDIP (Fig. 13). Here no PP spin–spin coupling can be simply detected in the ^{31}P NMR spectrum, due to the magnetic equivalence of the
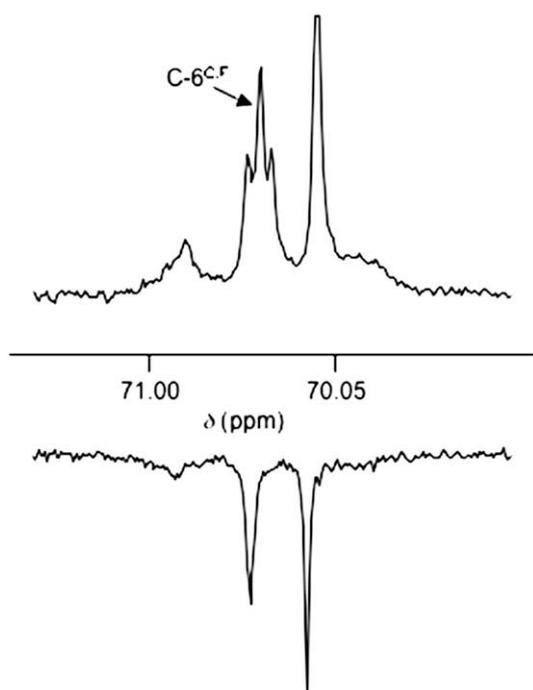

Fig. 14. Resonances of the $C_{6C,F}$ atoms in TRANSDIP: ^{13}C{^{1}H} (top) and ^{13}C{^{1}H,^{31}P} (bottom) NMR spectra recorded in CDCl$_3$ at 125.8 MHz.

phosphorus nuclei [25]. However, the C-4, C-5 and C-6 atoms of the P-bridged A, B, D, E glucose units display spin–spin couplings with both phosphorus atoms in the ^{13}C NMR spectrum, an observation that can only be rationalized by the existence of P,P orbital overlap. Moreover, a neat spin−spin coupling J(P,C) = 3.5 Hz between the C-6^C atom (equivalent to C-6^F) and both phosphorus atoms was also detected (see Fig. 14), thus indicating that both C-6 atoms lie in close proximity to the P atoms. The triplet observed reflects the equivalence of the two phosphorus atoms regarding the carbon atoms, and also evidences an unexpected extent of the orbital overlap.

The ''through-bond'' contribution to PC spin-spin coupling is likely to be negligible given the eight-bond separation existing between the C$_6$ atoms of glucose units C and F (Fig. 13) and the two phosphorus atoms. Molecular mechanics calculations (MM2), as well as X-ray crystal structures of TRANSDIP metal complexes [26], confirmed that the C-6^{C,F} atoms are close to both phosphorus atoms (averaged P···C separation: 4.8 Å, see Fig. 15).

The J(P,C-6^{C,F}) coupling constant of 3.5 Hz is somewhat smaller than the ''through-space'' J(P,C) value (5.5 Hz) observed for the aforementioned ferrocenyl triphosphane, suggesting a longer P···C separation in the case of TRANSDIP. The fact that only the C-6^{C,F} carbon atoms of the cyclodextrin give rise to such a direct interaction is a further indication of the *endo* orientation of the P lone-pairs as well as of the ligand rigidity. Overall, the ^{13}C{^{1}H} NMR spectrum gives valuable information on the structural features of this rigid diphosphane.

5. Advances in modelling TS couplings: distance dependence and real-space function visualization

As mentioned in Section 2.2, the overlap interaction of fluorine lone-pairs has been quantitatively estimated
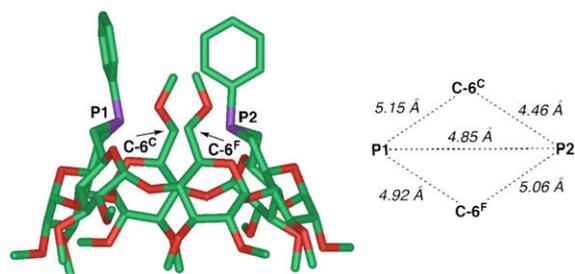

Fig. 15. Minimized structure of TRANSDIP (left, MM2 using Spartan 1.0.3.) and the corresponding calculated P···P and P···C$_{6C,F}$ distances.
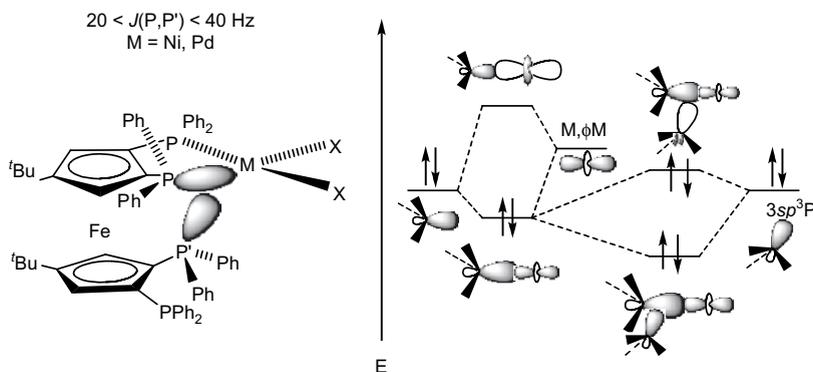
Fig. 16. Extension of Mallory's lone-pair overlap interaction model to polyphosphane coordination complexes (left), and schematic orbital diagram involving a transition metal orbital contribution (right).

for a number of constrained molecules. Computational methods were used for estimating the distances between the ''through-space'' coupled fluorine atoms. This allowed to establish exponential relationships between calculated internuclear distances and observed $J(F,F)$ couplings [3g,7].

The first d P···P′/$J(P,P)$ correlation between ''through-space'' interacting phosphorus nuclei was proposed recently in a publication dealing with complexes derived from Fc(P)$_4$tBu (see Section 3.1). In this work, the model developed by Mallory [16] was extended to show that ''through-space'' nuclear spin couplings do not necessarily require the presence of two lone-pair orbitals. Indeed, a lone-pair with an appropriate orientation may interact with electrons of a P−M bond, a ''through-space'' interaction taking place within a three-centre [P,P′,M] system. This concept (see Fig. 16), which extends the model developed for purely organic compounds is also consistent with the existence of PC couplings, the interaction involving possibly a C−C or a C−H bond.

As in the case of the fluorine compounds [2], overlap between P-centred electron clouds generates significant Fermi contact (FC) interactions. It is worth noting that the predominant role of the Fermi contact in nonbonded coupling has been confirmed by density functions interpretation [5b].

The $J(P,P)$ vs. d P···P′ correlation diagram shown in Fig. 17 was drawn using the data obtained for the above mentioned palladium complex (Table 1), as well as those corresponding to related nickel and palladium complexes [16,27]. The best fit was obtained for an exponential curve expressed by Eq. (2), with $J(P,P)$ in Hz and d P···P′ in Å.

$$J(P,P) = 8859.1e^{-1.5884d\ P···P} \tag{2}$$

The fitted data all correspond to experimentally determined values, which span a wide range of coupling constants (from 2 to 76 Hz) as well as distances (from 2.9 to 5.4 Å). Remarkably, the corresponding regression coefficient, $R^2 = 0.987$, compares with those obtained from computed data [3g,7].

It must be specified that this correlation constitutes, strictly speaking, only an approximation in the absence of a more developed tool taking into account that these TS couplings depend both on the *orientation of the lone-pair* and on the molecular orbitals (shape, symmetry energy) involved in the interaction. However, the phosphorus nucleus being a statistical centre for the electron clouds concerned, the resulting approximation allows in this case an effective estimation of TS spin coupling from the internuclear distance.

Recent work by Malkina and Malkin constitutes an interesting approach for an accurate visualization of spin couplings transmission [28]. These authors introduced a model based on real-space functions in three-
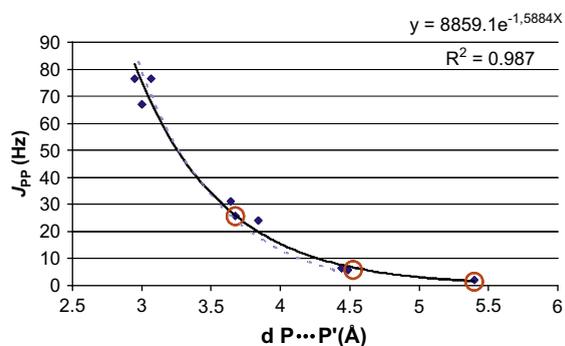

Fig. 17. Plot of $J(P,P)$ vs. d P···P′ ''through-space'' distances. The plot is fitted by the exponential relationship defined by Eq. (2) [27]. The dotted line corresponds to earlier results [16] and encircled values are examples from Table 1.
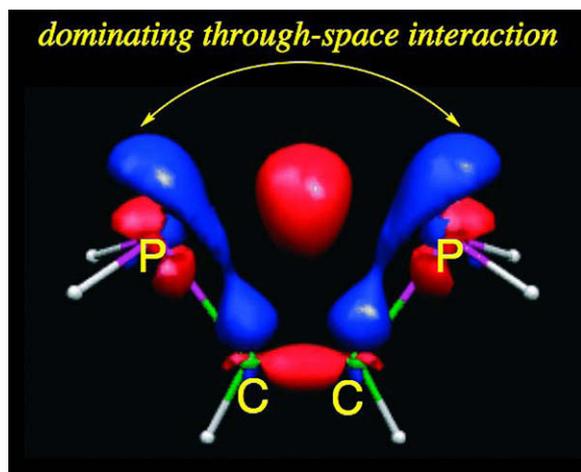
Fig. 18. Visualization of the *J*(P,P) coupling density (CED) in the $C_2H_2(PH_2)_2$ molecule from DFT calculations (taken from Ref. [28]).

dimensional space, which is appropriate for both localized and delocalized bonding situations. The indirect spin–spin coupling is expressed as the energy splitting between states with parallel and antiparallel nuclear spins. These energies are then written as an integral over an energy density called the coupling energy density (CED). The integral of CED over all space is equal to the reduced coupling constant. CED is a real-space function and can be visualized easily in 3D space. The CED was calculated using a double finite perturbation theory for various molecules, notably $C_2H_2(PH_2)_2$ (Fig. 18). The visualization clearly established that the "through-space" interaction between the two phosphorus nuclei dominates over the "through-bond" pathway [28].

Calculations aimed at 3D visualization of the above mentioned ferrocenylphosphane ligands and their complexes are currently underway.

6. Conclusion and perspectives

Both from a theoretical and an experimental point of view, the analysis of high-resolution NMR parameters is a critical issue. A deeper understanding of the relationship between coupling constants and molecular structure will greatly broaden future applications of high-resolution spectroscopy for the elucidation of molecular structures [29]. The *phosphinocalixarenes*, *phosphinocyclodextrins* and *ferrocenyl phosphanes* presented herein may contribute to furthering our knowledge about nonbonded coupling. The important structural information provided by careful analysis of the corresponding NMR spectra should encourage researchers to systematically pay more attention to all those *constrained* molecules in which nonbonded spin–spin couplings are likely to occur.

Overall, it may be anticipated that future studies in this field will ultimately allow easier and non-ambiguous discrimination between "through-bond" and "through-space" contributions in every type of molecule.

Acknowledgements

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