

DYNAMIC PHENOMENA IN BARRELENEPHOSPHINYL RADICALS: A COMPLEMENTARY APPROACH BY DENSITY MATRIX ANALYSIS OF EPR SPECTRA AND DFT CALCULATIONS

MARCIN BRYNDA¹, COSMINA DUTAN², THÉO BERCLAZ², MICHEL GEOFFROY²

¹Department of Chemistry, University of California, Davis, Davis CA 95616, USA

²Department of Physical Chemistry, University of Geneva, 30 quai Ernest Ansermet, 1211 Geneva, Switzerland

The paper shows the possibilities of the complementary use of the density matrix formalism for the simulation of the anisotropic EPR spectra and the DFT potential energy surface calculations to obtain a detailed picture of the motions of radical molecules. The combined approach is illustrated by a comparative EPR study of three phosphorus derivatives of barrelene. Three compounds were chosen as the model molecules for the observation of different temperature dependent dynamics of radical fragment. Each molecule based on the same barrelene skeleton has a different set of substituents which by influencing the local chemical environment are likely to modify the internal dynamics. The temperature dependent EPR spectra are simulated by means of the density matrix formalism and the geometry of radicals are calculated with DFT. The motion is described in terms of rotational barriers, DFT calculated energy profiles and hypothetical intramolecular distortions. These two approaches lead to a similar microscopic picture of the intramolecular radical motion.

INTRODUCTION

The details of the molecular dynamics are essential for the understanding of various complex chemical phenomena. Whereas NMR is a well established and a powerful tool in investigations of molecular motion (Ishima & Torchia, 2000; Palmer, 2001), the use of the EPR techniques for the study of the motion in radicals is far less widespread.

The knowledge of the details of the motion in radicals is of interest not only for highlighting the dynamics itself but also for the comprehension of motion-related changes in complex biological systems. In such systems, several paramagnetic species subjected to internal dynamics are usually involved. The use of EPR techniques allows one to determine not only the rotational or exchange correlation times τ of the specific paramagnetic molecule but also to obtain detailed information concerning the type of motion the molecule undergoes. A variety of biochemical problems such as those concerning enzymes, where some paramagnetic species may be transiently formed within the catalytic cycle, or proteins, the dynamics of which can be studied by the use of an external spin label, can be investigated by EPR (Prisner, Rohrer & MacMillan, 2001). It is well known that the motion of a nitroxide spin label bound to a protein is hindered, depending on the specific position of the spin label. Therefore, measurements of the spin label related dynamics can help in obtaining de-

tailed information not only on the molecule itself, but also on the surrounding protein backbone (Borbat, Costa-Filho, Earle, Moscicki & Freed, 2001). EPR methods can also be used to characterize the protein-protein and protein-lipid interactions by observing the changes in rotational diffusion of the paramagnetic labels (Marsh, 2001). Data concerning the dynamics of lipid molecules can also be extracted from the EPR lineshape analysis of a variety of lyotropic phases (Usova, Persson & Westlund, 2000), if different complex dynamics (internal reorientation, lateral diffusion) are present.

Several models have been developed to interpret the NMR and EPR lineshapes arising from dynamic phenomena. This can be achieved by the use of the modified Bloch equations as long as one is dealing with adiabatic exchange. Unfortunately, these equations can not describe the non-adiabatic exchange processes such the ones observed in solids. For such systems a more general density matrix formalism is necessary.

The use of the density matrix techniques for the interpretation of NMR and EPR lineshapes was pioneered in several research groups (Kaplan, 1958a, b; Alexander, 1962a, b; Johnson, 1964) in the early sixties. In 1965 Binstch unified the theories developed by Kaplan, Alexander and Johnson (Binstch, 1969) by showing that in the case of chemical exchange, a single NMR equation developed in Hilbert space that describes the exchange-

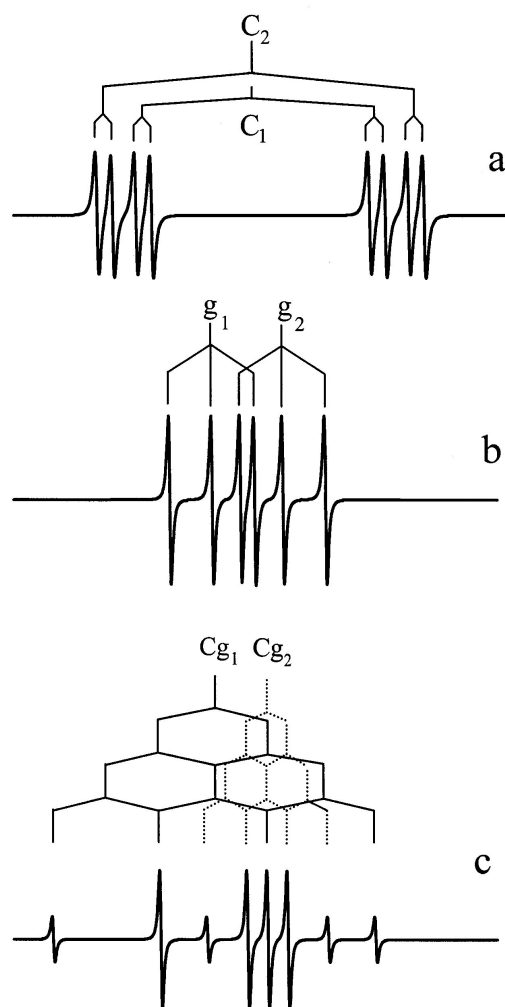


Fig. 1 Schematic representation of the EPR spectra resulting from two conformations of the same radical. (a) difference in the hyperfine coupling constants; (b) difference in the g values; (c) simultaneous presence of both mechanisms.

related lineshape can be rewritten in the Liouville space suggested by Fano (Fano, 1964). Simulations of EPR spectra by solving the time dependent stochastic Liouville equation were subsequently used by several authors. Some attempts were made to make a general computer simulation program, but only an isotropic case allowing the simulation of a lineshape from a multi-site exchange phenomena in solution was fully developed (Heinzer, 1971). In the early stage of development, the limiting factor to a wider use of density matrix techniques was the numerical problem of diagonalization of complex non-Hermitian matrices. Nowadays, the amazing acceleration in CPU performance allows one to overcome this limitation even for very complicated spectral patterns.

The use of the density functional theory recently proved to be a very useful tool for the calculations

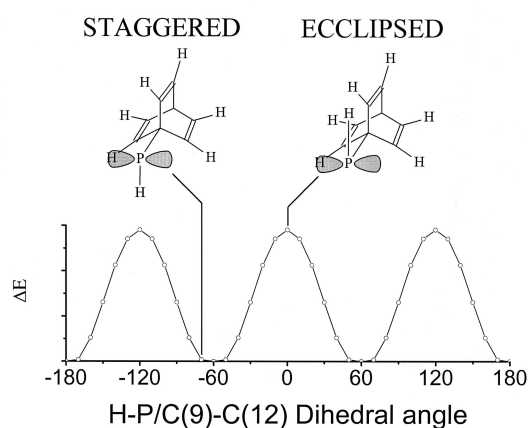


Fig. 2. Schematic representation of the potential energy variation as a function of HP/C(9)C(12) angle with the staggered and eclipsed conformations of barrelenephosphinyl radical.

of the geometry and the EPR parameters of paramagnetic molecules (Barone, 1995; Nesse, 2001, 1997; Chentit, Sidorenkova, Choua, Geoffroy, Ellinger & Bernardinelli, 2001). In this paper we show how the complementary use of the density matrix technique for the simulation of the EPR spectra together with quantum chemistry calculations can give a detailed picture of the motions of radical molecules. Moreover, this approach can help us to understand the influence of the molecular environment on intramolecular motions.

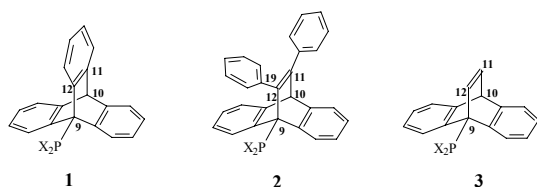
MOLECULAR MOTION AND EPR LINESHAPE

A simplest model for the analysis proposed here concerns a single radical trapped in the solid state which can adopt two or more different conformations. When no chemical exchange is present (e.g. frozen configuration at low temperature), the recorded spectrum of such a radical should be a superposition of single spectra corresponding to every considered conformation. In the simplest case the differences between different sites can be reflected in the spectrum in several ways (i) by the difference in the hyperfine coupling constants (Fig. 1a); (ii) by the difference in the g values (Fig. 1b); (iii) by simultaneous appearance of both factors (Fig. 1c). This latter case can lead to highly complicated patterns, especially if a large number of sites with similar values of g and hyperfine tensors are present. If the molecule undergoes a chemical exchange, every configurational site will be occupied for a certain time (exchange correlation time τ) and the corresponding EPR spectrum will arise from the average tensor composed of

single configurational tensors mixed together by the appropriate exchange operators.

MODEL

The investigation of dynamic phenomena in radicals presents some major difficulties. The main ones are the low stability of radicals and the simultaneous presence of intra- and intermolecular motion. To overcome these difficulties some preliminary conditions are required: one single radical undergoing a well specified motion must be created on the selected molecule with the rigid backbone. In order to make the description sufficiently detailed, the radical must be trapped in the solid state. To bring together these conditions, our choice was focused on the derivatives of barrelene. Their perfect stability, high molecular symmetry and relatively easy synthesis make the barrelene derivatives molecules of choice for the study of the intra-molecular motion. The easy inclusion of a variety of substituents in 9 position makes possible a handling of mobile fragment C-Y-X_n (where Y = P, C, Ge, Si, As, X = H, D) which can easily be made paramagnetic by the X-irradiation of the corresponding diamagnetic molecule. We restrict our analysis to a set of simple model molecules which served as a basis for the study of the approach described above. In this paper, we present the results obtained with radicals created on the phosphorus derivatives of barrelene. It was already proved that the irradiation of crystalline compounds containing a P-H (P-D) bond leads to the homolytic scission of this bond and formation of the corresponding phosphorous-centered radical (Geoffroy & Lucken, 1972). In order to study the internal hindered rotation of the PH (PD) fragment around the C-P bond, we have synthesised a series of barrelene derivatives with the PH₂ (PD₂) fragment bound to the sp³-carbon C(9) of the barrelene skeleton. Radicals X = H (**R1**, **R2**, **R3**) or X = D (**R'1**, **R'2**) used for this study were obtained by X-irradiation (Scheme 2) of the corresponding phosphines **1**, **2** and **3** (Scheme 1).



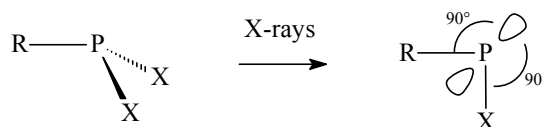
Scheme 1

This particular choice was adopted in order to highlight the influence of the molecular environment on the possible motion that the rotating

paramagnetic fragment will undergo. The tribenzobarrelene **1** (commonly called triptycene) has a totally symmetric backbone with a C₃ threefold axis. This symmetry was broken in compound **2** where one of the benzene rings was substituted by two phenyls bound to the C(11)-C(12) double bond in order to increase the possible interaction between the rotating PH fragment and the neighbouring benzene ring. The total suppression of the steric constraint was achieved in compound **3** where the presence of an ethylenic bond modifies the symmetry from the ternary C₃ threefold axis symmetry (**1**) to the planar symmetry (**3**).

The phosphinyl radical is characterized by a large anisotropic hyperfine coupling $T_{||} \sim 800$ MHz and an isotropic coupling A_{iso} close to 300 MHz. According to the ab-initio calculations made on the phosphinyl radical (Bhat *et al.*, 1994; Ramakrishnan, Jouaiti, Geoffroy & Bernardinelli, 1996), the C-P and P-H bonds form an angle of 90° with the phosphorus P_z orbital containing the single electron (Scheme 2).

The schematic energy profile for selected values of the C(9)PH/PC(9)C(19) dihedral angle θ , calculated by DFT for the barrelenephosphinyl radical is shown in Fig. 2. The staggered conformation (a) corresponds to the minimum energy, whereas the maximum energy is reached with the eclipsed conformation (b).



Scheme 2

METHODS

The synthesis and single crystal growth of phosphines **1**, **2** and **3** and the experimental details of the EPR studies of corresponding radicals were described elsewhere (Brynda, Berclaz & Geoffroy, 2000; Brynda, Berclaz, Geoffroy & Bernardinelli, 1998; Brynda, Geoffroy & Bernardinelli, 1999). The variable temperature spectra were recorded in the temperature range from 40 to 300 K. For each spectrum obtained at a given temperature, the parameters such as the populations of every site and the correlations times were fitted by comparison with simulated spectra obtained by means of the density matrix formalism. An ensemble of these parameters was used for the calculations of the rotational barriers. These calculations were carried out by estimating the temperature dependent corre-

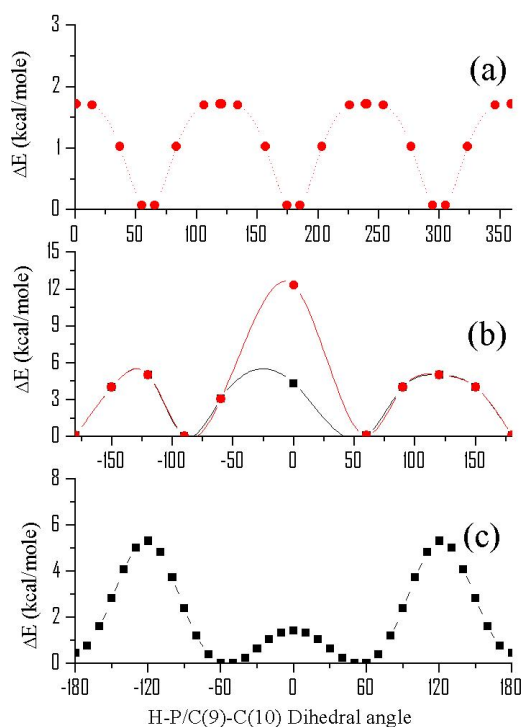


Fig. 3 DFT calculated variation of the potential energy of the phosphinyl radicals as a function of the HP/C(9)C(12) dihedral angle: (a) R1; (b) R2, circles correspond to the energy profile obtained after 15° rotation of the benzene ring around the C(12)-C(19) bond; (c) R3.

lation times τ at variable temperature and plotting the Arrhenius plot $\tau = f(1/T)$.

Quantum chemistry calculations

The DFT calculations were performed with the Gaussian98 package (Gaussian 98, Revision A.7, 1998) using B-3LYP exchange-correlation functional with 3-21G* basis set. The geometry of the radicals were optimised by partial (**R1**, **R2**) or total (**R3**) relaxation of the structure. The main geometric features for the optimised structures are presented in Table 1. The calculated geometry (except for the radical fragment C-P-H) is very close to that obtained from the crystal structure.

Simulations

The experimental spectra at variable temperature were simulated using the density matrix formalism in Liouville space. The lineshape $I(\omega)$ for the anisotropic spectrum is obtained as the real part of the trace of ρ^{+-} .

$$I(\omega) = \text{Re}[\text{Tr}(\rho^{+-} \cdot S^+)] = \text{Re}[\text{Tr}(\rho^{+-})],$$

where

Table 1 Selected bond lengths and bond angles calculated by DFT for R1, R2 and R3

	CPH angle	PH bond length [Å]	CP bond length [Å]
R1	95.5°	1.43	1.88
R2	96.3°	1.41	1.88
R3	95.4°	1.43	1.87

$$\rho^{+-} = iI_0 \cdot [U^{-1}\Lambda U - i\omega \cdot 1]^{-1} P$$

Λ contains the line positions, the exchange parameters and the line widths expressed in terms of $1/T_2$ and can be diagonalized once for a given simulation. The calculation of the spectra is then reduced to the inversion of a single diagonal matrix and can be easily performed for all the range of frequencies ω .

RESULTS AND DISCUSSION

The comparison of the experimental and simulated variable temperature spectra allowed us to determine a set of exchange parameters τ_{ij} and site populations P_i for every temperature. This led us to the experimental rotation barriers which were compared with those calculated by DFT (Fig. 3).

As an example, the temperature dependence of the experimental EPR spectrum of **R'1** is shown in Fig. 4a together with the spectra (Fig. 4b) simulated by density matrix formalism and the corresponding correlations times τ . At 110 K, the spectrum exhibits a set of 3 doublets showing a hyperfine coupling to a ^{31}P nucleus, corresponding to three staggered conformations (I,J,K) of the same phosphinyl radical, trapped in 3 directions separated by an angle of 120°, as predicted by the molecular symmetry of triptycene. Increasing the temperature from 110 to 170 K is accompanied by the increase of the line width of three sets of doublets. Between 170 and 190 K the three components of the spectrum can no more be distinguished due to the significant broadening of the spectral lines. Finally, above 180 K a single doublet whose width narrows with increasing temperature appears. The corresponding spectra were simulated by assuming that the three sites (I, J, K) were equally populated. The number of parameters to adjust in the simulation is reduced to one, since the populations of three sites and corresponding correlations times are the same for each site: $P_I = P_J = P_K$ and $\tau_{IJ} = \tau_{IK} = \tau_{JK}$. As expected, the calculated energy profile for the triptycene is totally

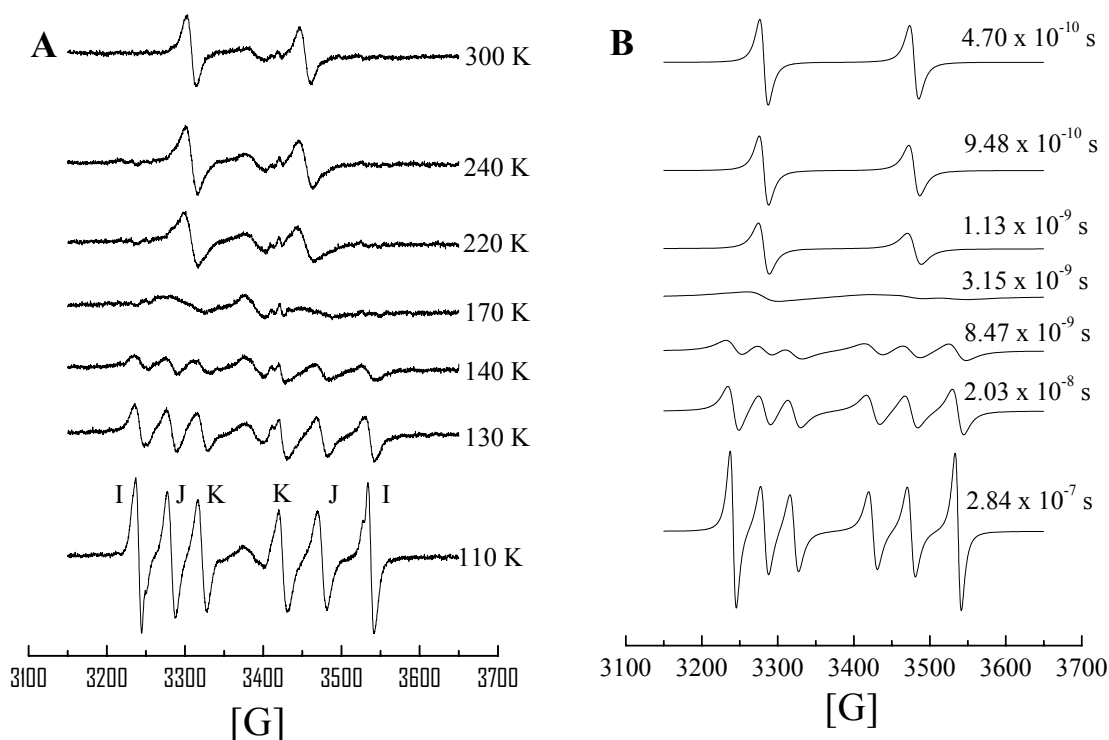


Fig. 4 Experimental (a) and simulated (b) variable temperature spectra of R'1 with corresponding temperatures and correlation times.

symmetric and consists of three minima corresponding to three staggered conformations of the phosphinyl radical. The energy barrier calculated from the Arrhenius plot is 2.7 kcal/mole. The DFT calculations give the slightly lower rotational barrier of 1.7 kcal/mole.

The situation is less obvious in R'2 where the potential curve calculated with DFT shows three quasi equivalent minima separated by slightly different rotational barriers. Surprisingly, the experimental spectra at 77 K exhibits only two doublets of inequivalent intensity. The additional doublet corresponding to the third site, suggested by the DFT calculations, is not observed at this tempera-

ture. That implies that at this temperature the third hypothetical site remains unoccupied. This is entirely confirmed by the simulations of the experimental spectra at low temperatures. Whereas only two sites must be considered to reproduce the measured lineshape of frozen configurations at low temperature, the simulation of the spectra at higher temperature requires the introduction of the third site with the population governed by the Boltzmann distribution. It then becomes obvious that the third position is not populated at low temperature when the motion is frozen, but its population grows as the temperature is raised. The change in the populations of three sites is also ac-

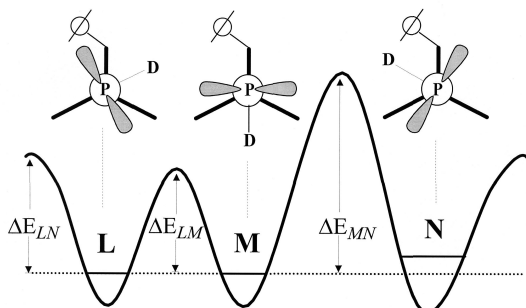


Fig. 5 Schematic representation of the potential energy variation of R'2 as a function of the HP/C(9)C(12) dihedral angle. Experimental rotation barriers: $\Delta E_{LN} = 2.46$ [kcal/mol]; $\Delta E_{LM} = 2.37$ [kcal/mol]; $\Delta E_{MN} = 2.74$ [kcal/mol].

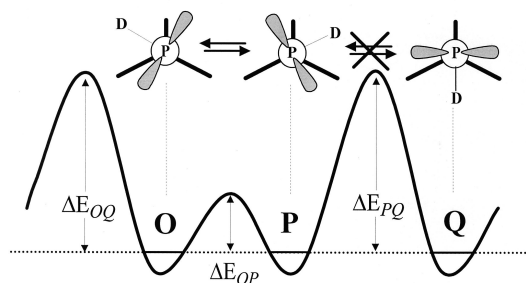


Fig. 6 Schematic representation of the potential energy variation of R'3 as a function of the HP/C(9)C(12) dihedral angle. Experimental rotation barrier: $\Delta E_{OP} = 0.51$ [kcal/mol];

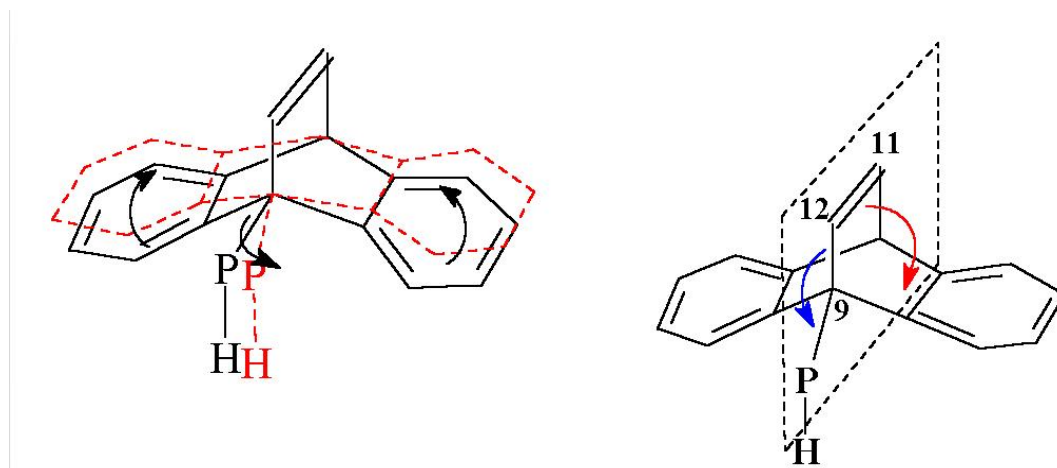


Fig. 7 Schematic representation of the distortion of the geometry of **R2** with the variation of the HP/C(9)C(12) torsional angle.

accompanied by exchange phenomena between three conformations. This is illustrated in Fig. 5. At first, exchange only occurs between sites L and M which have the same populations. With increasing temperature, the third site N starts to participate in the exchange process. The experimental rotational barriers are similar for the jumps between sites L and M and between sites L and N but a higher barrier for the jump between sites M and N are observed. This effect (which was not shown by the DFT calculations on the model structure **R2**), led us to consider that the benzene ring bound to C(12) carbon is not totally rigid but can undergo a slight reorientation which could result in a steric constraint between a proton bound to the phosphorus and this benzene ring. To verify this hypothesis we have performed a set of DFT calculations on **R2** by rotating the plane of the benzene ring bound to the C(12) of 15° around the C(12)-C(19) bond. This curve (plain circles line Fig. 3b) shows clearly an important increase in the energy barrier at this position and suggests that a slight reorientation of the benzene ring occurs in the crystal matrix.

The suppression of the steric constraint due to one of the benzene rings on the barrelene skeleton in compound **3** results in a significant lowering of the rotational barrier above this position observed in the radical **R3**. The experimental spectrum at 40 K exhibits only a pair of doublets of doublets which exhibit a hyperfine coupling with ^{31}P and ^1H nuclei. All the 8 lines are of equal intensity and correspond to two staggered conformations of the PH fragment (Fig. 6). A careful analysis of the spectra between 40 and 300 K suggests that only these two configurational sites are occupied in this temperature range. This hypothesis is confirmed by the simulation of the temperature dependent

spectra. The spectrum can be easily simulated over the whole temperatures range using the simple two sites model with equal population of two sites. Moreover, the inclusion of the third hypothetic site corresponding to the staggered conformation Q, even with very small population, drastically modifies the simulated spectrum which becomes very different from the measured one. The schematic energy profile (Fig. 6) shows only a small energy difference between sites O and P but a higher energy barrier between sites P and Q. This is in agreement with the experimentally observed exchange mechanism, where a simple jump between two sites occurs whereas the third hypothetic site remains unoccupied even at high temperature.

The decomposition of the hyperfine tensors at low and room temperature into anisotropic and isotropic parts permits the extraction of the phosphorus isotropic coupling constants A_{iso} at both temperatures. Surprisingly, the ^{31}P A_{iso} values at 40 K and at 300 K are not the same. The difference that appears between the traces of ^{31}P tensors measured at 77 K and at room temperature amounts to 28 MHz. To elucidate this difference, which was also observed in **R1** (30 MHz) and **R2** (26 MHz), we performed a set of additional DFT calculations on the dibenzobarrelene radical **R3** with total relaxation of the molecule geometry by varying the HPC(9)/PC(9)C(12) ϕ dihedral angle. The obtained geometrical features show clearly that the rotational motion of the P-H fragment is accompanied by a small distortion of the geometry of the dibenzobarrelene skeleton. As shown in the Fig. 7 both the PC(9)C(12) valence angle and the dihedral angle between two planes containing benzene rings of dibenzobarrelene are modified by jumps between two sites. This suggests that the small change in the chemical environment of the

C-P-H fragment could be responsible for the observed difference in the isotropic hyperfine coupling constant A_{iso} at low and at room temperature.

CONCLUSIONS AND PERSPECTIVES

In this paper, we have shown that the complementary use of density matrix techniques for the simulation of the variable temperature EPR spectra combined with quantum chemistry calculations to obtain the rotational barriers and the geometry of radical molecules, can give a detailed and quantitative picture of the motion in radicals. Moreover, such phenomena as the impact of the chemical environment (e.g. steric constraints, modification of local structure) on the molecular motions can be investigated using this approach. The use of the optimisation algorithms which permit the extraction of parameters such as correlations times or exchange constants by means of the automated procedures (Rockenbauer, Szabo-Planka, Arkosi & Korecz, 2001; Rockenbauer, 1999; Soulié, Berclaz & Geoffroy, 1996) seems to be a promising method for the study of molecular motion in complex biological systems. The possibility of combining the density matrix formalism with the optimisation program in order to extract the exchange parameters by automatically fitting the experimental spectra is currently under investigation.

Acknowledgments

We gratefully acknowledge the help of Dr G. Bernardinelli from the Crystallographic Laboratory for crystal structures. We also thank the Swiss National Science Foundation for financial support.

REFERENCES

- Alexander S. (1962a). Exchange of interacting nuclear spins in nuclear magnetic resonance (N.M.R.).I. Intramolecular exchange. *J. Chem. Phys.*, **37**, 967-974.
- Alexander S. (1962b). Exchange of interacting nuclear spins in nuclear magnetic resonance (N.M.R.).II. Chemical exchange. *J. Chem. Phys.* **37**, 974-980.
- Barone V. (1995). in Recent advances in Density Functional Methods, Vol. I, edited by D.P. Chong World Scientific, Singapour, 287-334.
- Bintsch G. (1969). Title. *J. Am. Chem. Soc.*, **91**, 1304.
- Bhat S., Berclaz T., Jouaiti A. & Geoffroy M. (1994). Radical reactions in an x-irradiated phosphalkene: a single-crystal ESR study. *Helv. Chim. Acta*, **77**, 372-382.
- Borbat P. P., Costa-Filho A. J., Earle K. A., Moscicki J. K., Freed J. H. (2001). Electron spin resonance in studies of membranes and proteins. *Science*, **291**, 266-269.
- Brynda M., Berclaz T. & Geoffroy M. (2000). Intramolecular motion in dibenzobarrelenephosphinyl radical: a single crystal EPR study at variable temperature. *Chem. Phys. Lett.*, **323**, 474-481.
- Brynda M., Berclaz T., Geoffroy M. & Bernardinelli G. (1998). Hindered rotation around C-PH bond: A single crystal EPR study of the Diphenyldibenzobarrelenephosphinyl radical. *J. Phys. Chem. A*, **102**, 8245-8250.
- Brynda M., Geoffroy M. & Bernardinelli G. (1999). Air-stable primary phosphines and germanes: synthesis and crystal structures of dibenzobarrelenephosphine and tribenzobarrelenegermane. *Chem. Commun.*, **1999**, 961-962.
- Chentit M., Sidorenkova H., Choua S., Geoffroy M., Ellinger Y., Bernardinelli G. (2001). EPR and theoretical studies of the reduction product of the fulvenephosphaallene system. *J. Organomet. Chem.*, **634**, 136-144.
- Neese F. (2001). Prediction of electron paramagnetic resonance g values using coupled perturbed Hartree-Fock and Kohn-Sham theory. *J. Chem. Phys.*, **115**, 11080-11096.
- Fano U. (1964). Liouville representation of quantum mechanics with application to relaxation processes [In:] E.R. Caianiello, (Ed.) *Lectures on the many-body problem* (pp. 217-239, Vol. II), New York: Academic Press, Inc.
- Heinzer J. (1971). Fast computation of exchange-broadened isotropic E.S.R. spectra. *Mol. Phys.*, **22**, 167-177.
- Geoffroy M. & Lucken E.A.C. (1972). The electron spin resonance spectra of X-irradiated phenylphosphinic acid and its salts. *Mol. Phys.*, **24**, 335-340.
- Ishima R. & Torchia D. (2000). Protein dynamics from NMR. *Nat. Struct. Biol.*, **7**, 740-743.
- Johnson C. S. (1964). Calculation of nuclear magnetic resonance spectra for coupled nuclear spins in intramolecular reactions. *J. Chem. Phys.*, **41**, 3277-3278.
- Kaplan J. I. (1958a). Generalized Bloch-type equations for chemical exchange. *J. Chem. Phys.*, **29**, 462.
- Kaplan J. I. (1958b). Exchange broadening in nuclear magnetic resonance. *J. Chem. Phys.*, **28**, 278-282.
- Marsh D. (2001). Application of electron spin resonance for investigating peptide-lipid concentrations, and correlation with thermodynamics. *Biochem. Soc. Trans.*, **29**, 582-589.
- Palmer A. G. (2001). NMR probes of molecular dynamics: overview and comparison with other techniques. *Annu. Rev. Biophys. Biomol. Struct.*, **30**, 129-155.
- Prisner T., Rohrer M. & MacMillan F. (2001) Pulsed EPR spectroscopy: Biological applications. *Annu. Rev. Phys. Chem.*, **52**, 279-313.
- Ramakrishnan G., Jouaiti A., Geoffroy M. & Bernardinelli G. (1996). 9-Substitued triptycene as a probe for the study of internal rotation around a C-PH bond in the solid state. A single crystal EPR study at variable temperature. *J. Phys. Chem.*, **100**, 10861-10868.

- Rockenbauer A., Szabo-Planka T., Arkosi Z. & Korecz L. (2001) A two-dimensional (magnetic field and concentration) Electron Paramagnetic Resonance method for analysis of multispecies complex equilibrium systems. Information content of EPR spectra. *J. Am. Chem. Soc.*, **123**, 7646-7654.
- Rockenbauer A. (1999) Determination of chemical exchange parameters in ESR spectroscopy. *Mol. Phys. Rep.*, **26**, 117-127.
- Soulié E., Berclaz T. & Geoffroy M. (1996). Comparison of two algorithms for non-linear least square fitting. *AIP Conference Proceedings*, Eds. Bernardi F., Rivail J. L., *Computational Chemistry*, **330**, p. 627.
- Usova N., Persson L. & Westlund P. O. (2000). Theory of slow-motion EPR lineshapes for studies of membrane curvature. *Phys. Chem. Chem. Phys.*, **2**, 2785-2793.
- Gaussian 98, Revision A.7, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, Gaussian, Inc., Pittsburgh PA, 1998.