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Isomerism of (π-1,3-dimethylallyl)(phosphinooxazoline)Pd complexes: a comparison between experiment and theory

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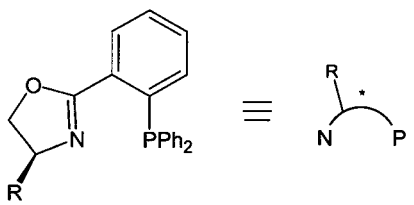
Dedicated to Professor Rolf Gleiter on the occasion of his 65th birthday

Abstract

Conformational analyses of two (π-1,3-dimethylallyl)(phosphinooxazoline)Pd complexes were carried out using QM/MM computations and a self-consistent reaction field (SCRF) solvation model. The computed isomer ratios and geometries are in good agreement with experimental NMR and X-ray data. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: π-Allyl complexes; Palladium; Quantum chemical calculations

The Pd-catalyzed asymmetric allylic substitution is frequently employed in organic synthesis [1]. Phosphinooxazoline (PHOX) ligands (cf. Fig. 1) are being widely used in this process [2]. Due to the modular structure and the efficient synthesis of PHOX ligands, their electronic and steric properties can be readily varied. The outcome of an allylic substitution is crucially dependent on the isomer distribution of intermediary π-allyl complexes. In the case of (π-1,3-dialkylallyl)Pd complexes (Fig. 2) there are eight possible isomers. The reaction of the mixture of these fast equilibrating complexes with soft C-nucleophiles, e.g. sodium dimethylmalonate, gives rise to products with *trans* configuration of the double bond with enantioselectivity typically in the range 80:20 and 85:15 with ligands **1** and **2**, respectively (1,3-dimethylallyl system). This value is close to the ratio of the *exo–syn–syn* isomer to the sum of the other isomers. Assuming preferential reaction at the allylic carbon (C3) *trans* to P, as was demonstrated for the 1,3-diphenylallyl system, it is likely that the major enantiomer of the product arises from the *exo–syn–syn* isomer and the minor enantiomer from the *endo–syn–syn* and *exo–syn–anti* isomers [3]. Thus, the ratio of the resultant products is correlated to the ratio of the isomeric Pd complexes. Accordingly, it would be of great value for the design of new ligands if the isomer distribution could be predicted with reasonable accuracy. We have previously found that this is indeed possible with high-level quantum chemical computations [4]. In order to reduce the computational expenditure we have now explored applicability of an integrated quantum mechanics/molecular mechanics (QM/MM) method by studying the isomer distributions of representative cationic (π-allyl)(PHOX)Pd complexes of ligands **1** and **2** (cf. Fig. 1). X-ray and NMR data of these complexes are available [4,5].



1 R = i-Pr

2 R = t-Bu

Fig. 1. PHOX ligands.

The QM/MM scheme allows large molecules to be studied while keeping the computational cost relatively

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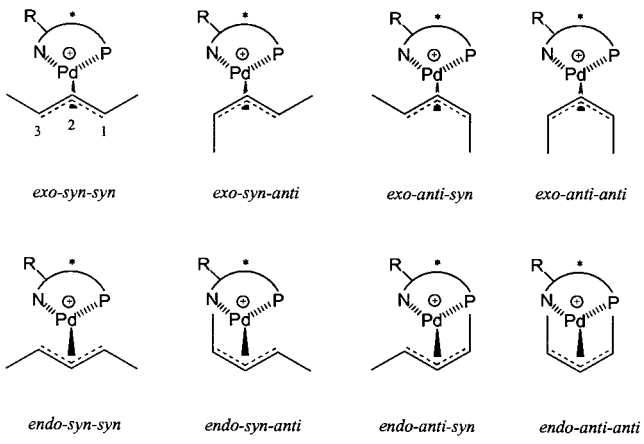

Fig. 2. Schematic plot of the formulas and descriptors [15] of the eight possible isomers of (π-1,3-dimethylallyl)Pd complexes.

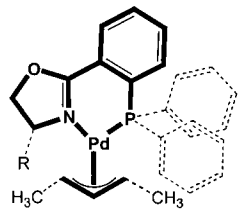

Fig. 3. QM/MM partition used in the computations, shown for complex (π-1,3-dimethylallyl)(**1**)Pd^+. The QM region is represented by thick and the MM part by dashed lines.

low and is becoming a powerful tool for the theoretical study of catalytic processes [6]. In this scheme the metal ion environment is described at QM level while the rest of the molecule, presumed to exert mainly steric effects, is treated by molecular mechanics. To our knowledge, the hybrid QM/MM method has not been applied yet to the study of (π-allyl)Pd complexes, although these

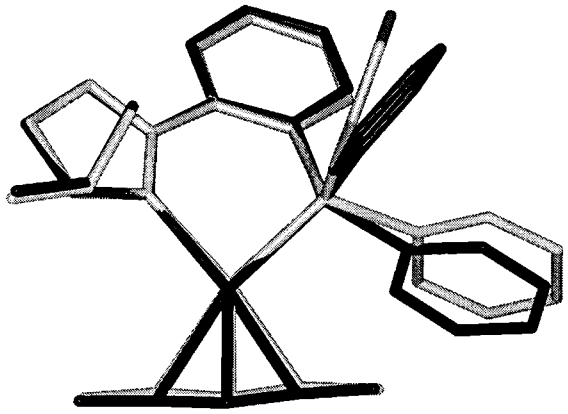

Fig. 4. Superposition of the X-ray (gray) and QM/MM (black) structures of complex (π-1,3-dimethylallyl)(**1**)Pd^+. Hydrogen atoms are omitted; in the crystal, the solvated counter ion is in close proximity to the phenyl groups.

have been investigated with other theoretical methods [7].

Because of the neglect of electronic effects in the MM part of the molecule, the frontier between the QM and MM regions must be chosen with great care. Fig. 3 shows the QM/MM partition employed: the QM part included the dihydrooxazole ring, the phenylene ring and the three allylic atoms C1–C3. The phenyl groups at phosphorus, the substituent of the dihydrooxazole ring and the terminal methyl groups of the allylic moiety were treated with molecular mechanics.

The calculations were performed with the GAUSSIAN 98 [8] program package and consisted in a complete optimization and conformational search of the (π-1,3-dimethylallyl)Pd^+ complexes of ligands **1** and **2** using the ONIOM [9] method at B3LYP level [10]; the basis set used was LANL2DZ + ECP for Pd and P as well as 3-21G for the other atoms. For each equilibrium PCM

Table 1
Selected bond lengths (Å) and bond angles (°) for the *exo–syn–syn* isomer of complex (π-1,3-dimethylallyl)(**1**)Pd^+, determined by X-ray analysis and DFT and QM/MM calculations with various basis sets

	X-ray	B3LYP	QM/MM		
		LANL2DZ+3-21G	LANL2DZ+3-21G	LANL2DZ	LANL2DZ+6-31G*
Bond lengths					
Pd–N	2.123	2.139	2.161	2.168	2.188
Pd–P	2.266	2.402	2.380	2.379	2.402
Pd–C1	2.136	2.202	2.189	2.176	2.197
Pd–C2	2.164	2.248	2.272	2.300	2.264
Pd–C3	2.264	2.336	2.327	2.487	2.333
C1–C2	1.409	1.426	1.430	1.442	1.420
C2–C3	1.381	1.399	1.400	1.401	1.397
Bond angles					
N–Pd–P	87.8	86.9	83.2	83.4	81.2
C1–Pd–C3	67.6	65.2	64.8	63.7	65.1
C1–C2–C3	122.8	120.0	117.6	120.9	120.1

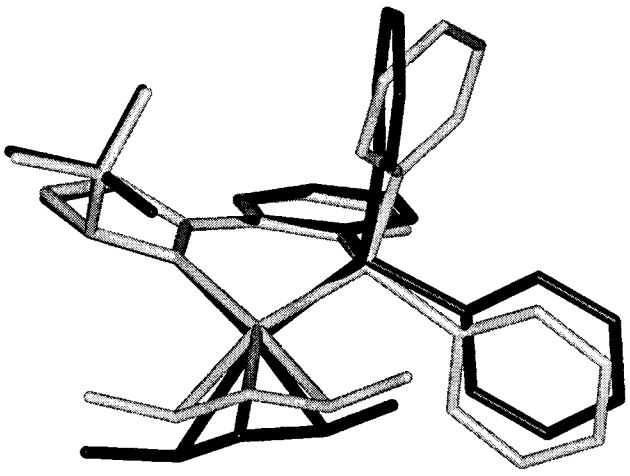

Fig. 5. Superposition of the computed most stable isomers of complexes (π-1,3-dimethylallyl)(**1**)Pd^+ (gray) and (π-1,3-dimethylallyl)(**2**)Pd^+ (black).

[11] solvation single point energies were computed at B3LYP level using LANL2DZ + ECP basis set for Pd and P as well as 6-31G* for all other atoms [12]. The PCM calculations were carried out for THF as solvent in order to compare the results with experimental data. The Onsager solvating model was also tested and gave unsatisfactory results [13]. Previous investigations of related model Pd complexes have demonstrated the suitability of B3LYP [7d,7f,14].

In Table 1 structures of the *exo–syn–syn* isomer of the complex (π-1,3-dimethylallyl)(**1**)Pd^+ obtained by QM/MM optimizations with different basis sets are compared with crystallographic data [4] (Section 1) and the result of a full DFT optimization. Conformational analyses show that the isopropyl group adopts a preferred conformation with its hydrogen pointing towards the Pd center, probably in order to minimize steric interactions. The same conformational preference was found in the NMR and X-ray studies of all Pd complexes of ligand **1** [4,5]. Fig. 4 shows the superposition of the X-ray and the QM/MM structure. It is apparent that the QM/MM geometry is in good agreement with the crystal structure. In addition, it is of interest to note that the geometry obtained from the hybrid QM/MM optimizations is *very similar* to that obtained with a full DFT optimization. Surprisingly, the best agreement with experimental geometric data was obtained with the relatively small 3-21G basis set for C, N, O and H.

In Fig. 5, geometries of the computed *exo–syn–syn* isomers of the (π-1,3-dimethylallyl)Pd^+ complexes of ligands **1** and **2** are compared. The structures are very similar in the dihydrooxazole and phenylene moieties, however, they differ in the dihedral angle of the axial phenyl group (Pd–P–C–C) by ca. 45° and in the location of the allyl group. These differences are due to higher steric effect of the *tert*-butyl group. These effects are also apparent from X-ray structures [4,5].

A complete evaluation of all possible isomers of the (π-1,3-dimethylallyl)Pd^+ complexes with ligands **1** and **2** was performed. Table 2 displays the calculated relative energies (E_{rel}) and experimentally determined populations. The computed relative energies are in good agreement with the experimental results for the most abundant, the *syn–syn* isomers. For the minor isomers, there are two cases where the stability order is reversed: for isomers *exo–syn–anti* and *endo–anti–syn* of (π-1,3-dimethylallyl)(**1**)Pd^+ and isomers *endo–syn–syn* and *exo–syn–anti* of (π-1,3-dimethylallyl)(**2**)Pd^+. In the former case, the difference is only 0.1 kcal mol^{-1}; in the latter case, the experimentally determined populations are almost equal but the calculated energy values differ by 1 kcal mol^{-1}. Isomers with $E_{rel} > 3$ kcal mol^{-1} are beyond experimental detection. This fact is reproduced by the calculations.

In conclusion, the QM/MM scheme is a powerful tool to study isomerism of (π-allyl)Pd complexes. It gives excellent geometric parameters and, when combined with the PCM solvating model, reproduces the experimental populations of isomers in solution quite well.

Table 2
Experimental populations and calculated relative energies of isomers of complexes (π-1,3-dimethylallyl)(**1**)Pd^+ and (π-1,3-dimethylallyl)(**2**)Pd^+

Isomer	(π-1,3-dimethylallyl)(**1**)Pd^+		(π-1,3-dimethylallyl)(**2**)Pd^+	
	NMR (%)	E_{rel} (kcal mol^{-1})	NMR (%)	E_{rel} (kcal mol^{-1})
exo–syn–syn	69.8	0.0	75.4	0.0
endo–syn–syn	18	+1.3	8.3	+1.4
exo–syn–anti	7.8	+2.0	10.2	+2.4
endo–anti–syn	4	+1.9	6	+2.6
endo–syn–anti	<0.2	+2.8	–	+5.6
exo–anti–syn	<0.2	+3.5	–	+5.7
endo–anti–anti	–	+6.9	–	+9.1
exo–anti–anti	–	+8.7	–	+9.4

1. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC nos. 155381 and 155382 for compounds [(π-1,3-dimethylallyl)(**1**)Pd]ClO_4 and[(π-1,3-dimethylallyl)(**2**)Pd]ClO_4, respectively. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

Acknowledgements

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[15] The terms *exo* and *endo* refer to the relative orientation of the bond C2–H with respect to the bond C4–R of the dihydrooxazole moiety. The substituents at the terminal allyl carbon atoms can adopt a *syn* or an *anti* orientation with respect to the allylic hydrogen at C2.