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Catalysis of Allylic Substitutions by Pd Complexes of Oxazolines Containing an Additional P, S, or Se Center. X-Ray Crystal Structures and Solution Structures of Chiral π-Allyl Palladium Complexes of Phosphinoaryloxazolines

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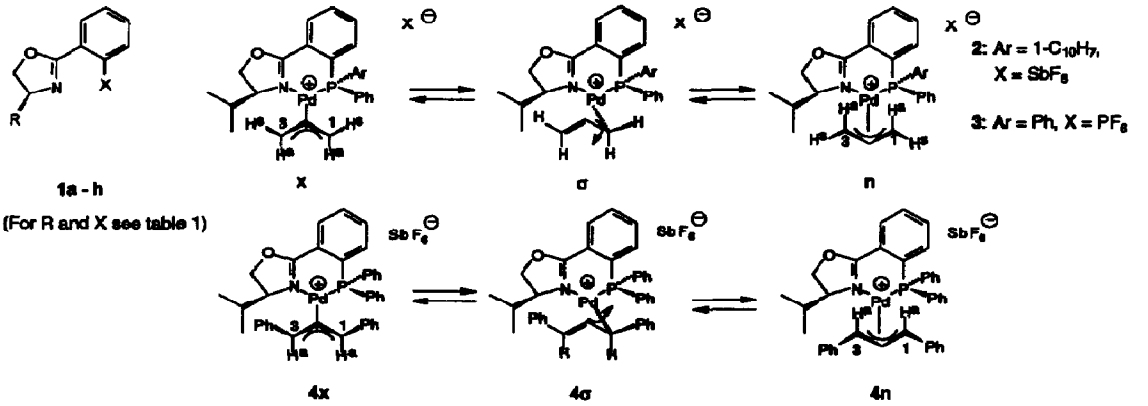
Abstract: Allylic alkylations with Pd complexes of chiral oxazolines with an additional donor P, S, or Se center are reported. Crystal and solution structures of palladium π-allyl complexes of phosphinoaryloxazolines were determined by X-ray crystallography and cross relaxation experiments, respectively. From the results conclusions concerning the steric course of allylic substitutions are drawn.

Recently we and others introduced phosphinoalkyl- and phosphinoaryloxazolines (**1**) as first members of a new class of chiral ligands, and demonstrated especially for the latter outstanding performance with respect to both reactivity and enantioselectivity in some Pd complex catalyzed allylic substitution reactions[1]. In the meantime, we have prepared additional ligands by varying R and X of **1**, widened the range of applications to i.a. N nucleophiles and were able to determine crystal and solution structures for the π-allyl Pd complexes **2**, **3** and **4** that were previously described[1a]. We hoped to aid by these studies mechanistic rationalization of the reactions of complexes **4** and analogous intermediates which required assessment of relative rates of reactions at C1 and C3 of the rapidly interconverting isomers **4x** and **4n**[2].



The first issue addressed was the relative influence of the substituents near the hard (N) and soft (X) center. Results are presented in Table 1. The steric course of the reaction, generally in favor of the product with (*S*) configuration, was found to be surprisingly insensitive to the nature of the soft ligand. Thus, the configuration of a stereogenic phosphorus atom (entries 2 and 3) is unimportant[3] and replacement of phosphorus by sulfur (entries 5, 6), as already apparent from studies by Williams[4], or selenium (entry 7) only reduces reactivity but not enantioselectivity. A monodentate ligand (entry 9) was, however, not effective. From these results we infere that the steric course is controlled by the oxazoline moiety and the soft ligand is mainly important for reactivity.

High quality crystals of the allylic complexes **2** and **4** were obtained by slow evaporation of solutions in CH_2Cl_2/ethyl acetate. Their X-ray crystal structures are described in Fig. 1. Remarkably, the crystal of **2** contained a disordered structure with both diastereomeric complexes. In the case of **4**, the *exo* isomer **4x** was found in the crystal. By dissolving a crystal at -78 °C and equilibration at higher temperature it was established that **4x** is more stable than **4n** (see below) which is in contrast to intuitive expectation. Selected bond lengths and angles are given in Table 2. The bond lengths between Pd and the allylic termini are within the range found for allylic complexes of NN and PP chelate ligands[5], i.e. the bond *trans* to P (225 ± 1 pm) is longer than the bond *trans* to N (213 ± 1 pm). The allylic plane forms an angle of 122 (2)/110 (4) deg with the coordination plane of Pd. In structure **4** there is a severe steric interaction between the phenyl group at C-1 of the allyl group and the equatorial phenyl group at P, which drives the allylic phenyl group out of co-planarity with the allylic system (torsion angle: 46 deg).

NMR investigations were carried out with a variety of methods[6] and furnished interesting results:

- The allylic complex **3** shows broad lines at room temperature. At -23 °C two sets of signals corresponding to the isomers **3x** and **3n** (ratio ca. 1:1) are observed. Almost all ^1H and ^{13}C resonances could be assigned[7].
- The complex **4** displays an 8 : 1 ratio of the two species **4x** and **4n** at room temperature, respectively (C_4D_8O). The ratio increases upon lowering of temperature. Assignment of the structures was unambiguously possible[7].

With the chemical shift data of all relevant species known, it was possible to shed some light on the processes involved in the interconversion of the *endo* and *exo* isomers. Assuming a π-σ-π process of interconversion, various possibilities have to be considered: formation of the σ bond to C1 or C3 and rotation around the allylic C-C single bond or the Pd-C bond. Careful analysis of the NOESY and ROESY data allowed to draw the following conclusions:

- Interconversion of **3x** and **3n** occurs via the σ-complex **3σ**, *i.e.*, by opening of the Pd-C bond *trans* to the phosphorus atom. From ROESY and NOESY spectra it follows that **3x** and **3n** interconvert at - 23 °C with a rate of 0.6 s^{-1} by rotation around the C1-C2 bond. In accordance with this motion only those cross peaks relating protons represented by the filled circles are observed (Fig. 2, the peak in brackets is obscured by overlap).

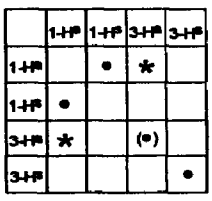


Fig. 2.

- In contrast, the 1,3-diphenyl allylic system **4** interconverts *via* the Pd-C-rotation mechanism (rate: 1.6 s^{-1} at +25 °C, cf. Fig. 2, corresponding cross peaks marked by asterisks).

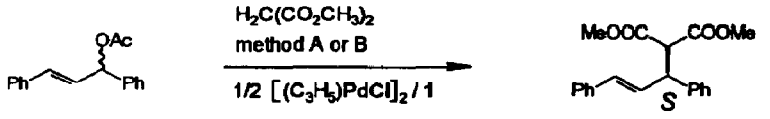


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Table 1. Allylic alkylation of dimethyl malonate with 1,3-diphenyl-2-propenyl acetate (5).

Entry	Ligand	R	X	Method	Molequiv. of Pd	Ratio of ligand/Pd	t [h]	Yield[d] [%]	% ee[e] (Config.)
1	1a	i-Pr	PPh_2	A[a]	0.02	1.2	1	98	98 (S)
2	1b	i-Pr	R_P-P(1-$C_{10}H_7$)Ph	A[b]	0.01	1.2	23	88	77 (S)
3	1c	i-Pr	S_P-P(1-$C_{10}H_7$)Ph	A[b]	0.02	1.2	21	98	77.5 (S)
4	1d	i-Pr	P(1-$C_{10}H_7$)$_2$[f]	A	0.02	1.1	120	36	90 (S)
5	1e	i-Pr	SPh	A	0.02	1.1	96	17	82 (S)
6	1e	i-Pr	SPh	A	0.02	5.0	96	49	79 (S)
7	1f	i-Pr	SePh	B[c]	0.01	2.0	72	50-84	95 (S)
8	1g	$(CH_2)_2SCH_3$	PPh_2	A	0.02	1.1	20	76	96 (S)
9	1h	i-Pr	H	B	0.015	2.0	120	3	2 (S)

a) Reaction of 1 mmol of 5 with 3 mmol of dimethyl malonate, 3 mmol of N,O-bis-trimethylsilylacetamide (BSA) and 10 µmol of H_3CCOOK in 2 ml of THF at room temperature. b) The solvent was CH_2Cl_2. c) Reaction of 1 mmol of 5 with 2 mmol of sodium dimethyl malonate in 2 ml of THF at room temperature. d) Yields refer to product after isolation and chromatographic purification. e) Enantiomeric excess was determined by ^1H NMR ($CDCl_3$) using Eu(hfc)$_3$ as shift reagent or by HPLC analysis on Daicel Chiralcel OD-H (n-hexane:i-propanol 99:1, flow 0.5 ml/min). f) Ligand 1d was provided by Mr. Th. Langer of our laboratory.

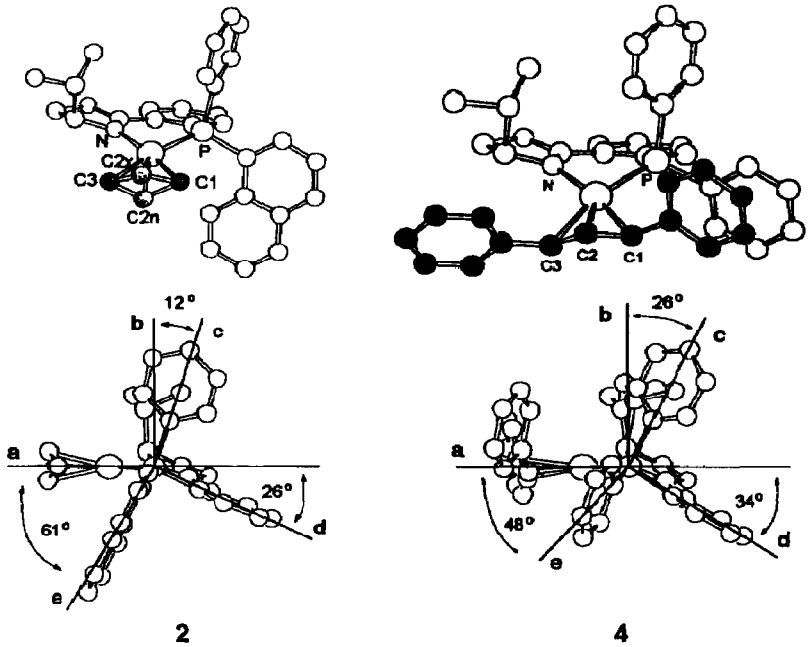


Fig. 1. Crystal structures of complexes **2** and **4**.

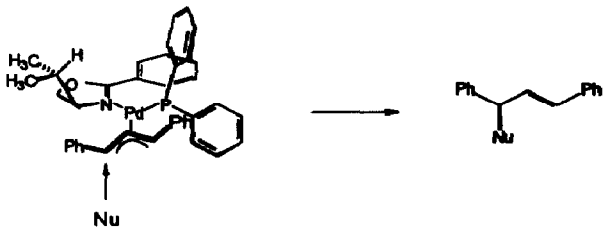
Anions and hydrogen atoms are omitted for clarity. Front and side views are given. In **2** both **2x** and **2n** are present in the crystal with all atoms except C2x and C2n, respectively, at identical positions.

In the side view, the horizontal line (a) marks the coordination plane spanned by C1, C3, Pd, P and N. The vertical line (b) is erected perpendicularly to the coordination plane at the P atom. Further lines are given to demonstrate differences in orientation of the ligand framework (c, d, e) to the coordination plane in **2** and **4**. The angle between a and d is mainly determined by the necessity of bond angles near 90 ° at Pd and steric effects. Axial disposition of the isopropyl group is a consequence of steric interactions of this group with ligands at Pd.

Table 2. Selected bond distances and bond angles.

	Distance [pm]			Angle [°]	
	2	**4**		**2**	**4**
Pd - N	207.7 (0.7)	209.0 (3.3)	N - Pd - P	88.9 (0.2)	88.6 (1.6)
Pd - P	226.8 (0.2)	226.2 (3.8)	P - Pd - C1	99.9 (0.3)	100.4 (0.8)
Pd - C1	211.9 (1.0)	214.3 (3.4)	C1 - Pd - C3	67.9 (0.4)	66.6 (1.0)
Pd - C2x	217.3 (2.2)	217.9 (5.5)	C3 - Pd - N	103.3 (0.3)	103.5 (0.7)
Pd - C2n	220.0 (1.7)	-		360.0	359.1
Pd - C3	224.0 (1.0)	226.3 (3.5)			

Experiments were carried out to determine the course of nucleophilic attack of dimethyl malonate, *i.e.*, to solve the question of the relative rates of nucleophilic attack at C1 or C3 of the diastereomeric π-allyl complexes **4x** and **4n**[8]. Unfortunately, interconversion of the isomers was found to be at least 50 times faster than nucleophilic attack so that no decision was possible. The results of the preparative experiments and the NMR work, *i.e.*, particular importance of the oxazoline moiety and opening of the Pd-C3 bond, *i.e.*, the bond *trans* to P, upon formation of the σ-complex, indicate that attack *trans* to the Pd-P bond is easier than *trans* to the Pd-N bond[9]. From the (*S*)-configuration of the predominant reaction product it follows that the *exo* isomer **3x** is the more reactive conformer. The same conclusion can be drawn by applying Bosnich's postulate[10] that the transition state of nucleophilic attack resembles the π-allyl intermediate; accordingly, it is the major diastereomer, here **4x**, that gives the major enantiomeric product; if so, attack of the nucleophile must occur *trans* to the Pd-P bond in order to give rise to the observed (*S*) enantiomer.



The same conclusion was independently derived by A. Pfaltz[11] for phosphinoaryloxazolines and by J.M. Brown for a different type of PN ligand (diphenylphosphinonaphthylisochinoline) with a somewhat different set of arguments[12].

References and Notes

1 (a) J. Sprinz, G. Helmchen, *Tetrahedron Lett.* **1993**, *34*, 1769; (b) P. von Matt, A. Pfaltz, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 566. (c) G.J. Dawson, C.G. Frost, J.M.J. Williams, S.J. Coote, *Tetrahedron Lett.* **1993**, *34*, 3149.

2 The terms *endo* and *exo* were used by Faller for the description of diastereomeric π-allyl complexes: (a) R. D. Adams, D. F. Chodosh, J. W. Faller, A. M. Rosan, *J. Am. Chem. Soc.* **1979**, *101*, 2570; (b) J. W. Faller, K.-H. Chao, *J. Am. Chem. Soc.* **1983**, *105*, 3893.

3 This observation is not true in general. With 3-cyclohexenyl acetate a very low degree of enantioselectivity is obtained with ligand **1a**; the ligands **1b** and **1c** raise the ee to levels of >50 % and yield products of opposite configuration; unpublished results of P. Sennhenn of our group.

4 (a) C.G. Frost, J.M.J. Williams, *Tetrahedron Lett.* **1993**, *34*, 2015; (b) C.G. Frost, J.M.J. Williams, *Tetrahedron: Asymmetry* **1993**, *4*, 1785.

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6 1D- and 2D-NMR methods were applied including ^{31}P-decoupled ^{1}H-NMR spectra, DQF-COSY and a modified version of ROESY: J. Schleucher, J. Quant, S. Glaser, C. Griesinger, submitted.

7 ^{1}H NMR chemical shift data for allylic systems in the complexes **3** (400 MHz, $CDCl_3$) and **4** (400 MHz, C_4D_8O): **3x**: 5.95 (2-H), 4.90 (3-H^s), 3.92 (3-H^a), 3.69 (1-H^s), 2.84 (1-H^a); **3n**: 5.89 (2-H), 4.89 (3-H^s), 3.77 (3-H^a), 3.42 (1-H^s), 3.20 (1-H^a); **4x**: 7.23 (2-H), 5.94 (3-H^a), 4.49 (1-H^a); **4n**: 7.02 (2-H), 5.82 (3-H^a), 5.24 (1-H^a).

8 Saturation transfer and EXSY experiments were unsuccessful so far.

9 Reaction at the allylic C with the weaker (longer) bond to Pd was demonstrated by Pfaltz and coworkers with Pd complexes of C_2-symmetric bis(oxazoline) ligands; cf. ref. 5a.

10 P. R. Auburn, P. B. Mackenzie, B. Bosnich, *J. Am. Chem. Soc.* **1985**, *107*, 2033.

11 A. Pfaltz, lecture at the HCM launch symposium, Groningen, November 13, 1993.

12 J.M. Brown, D.I. Hulmes, P.J. Guiry, submitted; we thank Prof. Brown for a preprint.

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