Pergamon

Tetrahedron Letters, Vol. 37, No. 23, pp. 3985-3988, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)00762-9

Optically Active Sulfoximines in Enantioselective Palladium Catalysis

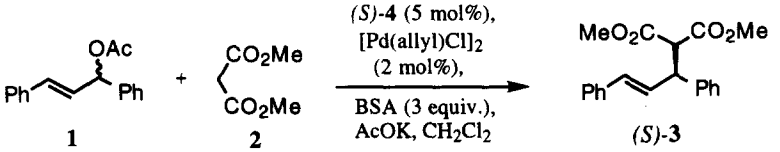
Carsten Bolm* [a], Daniel Kaufmann[a], Margareta Zehnder[b] and Markus Neuburger[b]

[a] *Fachbereich Chemie der Philipps-Universität Marburg, Hans-Meerwein-Straße, D-35032 Marburg (Germany)*
and
[b] *Institut für Anorganische Chemie, Universität Basel, Spitalstr. 51, CH-4056 Basel (Switzerland)*

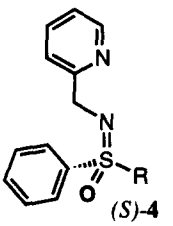
Key Words: Allylic substitution, palladium complex, asymmetric catalysis, enantioselective alkylation, sulfoximines

Abstract: Chiral sulfoximine/Pd-complexes catalyze enantioselective allylic alkylations. The corresponding products have been obtained in good yields with moderate enantioselectivities (up to 73% *ee*). The crystal structure of an allyl/Pd(II)-complex bearing a chelating sulfoximine is reported.

Various chelators have successfully been used as chiral ligands in palladium-catalyzed enantioselective allylic substitution reactions.[1] Among them, C_2-symmetric diphosphines[2] and P,N-oxazolines[3] gave the highest enantioselectivities. The use of dinitrogen-containing compounds[4] in palladium catalysis has also been studied.[5] The two nitrogens in these N,N-ligands were either identical (C_2-symmetric compounds) or their stereoelectronic properties were comparable. In this letter, we describe novel sulfoximine derivatives **4** having two significantly different donor atoms. Their ability to controle enantioselective Pd-catalyzed allylic substitutions has been investigated.



1 **2** *(S)*-**3**

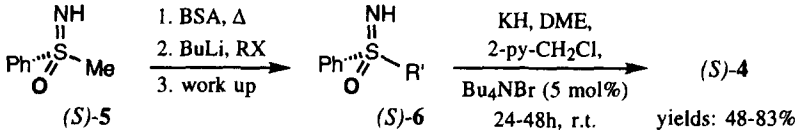


(S)-**4**

4a: R = -CH_3
4b: R = -$C_{19}H_{39}$
4c: R = -$CH(CH_3)_2$
4d: R = -$C(CH_3)_3$
4e: R = -$CH_2CH_2C_6H_5$
4f: R = -CH_2CH_2-*o*-$(CH_3O)C_6H_4$
4g: R = -CH_2CH_2-*o*-$(HO)C_6H_4$
4h: R = -$CH_2C(OH)(CH_3)_2$

Based on our previous results,[6,7] we expected sulfoximines **4** to bind to metals through the two nitrogens in a bidentate fashion. Selective coordination of the allyl fragment followed by its site-specific nucleophilic attack would then lead to the formation of optically active products.

We developed a reaction sequence by which both antipodes of **4** became available. Optically active **5** can be readily obtained by resolution of asymmetric synthesis.[8] N-silylation[9] of *(S)*-**5** followed by sequential C- and N-alkylation[8,10] gave *(S)*-**4** in moderate to good yields.



BSA = *N,O*-bis(trimethylsilyl)acetamide

The metal binding capability of sulfoximines of type **4** was revealed by the reaction of **4a** with $[Pd(allyl)Cl]_2$. A Pd(II)-π-allyl complex with one sulfoximine ligand was formed (with PF_6^- as counter ion). The molecular structure of this complex was unambiguously established by X-ray crystal structure determination.[11]

Figure 1. X-ray crystal structure of the Pd complex derived from **4a**.

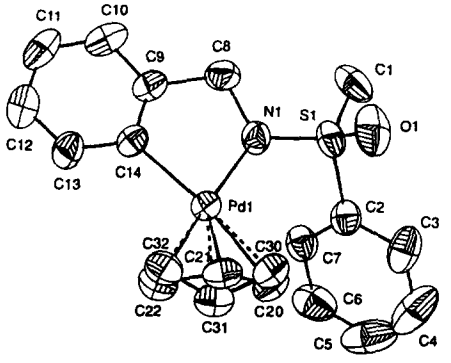


Table 1. Selected bond distances [Å].

Pd - C(20)	2.131(8)
Pd - C(21)	2.073(6)
Pd - C(22)	2.121(8)
Pd - C(30)	2.11(2)
Pd - C(31)	2.10(1)
Pd - C(32)	2.14(2)

The solid state structure of the disordered crystals shows two diastereomeric complexes which differ by the orientation of the allyl fragment (*endo* and *exo*). Both nitrogens are coordinated to the palladium center.[12] The dihedral angle between C8-N1-S1-C1 is -37.56° indicating that the orientation of the sulfoximine moity brings the S-methyl and the N-methylene groups into close proximity.[13] The Pd-N bond lenghths differ only slightly [Pd-N1: 2.096(4)Å; Pd-N2: 2.080(4)Å]. The Pd-to-C distances are listed in Table 1.

Next, we investigated the catalytic properties of the palladium complexes formed *in situ* from sulfoximines **4** and $[Pd(allyl)Cl]_2$. In the presence of 5 mol% of *(S)*-**4** and 2 mol% of the Pd-π-allyl-dimer, the reaction of 1,3-diphenyl-2-propenyl acetate (**1**) and the nucleophile generated from dimethyl malonate (**2**) by treatment with BSA and a small quantity of potassium acetate[14] afforded substitution product *(S)*-**3** in good yield with moderate enantiomeric excess (*ee*) (Table 2).

In all cases, the *(S)*-configurated product was obtained in excess. The enantioselectivity in the formation of **3** depends on various parameters: 1. *The substituent R at sulfur.* Linear and α-branched aliphatic R-groups (Table 2, entries 1-4) gave only low *ee* values (20-45%). The use of phenylethyl and substituted derivatives

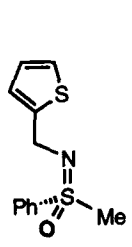
Table 2. Enantiomeric excesses of **3** resulting from asymmetric allylic alkylations of **1** using various sulfoximine/Pd(II)-complexes.

Entry	Sulfoximine	Temp. [°C]	Solvent	% Yield [a]	% *Ee* [b]	Config[c]
1	(*S*)-**4a**	r. t.	CH_2Cl_2	89	39	(*S*)
2	(*S*)-**4b**	r. t.	CH_2Cl_2	90	45	(*S*)
3	(*S*)-**4c**	r. t.	CH_2Cl_2	65	39	(*S*)
4	(*S*)-**4d**	r. t.	CH_2Cl_2	24	20	(*S*)
5	(*S*)-**4e**	r. t.	CH_2Cl_2	80	52	(*S*)
6	(*S*)-**4f**	r. t.	CH_2Cl_2	73	51	(*S*)
7	(*S*)-**4f**	r. t.	toluene	82	54	(*S*)
8	(*S*)-**4f**	-20	toluene	22	63	(*S*)
9	(*S*)-**4g**	r. t.	toluene	50	65	(*S*)
10	(*S*)-**4g**	-5	toluene	77	73	(*S*)
11	(*S*)-**4h**	r. t.	CH_2Cl_2	62	56	(*S*)

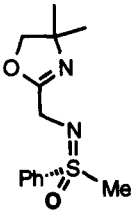
[a] Isolated by column chromatography. [b] *Ee* determ. by HPLC analysis using a chiral column (Chiralcel OD-H). [c] Abs. configuration determ. by comparison of optical rotations with literature value.

of this kind lead to better enantioselectivies (entries 5-11). The highest *ee* value was obtained with sulfoximine **4g** bearing a phenolic hydroxyl group.[15] Compared to that result the tertiary alcohol **4h** showed reduced enantioselectivity. 2. *The reaction temperature.* Most reactions were performed at room temperature. A decrease in temperature to -20°C led to an improved enantioselectivity, however, the product yield was lower due to reduced conversion of the starting materials. The best result (entry 10) was achieved in a reaction run at -5°C using **4g** as ligand. 3. *The solvent.* Reactions in toluene gave better results than those performed in dichloromethane or acetonitrile (For **4f**: 54%, 51%, 49% *ee*, respectively). 4. *The ligand-to-palladium ratio.* This effect is minor. Increasing the ratio of sulfoximine **4h** and Pd from 1:1 to 10:1 gave almost identical results (82% yield / 54% *ee* versus 88% yield / 56% *ee*).

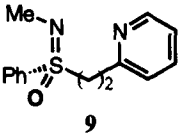
We also tested other sulfur-containing compounds such as sulfoximines **7**-**11** and sulfoxide **12** in this catalysis.[16,17] The *in situ* generated complexes were either inactive or gave **3** with very low *ee*. Yields and *ee* values are given below.



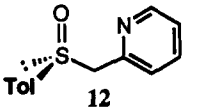
7
(no reaction)



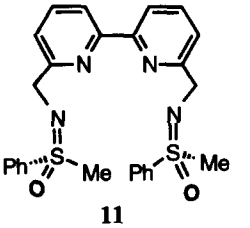
8
99% (35% *ee*)



9
11% (13% *ee*)



12
(no reaction)



11
56% (13% *ee*)

In conclusion, we have demonstrated that sulfoximines of type **4** can be used as chiral ligands in Pd-catalyzed allylic substitution reactions giving the product with moderate to good enantiomeric excess.

Acknowledgement: We are grateful to the DFG (SFB 260, Graduiertenkolleg) for support of our work. We thank Dr. P. Müller for samples of **7**, **8** and **11**.

References and Notes:

1. Reviews: (a) Review: Frost, C.G.; Howarth, J.; Williams, J.M.J. *Tetrahedron: Asymmetry* **1992**, *3*, 1089. (b) Reiser, O. *Angew. Chem.* **1993**, *105*, 576; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 547. (c) Heumann, A.; Réglier, M. *Tetrahedron* **1995**, *51*, 975. (d) See also in: Tsuji, J. *Palladium Reagents and Catalysis*, Wiley, Chichester **1995**.
2. For example: (a) Trost, B.M.; Organ, M.G.; O'Doherty, G.A. *J. Am. Chem. Soc.* **1995**, *117*, 9662. (b) Bolm, C.; Kaufmann, D.; Gessler, S.; Harms, K. *J. Organomet. Chem.* **1995**, *502*, 47. (c) Phosphites and phosphonites: Seebach, D.; Devaquet, E.; Ernst, A.; Hayakawa, M.; Kühnle, F.N.M.; Schweizer, W.B.; Weber, B. *Helv. Chim. Acta* **1995**, *78*, 1636 and references therein.
3. (a) Rieck, H.; Helmchen, G. *Angew. Chem.* **1995**, *107*, 2881; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2881. (b) Sprinz, J.; Kiefer, M.; Helmchen, G.; Reggelin, M.; Huttner, G.; Walter, O.; Zsolnai, L. *Tetrahedron Lett.* **1994**, *35*, 1523. (c) Dawson, G.J.; Frost, C.G.; Williams, J.M.J.; Coote, S.J. *Ibid.* **1993**, *34*, 3149. (d) von Matt, P.; Lloyd-Jones, G.C.; Minidis, A.B.E.; Pfaltz, A.; Macko, L.; Neuburger, M.; Zehnder, M.; Rüegger, H.; Pregosin, P.S. *Helv. Chim. Acta* **1995**, *78*, 265 and references therein.
4. Reviews: (a) Togni, A.; Vennanzi, L.M. *Angew. Chem.* **1994**, *106*, 517; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 497. (b) Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339.
5. (a) Togni, A. *Tetrahedron: Asymmetry* **1991**, *2*, 683. (b) Togni, A.; Rihs, G.; Pregosin, P.S.; Ammann, L. *Helv. Chim. Acta* **1990**, *73*, 723. (c) Bovens, M.; Togni, A.; Venanzi, L.M. *J. Organomet. Chem.* **1993**, 451, C28. (d) Müller, D.; Umbricht, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta* **1991**, *74*, 232. (e) Leutenegger, U.; Umbricht, G.; Fahrni, C.; von Matt, P.; Pfaltz, A. *Tetrahedron* **1992**, *48*, 2143. (f) Andersson, P.G.; Harden, A.; Tanner, D.; Norrby, P.-O. *Chem. Eur. J.* **1995**, *1*, 12. (g) Gamez, P.; Dunjic, B.; Fache, F.; Lemaire, M. *Tetrahedron: Asymmetry* **1995**, *6*, 1109. (h) Kang, J.; Cho, W.O.; Cho, H.G. *Ibid.* **1994**, *5*, 1347. (i) Kubota, H.; Nakajima, M.; Koga, K. *Tetrahedron Lett*, **1993**, *34*, 8135. (j) Tanner, D.; Andersson, P.G.; Harden, A.; Somfai, P. *Ibid.* **1994**, *35*, 4631.
6. (a) Zehnder, M.; Bolm, C.; Schaffner, S.; Kaufmann, D.; Müller, J. *Liebigs Ann.* **1995**, 125. (b) Bolm, C.; Müller, J.; Zehnder, M.; Neuburger, M.A. *Chem. Eur. J.* **1995**, *1*, 312. (c) Schaffner, S. Dissertation, University of Basel **1993**.
7. Kaufmann, D. Dissertation, University of Marburg, **1996**.
8. Reviews: (a) Johnson, C. R. *Aldrichim. Acta* **1985**, *18*, 3. (b) Johnson, C. R. *Acc. Chem. Res.* **1973**, *6*, 341. (c) Barbachyn, M. R.; Johnson, C. R. In *Asymmetric Synthesis*; *Vol. 4*, Morrison, J. D.; Scott, J., Eds.; Academic Press: New York, **1984**; pp 227. (d) Johnson, C. R. In *Comprehensive Organic Chemistry*; *Vol. 3*, Barton, D.; Ollis, W. D., Eds.; Pergamon Press: Oxford, **1979**; pp 223. (e) Oae, S.; Furukawa, N. *Sulfilimines and Related Derivatives*, ACS Monograph 179; American Chemical Society: Washington, **1983**; pp 297.
9. Hwang, K.-J.; Logusch, E.W.; Brannigan, L.H.; Thompson, M.R. *J. Org. Chem.* **1987**, *52*, 3435.
10. Johnson, C.R.; Lavergne, O., M. *J. Org. Chem.* **1993**, *58*, 1922.
11. Details of the crystal structure determination may be obtained from the Director of the Cambridge Crystallographic Data Center, University of Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW (UK) on quoting the full journal citation.
12. Selected examples of other X-ray crystal structures of Pd-π-allyl complexes with N,N-ligands: (a) Deaming, A.J.; Rothwell, I.P.; Hursthouse, M.B.; Backer-Dirks, J.D.J. *J. Chem. Soc. Chem. Commun.* **1979**, 670. (b) Deaming, A.J.; Rothwell, I.P.; Hursthouse, M.B.; Malik, K.M.A. *J. Chem. Soc. Dalton Trans.* **1979**, 1899. (c) Murrall, N.W.; Welch, A.J. *J. Organomet. Chem.* **1986**, *301*, 109. (d) Ammann, C.J.; Pregosin, P.S.; Ruegger, H.; Albinati, A.; Lianza, F.; Kunz, R.W. *Ibid.* **1992**, *423*, 415. (e) Ref. 5b.
13. The solid state structures of related $ZnCl_2$-complexes have been determined. They show a trans-orientation of the S-CH_3 and N-CH_2 groups. Bolm, C.; Kaufmann, D.; Zehnder, M.; Neuburger, M.A.; Harms, K. unpublished.
14. (a) Trost, B. M.; Brickner, S. J. *J. Am. Chem. Soc.* **1983**, *105*, 568. (b) von Matt, P.; Pfaltz, A. *Angew. Chem.* **1993**, *105*, 614; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 556. (c) For a detailed procedure see: Brown, J. M.; Hulmes, D. I.; Guiry, P. J. *Tetrahedron* **1994**, *50*, 4493.
15. The importance of ligands with hydroxyl groups in Pd-catalyses has been demonstrated by Hayashi and coworkers. Review: Hayashi, T. *Pure Appl. Chem.* **1988**, *60*, 7.
16. Recently, a C_2-symmetric bis(sulfoxide) has successfully been used in Pd-catalysis: Tokunoh, R.; Sodeoka, M.; Aoe, K. i.; Shibasaki, M. *Tetrahedron Lett.* **1995**, *36* 8035.
17. For the use of a thienyl oxazoline ligand: Frost, C.G.; Williams, J.M.J. *Tetrahedron Lett.* **1993**, *34*, 2015.

(*Received in Germany* 15 *February* 1996; *accepted* 19 *April* 1996)