Pd-Catalyzed Enantioselective Hydro(het)arylation of Bicyclo[2.2.1]hept-2-ene: Influence of the Chiral Ligand, the Leaving Group, and the Solvent

Jan C. Namyslo and Dieter E. Kaufmann*

Institut für Organische Chemie, Technische Universität Clausthal,

Leibnizstraße 6, D-38678 Clausthal-Zellerfeld, Germany

Abstract:

The use of optically active biaryl bisphosphanes **10 - 12**, a diphenylphosphanylphenyloxazoline **8**, and a (ß-*N*-sulfonylaminomethyl)bisdiphenylphosphane **7** as ligands in the Pd-catalyzed Heck-type hydro(het)-arylation [1] of norbornene (**1**) with phenyl **2 [2]** and various hetaryl derivatives **3 - 5** exclusively leads to the formation of *exo*-2-(het)arylnorbornanes **6** with asymmetric inductions up to 86.4% ee. In addition to an investigation into the effects of different chiral ligands, a systematic study has been made on the influence of various (het)aryl compounds, leaving groups, and solvents on the chemical and optical yields of this reductive arylation.

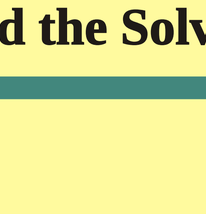
Table 1. Enantioselective Hydro(het)arylation of norbornene with up to 86% ee.

Entry	*Product*	*Aryl compound*	*Chiral ligand*	*Conds.*	*Time [h]*	*conv. [%]*	*yield[c] [%]*	*% ee[d]*
1	**6a**		**7**	a	2	100	37	80.9-82.4
2	**6a**		**7**	a (DMF)	10	100	31	79.3
3	**6a**		**7**	a (PC)	12	100	27	78.7
4	**6a**		**7**	a (THF)	16	100	44	79.5
5	**6a**		**7**	b	>24	20	13	77.7
6	**6a**	phenyl triflate (**2a**)	**8**	a	14	100	12	71.2
7	**6a**		**9**	a	14	100	58	23.7-24.8
8	**6a**		**10**	a	36	80	18	26.2-28.7
9	**6a**		**11**	a	12	100	17	34.5
10	**6a**		**12**	a	12	100	9	7.6-11.4
11	**6a**	phenyl nonaflate (**2b**)	**7**	a	4	100	47	80.2-86.4
12	**6a**		**7**	a (THF)	12	100	41	78.6
13	**6a**		**7**	a	12	100	55	42.6
14	**6a**	iodobenzene (**2c**)	**8**	a	10	100	16	46.9-49.5
15	**6a**		**12**	a	18	100	23	14.8
16	**6a**		**12**	a (DMF)	12	100	51	6.4-8.2
17	**6a**	$PhI(OAc)_2$ (**2e**)	**7**	a (HCOOK)	12	100	82	7.7
18	**6b**	3-pyridyl nonaflate (**3b**)	**7**	a	16	100	11	55.5
19	**6b**	3-pyridyl triflate (**3a**)	**7**	a	18	100	17	54.3-56.4
20	**6a**	bromobenzene (**2d**)	**7**	a	12	100	37	48.4-50.6
21	**6b**	3-bromopyridine (**3c**)	**7**	a	12	100	23	26.4
22	**6c**	3-bromothiophene (**4**)	**7**	a	11	100	40	61.6
23	**6d**	3-bromofuran (**5**)	**7**	a	12	100	39	46.4

[a] Solvent: dimethyl sulfoxide (DMSO), hydride source: formic acid; possible variations are noted: dimethylformamide (DMF), propylene carbonate (PC), tetrahydrofuran (THF). [b] Solvent: DMSO, hydride source: polymethylenehydrogensilane (PMHS). [c] Chemical yields refer to isolated products. [d] Optical yields determined by chiral GC.

(S)-Ms-Valphos [3]
(7)

(S)-2-(2-Diphenyl-phosphinophenyl)-4-isopropyl-oxazoline [4,5]
(8)



(S,S)-Chiraphos
(9)

(S)-BIBFUP
(10)

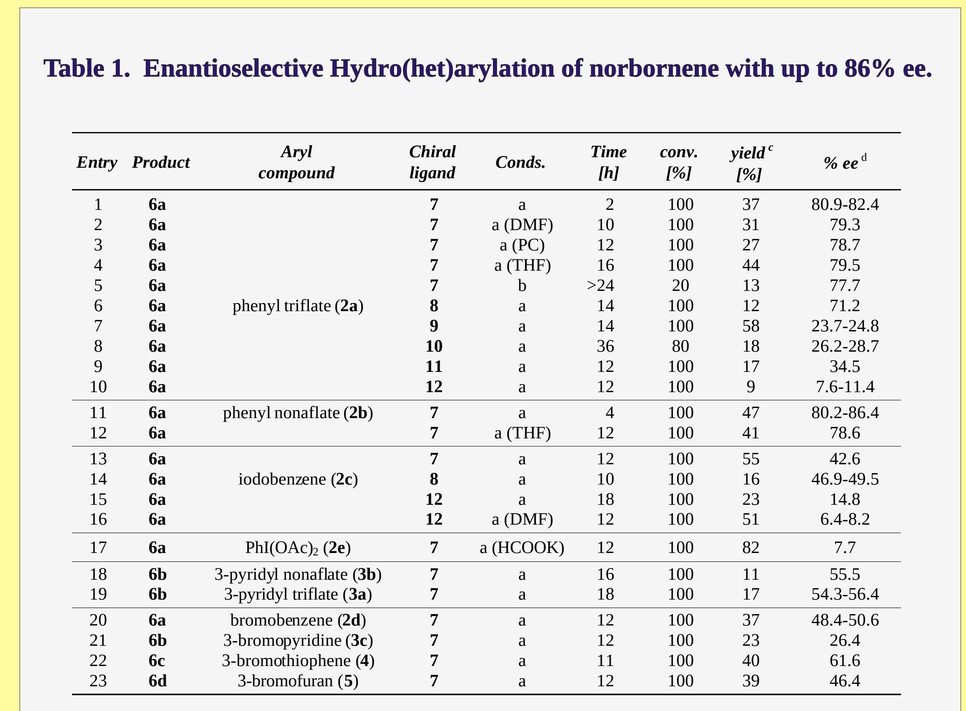
(R)-MeO-BIPHEP
(11)

(R)-BINAP
(12)

CHIRAL LIGANDS

activated and non-activated heteroaromatics

halides, sulfonates, and a iodonium diacetate



e.e. values were determined by chiral GC (25 m capillary column coated with heptakis-(6-*O*-methyl-2,3-di-*O*-pentyl)-γ-cyclodextrin) or oktakis-(6-*O*-methyl-2,3-di-*O*-pentyl)-γ-cyclodextrin)

Systematic studies

Variation of the Aryl Compound

To check the scope of this hydroarylation reaction, for the first time it was extended to a number of hetero-aromatic compounds, e.g. the 3-pyridyl derivatives **3a-c** and the bromides of the activated heteroaromatics thio-phene **4** and furan **5**. The new hetarylnorbornanes **6c, d** were obtained from the commercially available 3-bromo-aryl compounds **4, 5** in acceptable chemical (39 and 40%) and optical yields (46 - 62% ee).

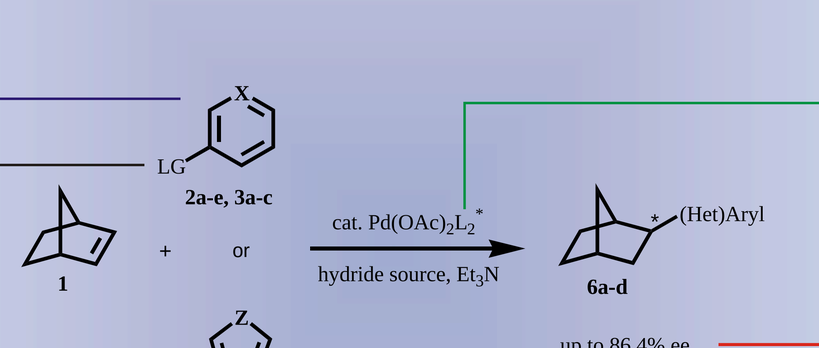
Effects of the Leaving Group and the Solvent

Besides aryl bromides and iodides we used sulfonates and furthermore tested two alternative leaving groups which are hitherto unknown in the field of hydro-arylations, i. e. both aryldiazonium salts and aryl-iodonium compounds. With phenyldiazonium tetrafluoro-borate, apart from biphenyl only trace amounts of the desired product were obtained, but using phenyliodonium diacetate **(2e)**, a maximum of product yield (82%) was found. Unfortunately, in this case the usually efficient ligand *(S)*-Ms-Valphos gave only poor optical yields (entry 17). Using phenyl sulfonates instead of iodo-benzene, the enantiomeric yield was improved from 43% to more than 80% ee.

An Undesirable Side-Reaction

Typically the product yield was 30-60%, although there was complete conversion of the starting material. It is worthy of note that there is a competing pathway under comparable reaction conditions, i.e. the reductive dehalogenation or the reduction of the sulfonates respectively.

The reduction of the leaving group



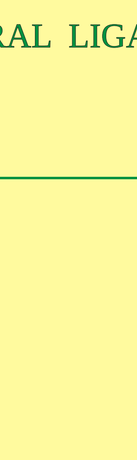


table 1, entry 11

References

[1] J. C. Namyslo, D. E. Kaufmann, *Chem. Ber.* **1997**, *130*, 1327-1331.
[2] H. Brunner, K. Kramler, *Synthesis* **1991**, 1121-1124.
[3] S. Sakuraba, T. Okada, T. Morimoto, K. Achiwa, *Chem. Pharm. Bull.* **1995**, *43*, 927-933.
[4] O. Loiseleur, P. Meier, A. Pfaltz, *Angew. Chem.* **1996**, *108*, 218-220; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 200-202.
[5] J. Sprinz, G. Helmchen, *Tetrahedron Letters* **1993**, *34*, 1769-1772.