Pergamon

Tetrahedron Letters 40 (1999) 7683–7686

TETRAHEDRON
LETTERS

Palladium-catalyzed Heck reaction in perfluorinated solvents

Johanne Moineau,[a] Gianluca Pozzi,[a,b] Silvio Quici [b] and Denis Sinou [a,*]

[a]*Laboratoire de Synthèse Asymétrique, associé au CNRS, CPE Lyon, Université Claude Bernard Lyon 1, 43, boulevard du 11 novembre 1918, 69622 Villeurbanne Cédex, France*

[b]*Centro CNR Sintesi e Stereochimica di Speciali Sistemi Organici, via Golgi 19, 20133 Milano, Italy*

Received 1 July 1999; accepted 20 August 1999

Abstract

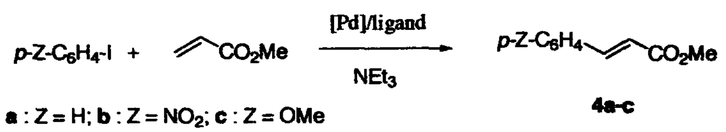
Palladium-catalyzed coupling reaction of aryl iodides with methyl acrylate, commonly designated as the Heck reaction, can be performed in perfluorinated solvents, using perfluorocarbon-soluble triarylphosphines as ligands. The easy separation and recycling of the catalyst is also possible.

Keywords: Heck reactions; palladium; perfluorinated solvents; perfluorinated ligands; recycling.

There is growing interest in the development of new liquid–liquid biphasic catalytic systems.[1] One of the most recent approaches in this field is based on the use of 'fluorous biphase systems' (FBS).[2] In this concept, the organometallic catalyst is solubilized in the fluorous phase via the use of perfluorinated ligands and is segregated from reagents and products, either during the whole process or during the work-up only. This approach has been successfully applied to the hydroformylation of alkenes,[2a,3] the hydroboration of alkenes,[4] the oligomerization of ethylene,[5] the palladium cross-coupling of organozinc bromides with aryl iodides,[6] the epoxidation of alkenes,[7,8] the oxidation of aldehydes,[7] thioethers[7] and alkanes,[9,10] the Wacker oxidation of alkenes,[11] and the palladium allylic alkylation.[12]

The Heck coupling reaction has emerged as one of the most powerful tools for the creation of carbon–carbon bonds.[13] In this communication, we describe our preliminary results concerning the extension of the FBS concept to the Heck reaction.

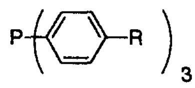
We first examined the palladium-catalyzed Heck coupling of iodobenzene with methyl acrylate in the presence of palladium complexes at 80°C (Eq. 1), using the perfluorinated phosphines **1–3**, whose synthesis was previously described,[6,14] as ligands (Scheme 1). The results are summarized in Table 1.



(1)

* Corresponding author. Tel: 33 (0)4 72446263; fax: 33 (0)4 72448160; e-mail: sinou@univ-lyon1.fr

0040-4039/99/$ - see front matter
PII: S0040-4039(99)01590-7



1 R = $OCH_2C_7F_{15}$ (% F = 58.7) **2** R = C_6F_{13} (% F = 60.9) **3** R = $O(CH_2)_2OCH_2CF_2[OCF(CF_3)CF_2]_p(OCF_2)_qOCF_3$

$\bar{p} = 3.38; \bar{q} = 0.11$

(% F = 56.1)

Scheme 1.

Table 1
Heck cross-coupling reaction under FBS conditions[a]

Entry[b]	Ar-I	Solvent	Ligand	Conversion of Ar-I (%)[c]	Selectivity in **4** (%)[c]
1[d]	C_6H_5-I	CH_3CN	**1**	84	89
2[d]	C_6H_5-I	CH_3CN	**2**	98	84
2a[e]		"	"	72	98
3	C_6H_5-I	CH_3CN/D-100	**1**	100	89
3a		"	"	85	88
3b		"	"	60	96
4	C_6H_5-I	CH_3CN/D-100	**2**	100	88
4a		"	"	92	90
4b		"	"	70	94
5	C_6H_5-I	CH_3CN/D-100	**3**	100	93
5a		"	"	60	85
5b		"	"	40	97
6	*p*-NO_2-C_6H_4-I	CH_3CN/D-100	**2**	100	78
6a		"	"	93	74
7	*p*-MeO-C_6H_4-I	CH_3CN/D-100	**2**	95	84
7a		"	"	75	84

[a] The reaction was conducted at 80 °C, for 4 h, in the presence of 10 μmol ligand, 2.5 μmol (2.3 mg) $Pd_2(dba)_3$, using 1 mmol (0.14 mL) Et_3N, 0.5 mmol Ar-I, 0.62 mmol (0.056 mL) methyl acrylate, in 4 mL solvent (2 ml of CH_3CN and 2 ml of D-100).

[b] Entries a and b correspond to the 1st and 2nd recycling of the catalyst, respectively.

[c] Determined by GC after calibration.

[d] $Pd(OAc)_2$ (1.1 mg, 5 μmol) was used as the catalyst precursor, together with 10 μmol equiv of ligand.

[e] The catalyst was extracted with D-100 (2 mL) and reused for the second run.

The complexes obtained by ligand exchange from $Pd(OAc)_2$ and phosphines **1** or **2** were active in the coupling of iodobenzene and methyl acrylate in CH_3CN at 80°C, giving the expected product **4** with a high selectivity (Table 1, entries 1 and 2). We observed that the extraction of the organic phase with the perfluorinated solvent D-100 (mainly *n*-perfluorooctane) gave a fluorous phase which again catalyzed the coupling reaction after addition of an acetonitrile solution of the substrates (Table 1, entry 2a).

The reaction was then performed directly in a two-phase system.[15] The fluorous-soluble palladium complexes were prepared by stirring $Pd(OAc)_2$ or $Pd_2(dba)_3$ and a solution of perfluorinated phosphine **1**, **2** or **3** in D-100 for 30 min at room temperature (ratio [Pd]/[P]=1/2). An acetonitrile solution of iodobenzene and methyl acrylate was added, and the two-phase system was stirred at 80°C for 4 h. The reaction mixture was cooled to 0°C, and the acetonitrile phase containing the coupling product **4** was easily separated by simple decantation, whereas the palladium catalyst remained in the fluorous phase. The three ligands gave complete conversion of iodobenzene in the first run, with high selectivity in compound **4** (Table 1, entries 3, 4 and 5). Recycling of the catalyst solution was also possible, although a decrease in activity was observed; this could be due to the formation of some metallic palladium or the loss of perfluorinated ligand in the acetonitrile phase. In order to avoid the deactivation of the catalyst, we prepared two catalysts from $Pd_2(dba)_3$ (2.5 μmol) and ligands **1** or **2** in excess (ratio [Pd]/[P]=1/4). However, when the reaction was carried out in a mixture CH_3CN–D-100, no coupling product was observed at all, although performing the reaction in CH_3CN with **1** gave, after 4 h, a moderate conversion (45%) of iodobenzene, with 100% selectivity in **4**. So an excess of perfluorinated phosphine exhibits a detrimental effect on the reaction. The loss of activity during the recycling was more pronounced for the catalyst obtained using **3** as the ligand; this is probably due to the higher solubility of this ligand, compared to **1** and **2**, in acetonitrile, matching the lower fluorine content of the ligands.

The coupling reaction was extended to *p*-nitrophenyl iodide and *p*-methoxyphenyl iodide, using perfluorinated ligand **2**. We observed for the first cycle a very high conversion and selectivity in compound **4** after 4 h, with a slight decrease in activity for the first recyling (Table 1, entries 6 and 7).

In summary we have observed that Heck coupling in perfluorinated solvents can proceed in the presence of palladium complexes of perfluorinated phosphines. The recycling of the catalyst was possible, although some loss of activity was observed. Work is presently in progress in order to circumvent this loss of activity and to extend this concept to other palladium-catalyzed reactions.

Acknowledgements

This work was supported by the CNRS (fellowship to G.P.) and Programme Galilée no. 99023. We wish to thank Ausimont S.p.A. Bollate (Italy) for generously providing some perfluorinated compounds.

References

1. (a) Cornils, B.; Herrmann, W. A. *Aqueous-Phase Organometallic Catalysis. Concepts and Applications*; VCH: Weinheim, 1996. (b) Cornils, B. *Angew. Chem., Int. Ed. Engl.* **1995**, *35*, 1575–1577.
2. (a) Horvàth, I. T.; Ràbai, J. *Science* **1994**, *266*, 72–75. (b) Cornils, B. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2057–2059. (c) Montanari, F.; Pozzi, G.; Quici, S. *Chim. Ind. (Milan)* **1998**, *80*, 469–475. (d) Horvàth, I. T. *Acc. Chem. Res.* **1998**, *31*, 641–650. (e) de Wolf, E.; van Koten, G.; Deelman, B. *J. Chem. Soc. Rev.* **1999**, *28*, 37–41.
3. Horvàth, I. T.; Kiss, G.; Cook, R. A.; Bond, J. E.; Stevens, P. A.; Ràbai, J.; Mozeleski, E. J. *J. Am. Chem. Soc.* **1998**, *120*, 3133–3143.
4. (a) Juliette, J. J. J.; Horvàth, I. T.; Gladysz, J. A. A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1610–1612. (b) Juliette, J. J. J.; Rutherford, D.; Horvàth, I. T.; Gladysz, J. A. *J. Am. Chem. Soc.* **1999**, *121*, 2696–2704.
5. Keim, W.; Vogt, M.; Wasserscheid, P.; Driessen-Hölscher, B. J. *J. Mol. Catal. A: Chem.* **1999**, *139*, 171–175.
6. Betzemeier, B.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2623–2624.
7. Klement, I.; Lütjens, H.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1454–1456.
8. (a) Pozzi, G.; Cinato, F.; Montanari, S. *Chem. Commun.* **1998**, 877–878. (b) Quici, S.; Cavazzini, M.; Ceragioli, S.; Montanari, F.; Pozzi, G. *Tetrahedron Lett.* **1999**, *40*, 3647–3650.

9. Vincent, J. M.; Rabion, A.; Yachandra, V. K.; Fish, R. H. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2346–2349.
10. Pozzi, G.; Cavazzini, M.; Quici, S.; Fontana, S. *Tetrahedron Lett.* **1997**, *38*, 7605–7608.
11. Betzemeier, B.; Lhermitte, F.; Knochel, P. *Tetrahedron Lett.* **1998**, *39*, 6667–6670.
12. Kling, R.; Sinou, D.; Pozzi, G.; Choplin, A.; Quignard, F.; Busch, S.; Kainz, S.; Koch, D.; Leitner, W. *Tetrahedron Lett.* **1998**, *39*, 9439–9442.
13. (a) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985. (b) Heck, R. F. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, pp. 833–863. (c) Tsuji, J. *Palladium Reagents and Catalysts: Innovations in Organic Synthesis*; Wiley: New York, 1995. (d) Herrmann, W. A. In *Applied Homogeneous Catalysis*; Cornils, B.; Herrmann, W. A., Eds.; Wiley: Weinheim, 1996; pp. 712–732. (e) Beller, M.; Riermeier, T. H.; Stark; G. In *Transition Metals for Organic Synthesis*; Beller, M.; Bolm, C., Eds.; Wiley: Weinheim, 1998; pp. 208–240. (f) De Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379–2411. (g) Crisp, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427–436.
14. Sinou, D.; Pozzi, G.; Hope, E. G.; Stuart, A. M. *Tetrahedron Lett.* **1999**, *40*, 849–852.

15. A typical procedure is as follow (Table 1, entry 4): A mixture of $Pd_2(dba)_3$ (2.3 mg, 2.5×10^{-3} mmol) and phosphine **2** (13.2 mg, 10^{-4} mmol) was stirred in D-100 (2 mL) at room temperature for 0.5 h. A solution of iodobenzene (102 mg, 0.5 mmol), methyl acrylate (54 mg, 0.62 mmol), and triethylamine (43 mg, 1 mmol), in acetonitrile (2 mL) was added. After being stirred at 80°C for 4 h, the reaction mixture was cooled to 0°C, and the acetonitrile phase was separated by simple decantation. For the recycling of the catalyst, another acetonitrile solution of reactants was simply added to the fluorous phase containing the catalyst.