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Asymmetric allylic alkylation in supercritical carbon dioxide using P*-chiral diamidophosphite ligands

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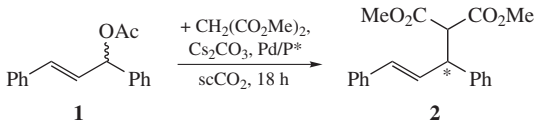
P*-Chiral diamidophosphite ligands in the Pd-catalyzed allylic alkylation of (*E*)-1,3-diphenylallyl acetate in supercritical carbon dioxide provide enantioselectivities up to 90% *ee*. The catalytic performance is affected greatly by temperature, CO_2 pressures and structure of catalysts.

Palladium-catalyzed allylic substitution (the Tsuji–Trost reaction) is a useful synthetic method for the formation of carbon–carbon and carbon–heteroatom bonds.[1] Application of chiral ligands on prochiral substrates provides good and even excellent asymmetric inductions.[1–3] One of the most promising family of such ligands is P*-chiral diamidophosphites prepared from cheap *S*-glutamic acid and proved to be very effective in the Pd-catalyzed allylic substitution reactions (up to 99% *ee*).[4,5] Another significant challenge in metal complex asymmetric catalysis is the use of alternative solvents often called as 'green media' for chemical transformations.[6] Supercritical carbon dioxide ($scCO_2$) presents a viable substitute for organic solvents, as it is non-toxic, inflammable, and relatively cheap, has a low critical temperature (31.1 °C) and an acceptable critical pressure (72.9 atm).[6,7] Recently, we showed that inexpensive phosphite-type ligands are highly effective in the Rh-catalyzed asymmetric hydrogenation of prochiral olefins (up to 99% *ee*) in $scCO_2$.[8]

The number of publications on classical C–C cross-coupling in $scCO_2$ is scarce and is limited to Heck, Suzuki, Sonogashira and Stille reactions (representative examples see in ref. 9). To the best of our knowledge, the Tsuji–Trost reaction in $scCO_2$ was not documented except for our recent single episode of alkylation of (*E*)-1,3-diphenylallyl acetate **1** with dimethyl malonate (up to 81% *ee* with 60% conversion) with the use of sophisticated carborane-tethered P*-chiral diamidophosphite palladium complex.[10] In the present work we report on the broader investigations of the same reaction (Scheme 1) using the series of simpler palladium cationic and neutral complexes with diamidophosphite ligands (Figure 1). Note that traditional versions of the Tsuji–Trost reaction involve use of fully deprotonated carbanion of CH-acid or combination of BSA–AcOK as a deprotonating system which seem inconsistent with electrophilic character of CO_2. Therefore, it seemed reasonable to use metal carbonates which provide sufficient quasi-stationary concentration of the required carbanion, although not fully deprotonating CH-acid (*cf.* ref. 11).



1 **2**

Scheme 1 Pd-catalyzed allylic alkylation of (*E*)-1,3-diphenylallylic acetate.

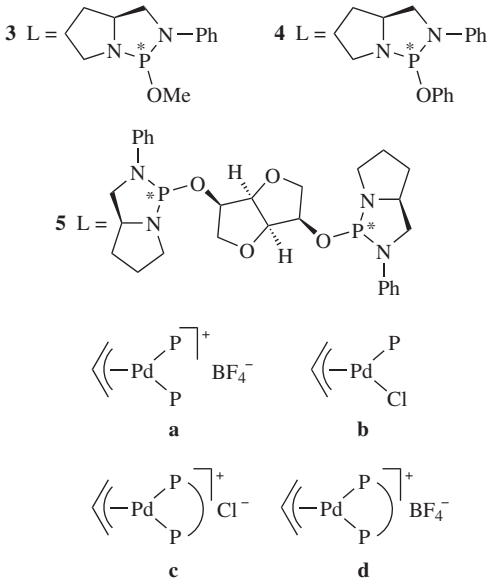


Figure 1 Cationic (**a**, **c**, **d**) and neutral (**b**) Pd-complexes with diamidophosphite ligands.

The use of the cationic palladium tetrafluoroborate complex **3a** (Figure 1) and Cs_2CO_3 at a low temperature (40 °C) and 170 atm CO_2 pressure yielded product **2** with 60% *ee*, though a moderate conversion of **1** was observed (Table 1, entry 1). To evaluate the effect of temperature with the aim of increasing conversion, temperature was raised from 40 to 60 °C. In this case, the same level of enantioselectivity was held but the conversion did increase (entry 2). Changing of CO_2 pressure to lower or higher values (from 170 to 110 atm or from 170 to 240 atm) at 60 °C resulted in a decrease in conversion, but the *ee* values remained the same (entries 2–4). Interestingly, the neutral complex **3b**, which can be prepared by simple mixing of ligand **3** and $[Pd(allyl)Cl]_2$ in $CHCl_3$ and evaporating the solvent, also gives 60% *ee* and an acceptable conversion at 60 °C and 170 atm pressure (entries 5 and 2).

Cationic complex **4a**† afforded product **2** with better enantioselectivity, as compared to **3a**, probably because of the higher steric bulkiness of the ligand **4** (Table 1, entries 2–4 and 6–7). Moreover, complete conversion was observed at 75 and 60 °C using 170 atm CO_2 pressure. The reaction at 240 atm pressure

Table 1 Pd-catalyzed enantioselective allylic alkylation of **1** with dimethyl malonate in $scCO_2$.

Entry	Catalyst	Pressure/ atm	*T*/°C	HPLC yield (%)	*ee* (%)
1	**3a**	170	40	60	60 (*S*)
2	**3a**	170	60	85	60 (*S*)
3	**3a**	240	60	25	58 (*S*)
4	**3a**	110	60	51	60 (*S*)
5	**3b**	170	60	70	60 (*S*)
6	**4a**	170	75	100	76 (*S*)
7	**4a**	170	60	100	76 (*S*)
8	**4a**	240	75	80	67 (*S*)
9	**5c**	170	60	100	90 (*S*)
10	**5d**	170	60	75	61 (*S*)
11	**5d**	170	75	84	61 (*S*)

using the same catalyst (**4a**) leads to a decrease in both the conversion and enantioselectivity (entries 6, 8).

Alkylation of **1** using complexes **5c** and **5d** with a bidentate ligand showed an unexpected result. In this case, the anion had a marked influence on enantioselectivity and reaction rate. Cationic complex **5c**† with chloride anion gave complete conversion of **1** in 18 h and high enantioselectivity (90% *ee*) was observed (Table 1, entry 9). The tetrafluoroborate cationic complex **5d** exhibited 61% *ee* and from moderate to good conversion (Table 1, entries 10, 11), with the conversion being higher at the temperature growth. Note that in the last cases the enantioselectivity remains independent of the temperature used, but raising temperature leads to improvement of conversion.

The results obtained are somewhat advantageous to the data of using the same catalysts under standard conditions[5(*b*),12] (THF or CH_2Cl_2, BSA–AcOK), when along with 90–98% *ee* values the conversion remained moderate on 48 h of the reaction time.

In conclusion, we have performed the Tsuji–Trost reaction in $scCO_2$ using P*-chiral diamidophosphite Pd complexes as the catalysts and Cs_2CO_3 as the base, providing thus satisfactory conversions and *ee* values of the product **2**. The results obtained with active substrate **1** is a challenge to evaluate scope and limitations of this procedure, which is definitely associated with solubility and solvation of the reaction components with $scCO_2$. Our preliminary experiment to react diethyl malonate with allyl acetate (less active than **1**) in $scCO_2$ under conditions of entry 2 (Table 1) gave 88% GC yield of the target diethyl allylmalonate, while diallylation did not occur. Attempted prenylation with 3-methylbut-1-en-3-yl acetate afforded only 4% of the product. Therefore, further screening of substrates, catalysts and reaction conditions is needed to promote using of $scCO_2$ as a cheap and inflammable medium in valuable Tsuji–Trost reaction.

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† Complexes **3a**, **3b** and **5d** were prepared according to the published procedures.[5(*a*),(*c*),12]

For **4a**: a solution of the ligand **4** (59 mg, 0.2 mmol) in CH_2Cl_2 (10 ml) was added dropwise over 15 min to a vigorously stirred solution of 18 mg (0.05 mmol) $[Pd(allyl)Cl]_2$ in CH_2Cl_2 (5 ml). The mixture was stirred for 10 min, followed by dropwise addition of $AgBF_4$ (20 mg, 0.1 mmol) in THF (5 ml) over 5 min. The mixture was stirred for additional 30 min, and the precipitate of AgCl was filtered off. The filtrate was concentrated at reduced pressure and dried *in vacuo* (1 Torr) for 30 min. Yield, 71 mg (87%). $^{31}P\{^1H\}$ NMR ($CDCl_3$), δ: 115.57. Found (%): C, 53.60; H, 5.30; N, 6.65. Calc. for $C_{37}H_{43}BF_4N_4O_2P_2Pd$ (%): C, 53.48; H, 5.22; N, 6.74. MS (ESI), *m*/*z* (%): 744 $[M - BF_4]^+$ (100), 703 $[M - BF_4 - allyl]^+$ (10).

For **5c**: a solution of the ligand **5** (55 mg, 0.1 mmol) in CH_2Cl_2 (10 ml) was added dropwise over 10 min to a vigorously stirred solution of $[Pd(allyl)Cl]_2$ (18 mg, 0.05 mmol) in CH_2Cl_2 (5 ml). The mixture was stirred for additional 10 min after which the solvent was evaporated under reduced pressure (40 Torr). The residue was washed with diethyl ether (5 ml) and dried in a vacuum (1 Torr, 30 min). Yield, 67 mg (92%). $^{31}P\{^1H\}$ NMR ($CDCl_3$), δ: 115.56. Found (%): C, 50.56; H, 5.65; N, 7.51. Calc. for $C_{31}H_{41}ClN_4O_4P_2Pd$ (%): C, 50.49; H, 5.60; N, 7.60. MS (ESI), *m*/*z* (%): 702 $[M - Cl]^+$ (20), 661 $[M - Cl - allyl]^+$ (100), 554 $[L]^+$ (3).

*Pd-catalyzed allylic alkylation of (*E*)-1,3-diphenylallyl acetate with dimethyl malonate in $scCO_2$.* Pd-catalyst (0.02 mmol), (*E*)-1,3-diphenylallyl acetate (0.1 ml, 0.5 mmol), dimethyl malonate (0.1 ml, 0.87 mmol) and Cs_2CO_3 (244 mg, 0.75 mmol) were placed open to air into a 10 ml autoclave. The vessel was filled with $scCO_2$ by means of a syringe-press to a total pressure of 60 atm. The mixture was allowed to equilibrate to the reaction temperature (30 min) and then additional CO_2 was added up to the required pressure. After this, the mixture was stirred for 18 h and the vessel was slowly depressurized. The resulting residue was stirred up with CH_2Cl_2 and the mixture was filtered through silica gel. The filtrate was concentrated in a vacuum to give the product **2** as yellow oil. Conversion of substrate **1** and enantiomeric excess (*ee*) of product **2** were determined using HPLC (Daicel Chiralcel OD-H column) as described previously.[13]

References

1 (*a*) B. M. Trost, *Acc. Chem. Res*., 1980, **13**, 385; (*b*) B. M. Trost and D. L. Van Vranken, *Chem. Rev.*, 1996, **96**, 395; (*c*) Z. Lu and S. Ma, *Angew. Chem. Int. Ed*., 2008, **47**, 258.

2 I. Ojima, *Catalytic Asymmetric Synthesis*, 2nd edn., Wiley-VCH, New York, 2000.

3 A. Boerner, *Phosphorus Ligands in Asymmetric Catalysis*, Wiley-VCH, Weinheim, 2008.

4 K. N. Gavrilov, O. G. Bondarev and A. I. Polosukhin, *Usp. Khim.*, 2004, **73**, 726 (*Russ. Chem. Rev.*, 2004, **73**, 671).

5 (*a*) V. N. Tsarev, S. E. Lyubimov, A. A. Shiryaev, S. V. Zheglov, O. G. Bondarev, V. A. Davankov, A. A. Kabro, S. K. Moiseev, V. N. Kalinin and K. N. Gavrilov, *Eur. J. Org. Chem*., 2004, 2214; (*b*) K. N. Gavrilov, V. N. Tsarev, A. A. Shiryaev, O. G. Bondarev, S. E. Lyubimov, E. B. Benetsky, A. A. Korlyukov, M. Yu. Antipin, V. A. Davankov and H.-J. Gais, *Eur. J. Inorg. Chem*., 2004, 629; (*c*) S. E. Lyubimov, V. A. Davankov and K. N. Gavrilov, *Tetrahedron Lett*., 2006, **47**, 2721; (*d*) S. E. Lyubimov, V. A. Davankov, M. G. Maksimova, P. V. Petrovskii and K. N. Gavrilov, *J. Mol. Catal. A: Chem*., 2006, **259**, 183; (*e*) K. N. Gavrilov, S. E. Lyubimov, O. G. Bondarev, M. G. Maksimova, S. V. Zheglov, P. V. Petrovskii, V. A. Davankov and M. T. Reetz, *Adv. Synth. Catal*., 2007, **349**, 609; (*f*) K. N. Gavrilov, S. E. Lyubimov, S. V. Zheglov, E. B. Benetsky, P. V. Petrovskii, E. A. Rastorguev, T. B. Grishina and V. A. Davankov, *Adv. Synth. Catal*., 2007, **349**, 1085.

6 (*a*) D. J. Cole-Hamilton, *Adv. Synth. Catal*., 2006, **348**, 1341; (*b*) E. J. Beckman, *J. Supercrit. Fluids*, 2004, **28**, 121; (*c*) J. Durand, E. Teuma and M. Gomez, *C. R. Chimie*, 2007, **10**, 152.

7 (*a*) T. Ikariya and Y. Kayaki, *Catalysis Surveys from Japan*, 2000, **4**, 39; (*b*) P. G. Jessop, *J. Supercrit. Fluids*, 2006, **38**, 211.

8 (*a*) S. E. Lyubimov, A. A. Tyutyunov, V. N. Kalinin, E. E. Said-Galiev, A. R. Khokhlov, P. V. Petrovskii and V. A. Davankov, *Tetrahedron Lett*., 2007, **48**, 8217; (*b*) S. E. Lyubimov, V. A. Davankov, E. E. Said-Galiev and A. R. Khokhlov, *Catal. Commun*., 2008, **9**, 1851; (*c*) S. E. Lyubimov, I. V. Kuchurov, V. A. Davankov and S. G. Zlotin, *J. Supercrit. Fluids*, 2009, **50**, 118.

9 (*a*) D. K. Morita, D. R. Pesiri, S. A. David, W. H. Glaze and W. Tumas, *Chem. Commun.*, 1998, 1397; (*b*) N. Shezad, R. S. Oakes, A. A. Clifford and C. M. Rayner, *Tetrahedron Lett*., 1999, **40**, 2221; (*c*) T. R. Early, R. S. Gordon, M. A. Carroll, A. B. Holmes, R. E. Shute and I. F. McConvey, *Chem. Commun*., 2001, 1966; (*d*) R. S. Gordon and A. B. Holmes, *Chem. Commun*., 2002, 640; (*e*) I. V. Kuchurov, A. A. Vasil'ev and S. G. Zlotin, *Mendeleev Commun*., 2010, **20**, 140.

10 S. E. Lyubimov, I. V. Kuchurov, A. A. Vasil'ev, A. A. Tyutyunov, V. N. Kalinin, V. A. Davankov and S. G. Zlotin, *J. Organomet. Chem*., 2009, **694**, 3047.

11 (*a*) S. A. Lebedev, L. F. Starosel'skaya and E. S. Petrov, *Zh. Org. Khim.*, 1986, **22**, 1565 [*J. Org. Chem. USSR* (*Engl. Transl.*), 1986, **22**, 1410]; (*b*) A. A. Vasil'ev, S. E. Lyubimov, E. P. Serebryakov, V. A. Davankov and S. G. Zlotin, *Mendeleev Commun*., 2009, **19**, 103; (*c*) A. A. Vasil'ev, S. E. Lyubimov, E. P. Serebryakov, V. A. Davankov, M. I. Struchkova and S. G. Zlotin, *Izv. Akad. Nauk, Ser. Khim.*, 2010, 592 (in Russian).

12 K. N. Gavrilov, S. V. Zheglov, P. A. Vologzhanin, E. A. Rastorguev, A. A. Shiryaev, M. G. Maksimova, S. E. Lyubimov, E. B. Benetsky, A. S. Safronov, P. V. Petrovskii, V. A. Davankov, B. Schaffner and A. Borner, *Izv. Akad. Nauk, Ser. Khim*., 2008, 2266 (*Russ. Chem. Bull., Int. Ed.*, 2008, **57**, 2311).

13 H. Kodama, T. Taiji, T. Ohta and I. Furukawa, *Tetrahedron: Asymmetry*, 2000, **11**, 4009.

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