

An Expedient Variant of Heck Reaction of Alkenyl Nonaflates: Homogeneous Ligand-Free Palladium Catalysis at Room Temperature

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Abstract: A mechanistic study on the ligand-free room-temperature Heck reaction of alkenyl nonafluorobutanesulfonates (nonaflates) is described. Kinetic data obtained from poisoning experiments, centrifugation and variation of catalyst loading consistently provide evidence for a homogeneous palladium catalysis unprecedented in Heck chemistry. The Heck reaction of alkenyl perfluorobutanesulfonates represents a remarkably robust, active and efficient catalytic system generally applicable to the coupling with a broad range of terminal olefins including non-activated ones under ambient conditions. It features insensitivity towards atmospheric oxygen and moisture, furnishing uniformly high yields of the anticipated coupling products without the necessity to purify commercial reagents and solvents.

Keywords: alkenyl nonaflates; catalyst poisoning; Heck reaction; homogeneous catalysis; kinetics; ligand-free catalysis

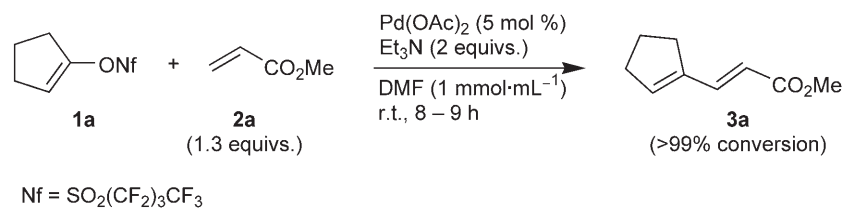
Coupling of olefins with aryl/alkenyl halides, commonly known as the Heck reaction, represents one of the basic tools in contemporary organic synthesis.^[1] The existing vast realm of the Heck chemistry can conventionally be subdivided to ligand-assisted and ligand-free catalysis. Ligands at palladium play a different role depending on the application. While the ligation is crucially important for enantioselective variants of the Heck reaction^[2] or activation of otherwise unreactive aryl chlorides,^[3] it often tends to deteriorate the desired coupling, causes side reactions and

deactivates the catalyst,^[4] in particular, when aryl iodides are used as substrates.^[5] From this standpoint, it is of no surprise that the fastest versions of Heck reaction known so far are described for ligand-free systems containing free halides (Cl[−] or Br[−] added as quaternary ammonium salts) which are believed to stabilize Pd(0)-species.^[1d]

Later on, it was shown that intermediary Pd nanoparticles as colloids are likely to be the true catalytic species in such systems.^[6] Owing to the recent advancements in the mechanistic study and design of robust and efficient low Pd-loading systems,^[7] the ligand-free Heck reaction became an emerging trend with particular promise for industrial applications.^[8] On the other hand, it was demonstrated in a number of well-documented cases that palladacycles^[7a,9] and pincer Pd(II) complexes^[10] are pre-catalysts and not the actual active species catalyzing the Heck reaction of aryl halides as it was believed earlier.^[11] Compelling evidence based on kinetic studies^[10,12] and quantitative poisoning experiments^[10] was obtained that the above complexes decompose under the reaction conditions to generate the actual catalytic species, Pd nanoparticles.

The above breakthroughs in understanding the nature of catalysis in the Heck chemistry of aryl halides^[13] and a lack of mechanistic insight in the underligated Heck reaction of aryl and alkenyl perfluoroalkanesulfonates^[14] prompted us to investigate the nature of Pd-catalysis for the latter substrates.

Herein, we report on the nature of the catalyst and the remarkable efficiency of our ligand- and additive-free system enabling room-temperature Heck coupling of readily available alkenyl nonaflates^[15] with electron-withdrawing, electron-rich as well as inactivated alkenes. Our primary objective within the scope



Scheme 1. A model room-temperature Heck reaction.

of this publication was to establish whether the reaction is effected by heterogeneous or homogeneous catalysis.

As a test case the reaction of cyclopentenyl nonaflate (**1a**) with methyl acrylate (**2a**) was chosen (Scheme 1). The model reaction was carried out under optimized conditions at ambient temperature (20–24 °C) with Et_3N as a base in $\text{DMF}^{[16]}$ resulting in clean and complete conversion of the starting nonaflate **1a** to the 1,3-diene ester **3a** within 8–9 h. The catalytic system employed features excellent reproducibility, robustness and insensitivity towards atmospheric oxygen and moisture. Reduced catalytic loading (0.5 mol%) appreciably slows down the room temperature reaction. Thus, in a typical example, it required 6 days to attain 88% conversion. However, a subsequent gentle heating at 50 °C rendered a complete conversion within 3 h indicating that the observed slow-down effect is not due to the irreversible deactivation of the catalyst. Noteworthy, the reaction mixtures remain essentially homogeneous during the entire course of the reactions regardless of the amount of Pd taken and in spite of the absence of Pd-colloid stabilizers.^[17]

The first indirect evidence for the homogeneous nature of the catalytic system studied herein comes from the comparative analysis of conversion rate as a function of catalyst loading in the model Heck reaction of nonaflate **1a** (Figure 1) vs. that of bromoben-

zene studied earlier.^[7] In the latter case, the reaction stops at an early stage when a high Pd loading is employed because aggregation leading to Pd clusters of low catalytic activity outruns the desired Heck coupling.^[7,18] A significantly different kinetic profile was obtained using our protocol with nonaflate **1a** as a substrate (Figure 1). It manifests a steady increase of the reaction rate with increasing catalyst-to-substrate rate even at high Pd concentrations. This result can be regarded as (negative) evidence for a kinetically stable homogeneous catalytic species lacking clustering.

To gain further insight into the catalyst identity we monitored the model reaction kinetics in the presence of different amounts of thiophene (Figure 2) and PPh_3 (Figure 3).

It has been generally accepted that quantitative kinetic data provide the most compelling evidence for the identity of the true catalyst.^[19] In a number of quantitative studies, well-established catalyst poisons such as PPh_3 , CS_2 or thiophene taken in amounts ≤ 1 equiv. (hereinafter, the amounts of the additives are expressed in equiv. relative to the Pd catalyst) or a large excess of metallic mercury were found to effectively quell the catalytic activity thus proving the heterogeneous nature of the Pd(0) catalysts in the Heck reactions of aryl halides.^[10,20] For this reason, we

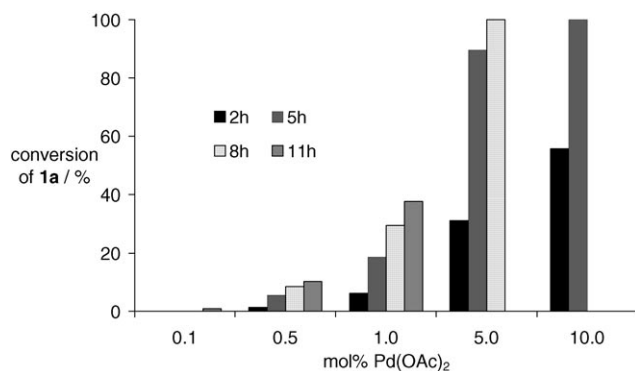


Figure 1. Effect of palladium catalyst loading on the conversion rate of the model reaction (see Scheme 1), at 24 °C.

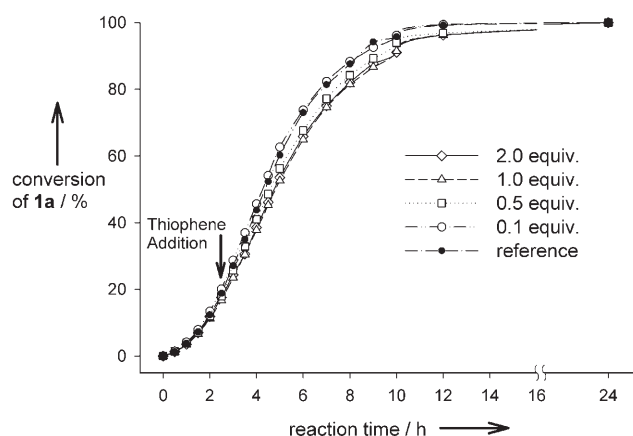


Figure 2. Kinetic profiles of the model reaction (see Scheme 1) in the presence of different amounts of thiophene (from 0.1 to 2 equivs.), at 20 °C.

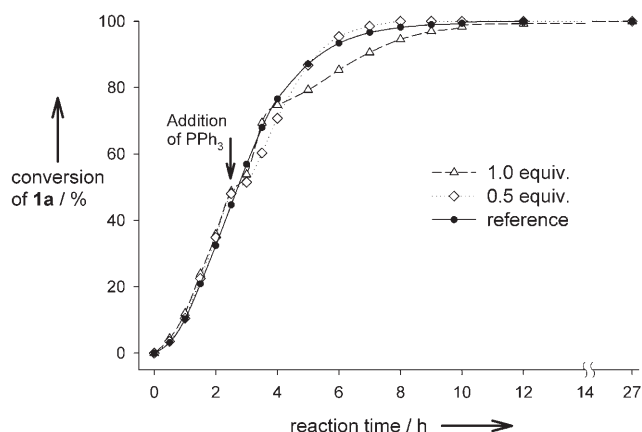


Figure 3. Kinetic profiles of the model reaction (see Scheme 1) in the presence of PPh_3 (0.5 and 1 equiv.), at 24°C .

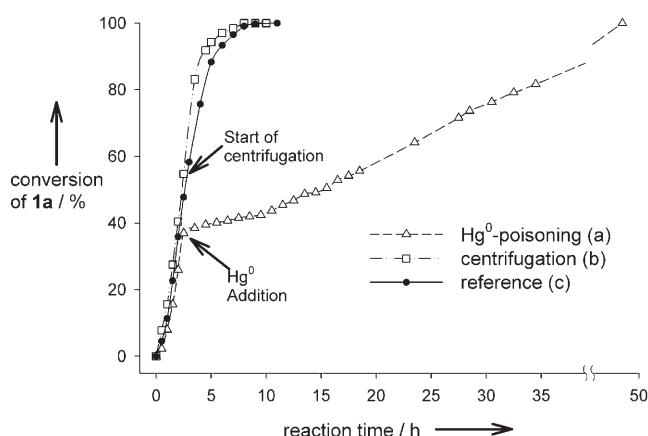


Figure 4. Kinetic profiles of the model reaction (see Scheme 1) subjected to Hg^0 poisoning (a) or centrifugation (b), at 24°C .

decided to apply these poisoning methods to the model reaction of nonaflate **1a** (Scheme 1).

The poisoning experiments (Figure 2 and Figure 3) clearly demonstrate that the heterogeneous catalyst poisons, PPh_3 and thiophene, added in amounts of up to 2.0 equivs. have minimal to no effect on the outcome and the rate of the standard Heck reaction of nonaflate **1a**. These observations dramatically contrast results obtained by Eberhard^[10b] who observed that $\ll 1$ equiv. of PPh_3 or thiophene is sufficient to fully suppress the activity of the heterogeneous Pd catalyst apparently resulting from decomposition of pincer Pd(II) complexes. On the other hand, the lack of poisoning with the above additives can be regarded as an evidence of a kinetically stable form of the homogeneous Pd(0) catalytic species throughout the entire course of the reaction.^[21,22]

Despite certain limitations on the applicability of $\text{Hg}(0)$ poisoning tests,^[23] we decided to investigate its

effect on our reaction system. Whereas the Heck reactions catalyzed by Pd colloids are instantaneously and completely suppressed after addition of mercury,^[10] no such dramatic effect was observed under our conditions. As shown in Figure 4, a treatment with 300 equivs. $\text{Hg}(0)$ ^[24] resulted in an appreciable slow-down effect. However, no irreversible loss of catalytic activity was observed, and the reaction did reach complete conversion.

Finally, centrifugation (14500 rpm, 25 min) of the slightly turbid reaction mixture at 55% completion (after 2.5 h) resulted in the formation of a tiny amount of a very fine dark-brown precipitate. The residue proved to be catalytically inactive after exposure to the freshly added reactants for 24 h at room temperature. The reaction rate in the clear homogeneous reaction mixture matched well that of the reference reaction indicating that the true catalytic species fully remains in solution (Figure 4, cf. curves b and c).

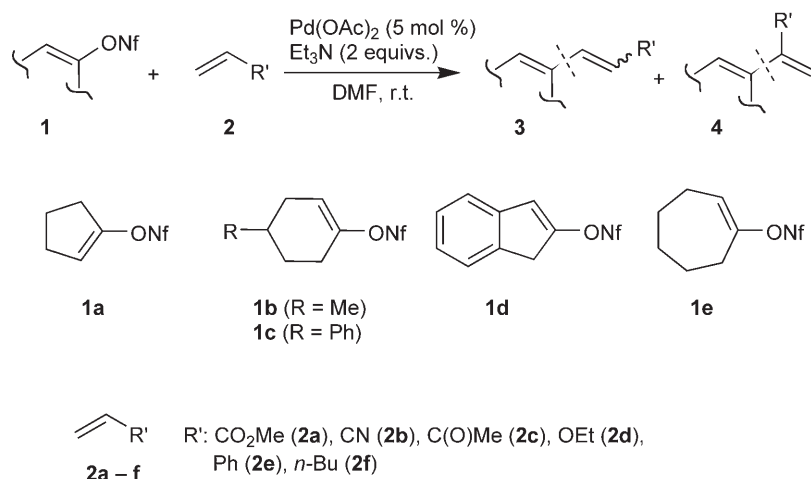
To test the generality of this ligand-free cross-coupling protocol, a range of substrates was submitted to the optimized reaction conditions. Gratifyingly, a number of alkenyl nonaflates **1** derived from cyclic ketones were found to react with terminal alkenes **2** (Scheme 2) to give the expected cross-coupling products in high yields (Table 1).

While selectivities follow typically observed trends,^[1h] we were surprised to learn that the catalytic system is active enough to effect the room-temperature Heck coupling even with poorly activated (styrene, **2e**) or non-activated (1-hexene, **2f**) olefins.

Attempts to extend our ligand-free system to aryl nonaflates met with no success so far. Thus exposure of phenyl nonaflate with methyl acrylate **2a** for 4 d at room temperature or heating for 2 h at 50°C did not furnish a detectable amount of product with the coupling reactants remaining intact.

At this stage, we would refrain from speculating on the structure of the catalyst in the Heck reaction of alkenyl nonaflates. As a working hypothesis, we suggest that Pd(0) exists in kinetically stable form, PdL_n in dynamic equilibrium with the reaction components ($\text{L} = 1,3\text{-diene } \mathbf{3a}$ or olefin **2a** or DMF or Et_3N) playing a role of weak ligands readily coordinating and dissociating and thus enabling an easy access of substrate to the coordinating sphere of Pd(0)-centre. With all likelihood, low-nucleophilic nonaflate anion accumulated during the reaction course does not coordinate to the catalytic Pd-species and thus does not affect the catalyst activity.^[30]

In conclusion, unlike the relevant ligand-free systems designed for Heck couplings of aryl halides,^[6,7] the room-temperature Heck reactions of alkenyl nonaflates described herein do not indicate signs of heterogeneous (colloidal Pd) catalysis. The catalytic system features remarkable activity, endurance and insensitivity to the established heterogeneous catalyst poi-



Scheme 2. Ligand-free room-temperature Heck reactions of alkenyl nonaflates **1** with terminal alkenes **2**.

Table 1. Reaction conditions and yields of the products **3** and **4** according to Scheme 2.

Entry	Reaction 1 + 2	Time	Products 3/4 (ratio, %:%)	Yield [%] ^[a]
1	1a + 2a	11 h	(<i>E</i>)- 3a ^[14f]	94
2	1a + 2b	16 h	3b , <i>E/Z</i> = 79:21	92
3	1a + 2c	13 h	(<i>E</i>)- 3c ^[25]	90
4	1a + 2d	18 h	(<i>E</i>)- 3d/4d (6:94)	86
5	1a + 2e	13 h	(<i>E</i>)- 3e ^[14f] / 4e (93:7)	86
6	1a + 2f	15 h	(<i>E</i>)- 3f ^[26] / 4f (56:31) ^[b]	84
7	1b + 2a	24 h	(<i>E</i>)- 3g	98
8	1b + 2e	24 h	(<i>E</i>)- 3h/4h (84:16)	98
9	1c + 2c	14 h	(<i>E</i>)- 3i ^[27]	98
10	1d + 2a	13 h	(<i>E</i>)- 3j	93
11	1d + 2e	15 h	(<i>E</i>)- 3k ^[28]	94
12	1e + 2a	13 h	(<i>E</i>)- 3l ^[14f]	92
13	1e + 2b	14 h	3m ^[14e] <i>E/Z</i> = (67:33)	87
14	1e + 2c	13 h	(<i>E</i>)- 3n ^[29]	94
15	1e + 2d	37 h	4o	91

^[a] Isolated yields.

^[b] Contains 13 mol % of the 1,4-diene product, 1-hex-2-enylcyclopentene.

sons. These results suggest that the coupling reactions are catalyzed by homogeneous Pd(0)-complex(es) of yet unidentified structure. The study on the structure of the catalyst and the Pd-intermediates is currently in progress.

From the synthetic viewpoint, the protocol described herein is simple, robust and generally applicable to the coupling of stable and easy-to-handle alkenyl nonaflates^[15] with electron-withdrawing, electron-rich as well as non-activated alkenes.

Experimental Section

General Procedure for the Syntheses of Dienes **3** from Alkenyl Nonaflates **1**

DMF (1 mL), Et₃N (202 mg, 2.00 mmol), alkenyl nonaflate **1** (1.00 mmol), alkene **2** (1.30 mmol), and Pd(OAc)₂ (11.2 mg, 0.05 mmol) were subsequently added to a screw-cap vial equipped with magnetic stirring bar. The reaction mixture was stirred for the designated amount of time (see Table 1) at ambient temperature. It was then subjected to aqueous work-up (pentane/water). The combined organic layers were washed with brine and dried with Na₂SO₄. The solvent was removed under reduced pressure and the residue purified by either column chromatography (silica gel) or Kugelrohr distillation, to give pure dienes **3**.

Acknowledgements

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References

- [1] a) G. D. Daves, A. Hallberg, *Chem. Rev.* **1989**, 89, 1433–1445; b) R. F. Heck, in: *Comprehensive Organic Synthesis*, Vol. 4, (Eds.: B. M. Trost, I. Fleming, M. F. Semmelhack), Pergamon Press, Oxford, **1991**, pp. 833–864; c) A. De Meijere, F. E. Meyer, *Angew. Chem.* **1994**, 106, 2473–2506; *Angew. Chem. Int. Ed. Engl.* **1994**, 33, 2379–2411; d) T. Jeffery, in: *Advances in Metal-Organic Chemistry*, Vol. 5, (Ed.: L. S. Liebeskind), JAI Press Inc, Greenwich, CT, **1996**; pp 153–260; e) S. Bräse, A. de Meijere, in: *Metal-Catalyzed Cross-Coupling Reactions*, (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, New York, **1998**, pp 99–166;

- f) J. T. Link, L. E. Overman, in: *Metal-Catalyzed Cross-Coupling Reactions*, (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, New York, **1998**, pp 231–269; g) M. T. Reetz, in: *Transition Metal Catalyzed Reactions*, (Eds.: S. G. Davies, S.-I. Murahashi), Blackwell Sci., Oxford, **1999**, pp 207–224; h) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009–3066; i) M. Beller, A. Zapf, T. H. Riermeier, in: *Transition Metals for Organic Synthesis*, Vol. 1, 2nd edn, (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **2004**, pp 271–305; j) N. Miyaoura, *Adv. Synth. Catal.* **2004**, *346*, 1522–1523.
- [2] M. Shibasaki, E. M. Vogl, T. Ohshima, *Adv. Synth. Catal.* **2004**, *346*, 1533–1552.
- [3] a) A. F. Littke, G. C. Fu, *J. Am. Chem. Soc.* **2001**, *123*, 6989–7000; b) A. F. Littke, G. C. Fu, *Angew. Chem.* **2002**, *114*, 4350–4386; *Angew. Chem. Int. Ed.* **2002**, *41*, 4176–4211.
- [4] a) W. A. Herrmann, C. Broßmer, K. Öfele, M. Beller, H. Fischer, *J. Organomet. Chem.* **1995**, *491*, C1–C4; b) K. Nishi, Y. Narukawa, H. Onoue, *Tetrahedron Lett.* **1996**, *37*, 2987–2988; c) A. Bråthe, L.-L. Gundersen, F. Rise, A. B. Eriksen, A. V. Vollsnes, L. Wang, *Tetrahedron* **1999**, *55*, 211–228.
- [5] L. S. Hegedus, *Palladium in Organic Synthesis*, in: *Organometallics in Synthesis – a Manual*, (Ed.: M. Schlosser), John Wiley & Sons Ltd., Chichester, **1994**, p 421.
- [6] a) M. T. Reetz, E. Westermann, *Angew. Chem.* **2000**, *112*, 170–173; *Angew. Chem. Int. Ed.* **2000**, *39*, 165–168; for the first report on the use of preformed colloids in Heck couplings, see: b) M. Beller, H. Fischer, K. Kühlein, C. P. Reisinger, W. A. Herrmann, *J. Organomet. Chem.* **1996**, *520*, 257–259.
- [7] a) M. T. Reetz, J. G. de Vries, *Chem. Commun.* **2004**, 1559–1563, and references cited therein; b) A. H. M. de Vries, J. M. C. A. Mulders, J. H. M. Mommers, H. J. W. Henderickx, J. G. de Vries, *Org. Lett.* **2003**, *5*, 3285–3288.
- [8] a) M. Beller, A. Zapf, in: *Handbook of Organopalladium Chemistry for Organic Synthesis*, Vol. 1, (Eds.: E.-i. Negishi, A. de Meijere), John Wiley & Sons, Chichester, **2002**, pp 1209–1222; b) J. G. de Vries, *Can. J. Chem.* **2001**, *79*, 1086–1092.
- [9] a) C. S. Consorti, F. R. Flores, J. Dupont, *J. Am. Chem. Soc.* **2005**, *127*, 12054–12065; b) C. S. Consorti, M. L. Zanini, S. Leal, G. Ebeling, J. Dupont, *Org. Lett.* **2003**, *5*, 983–986; c) C. Rocaboy, J. A. Gladysz, *New J. Chem.* **2003**, *27*, 39–49; d) C. Rocaboy, J. A. Gladysz, *Org. Lett.* **2002**, *4*, 1993–1996.
- [10] a) W. J. Sommer, K. Yu, J. S. Sears, Y. Ji, X. Zheng, R. J. Davis, C. David Sherrill, C. W. Jones, M. Weck, *Organometallics* **2005**, *24*, 4351–4361; b) M. R. Eberhard, *Org. Lett.* **2004**, *6*, 2125–2128.
- [11] W. A. Herrmann, C. Broßmer, K. Öfele, C.-P. Reisinger, T. Priermeier, M. Beller, H. Fischer, *Angew. Chem.* **1995**, *107*, 1989–1992; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1844–1847.
- [12] M. Nowotny, U. Hanefeld, H. van Koningsveld, T. Maschmeyer, *Chem. Commun.* **2000**, 1877–1878.
- [13] Current state of art in elucidation of active species in Heck and Suzuki coupling reactions is summarized in the recent review: a) N. T. S. Phan, M. Van Der Sluys, C. W. Jones, *Adv. Synth. Catal.* **2006**, *348*, 609–679; noteworthy, in the very recent account, a leaching of homogeneous Pd-species from Pd colloids in the ligand-free Heck reaction was proven by a molecular membrane technique: b) M. B. Thathagar, J. E. ten Elshof, G. Rothenberg, *Angew. Chem.* **2006**, *118*, 2952–2956; *Angew. Chem. Int. Ed.* **2006**, *45*, 2886–2890.
- [14] Heck reactions of alkenyl triflates (refs. a–d) and nonaflates (refs. e–g) are often carried out without phosphine added: a) A. Arcadi, E. Bernocchi, S. Cacchi, L. Caglioti, F. Marinelli, *Tetrahedron Lett.* **1990**, *31*, 2463–2466; b) S. Cacchi, G. Fabrizi, R. C. Larock, P. Pace, V. Reddy, *Synlett* **1998**, 888–890; c) R. C. Larock, H. Yang, P. Pace, K. Narayanan, C. E. Russell, S. Cacchi, G. Fabrizi, *Tetrahedron* **1998**, *54*, 7343–7356; d) T. Flessner, V. Ludwig, H. Siebeneicher, E. Winterfeldt, *Synthesis* **2002**, 1373–1378; e) M. Webel, H.-U. Reissig, *Synlett* **1997**, 1141–1142; f) I. M. Lyapkalo, M. Webel, H.-U. Reissig, *Eur. J. Org. Chem.* **2002**, 3646–3658; g) I. M. Lyapkalo, J. Högermeier, H.-U. Reissig, *Tetrahedron* **2004**, *60*, 7721–7729; a negative impact of PPh₃ on the reaction outcome was noticed earlier, see ref.^[4b].
- [15] A versatile methodology has been developed that enables an easy one-step access to alkenyl nonaflates from enolizable carbonyl compounds and a commercially available convenient technical product, nonafluorobutane-1-sulfonyl fluoride (NfF); a) *via* trimethylsilyl enol ethers: I. M. Lyapkalo, M. Webel, H.-U. Reissig, *Eur. J. Org. Chem.* **2002**, 1015–1025; b) *via* Li-enolates: I. M. Lyapkalo, M. Webel, H.-U. Reissig, *Synlett* **2001**, 1293–1295; c) using P-bases: I. M. Lyapkalo, M. A. K. Vogel, *Angew. Chem.* **2006**, *118*, 4124–4127; *Angew. Chem. Int. Ed.* **2006**, *45*, 4019–4023.
- [16] Effects of solvent, auxiliary base and additives on the reaction rate will be reported in a full account elsewhere.
- [17] The absence of colloid stabilizers (typically quaternary ammonium salts) in ligand-free Heck reactions of aryl halides leads to rapid formation of Pd-black with concomitant deterioration of the catalyst efficiency.^[1d,7b,9a]
- [18] As the aggregation process is higher order in Pd concentration than Heck coupling, by reasonable lowering the catalyst-to-substrate ratio significant improvement of the kinetics in favour of the Heck reaction was achieved.^[7b]
- [19] J. A. Widegren, R. G. Finke, *J. Mol. Catal. A: Chem.* **2003**, *198*, 317–341.
- [20] In the heterogeneous catalyst, only a fraction of the metal atoms on the surface is active. Therefore, (much) less than 1 equiv. of the catalytic poison (PPh₃, CS₂ or thiophene) is sufficient to block the active sites. Complete quenching of the catalytic activity with ≤ 1 equiv. of the above poisons was regarded as a solid evidence for the heterogeneous nature of the Pd(0)-catalyst in Heck coupling of aryl halides. Metallic mercury taken in a large excess amalgamates the colloidal metallic Pd thus deactivating it.
- [21] Despite gaining the evidence of a leaching of the homogeneous Pd-species from Pd colloids, the entity of the suggested Pd(0) catalyst upon completion of the catalytic cycle is still obscure. If it remains homogeneous and does not re-cluster to the Pd-nanoparticles, it

should not be affected by the quantitative heterogeneous catalyst poisons. However no poisoning experiments with PPh_3 , CS_2 or thiophene were reported.

- [22] Indeed, a single-metal $\text{Pd}(0)$ -complex efficiently catalyzing a hydrogenation of alkenes was regarded as a truly homogeneous catalyst based on its insensitivity towards poisoning with thiophene: R. van Asselt, C. J. Elsevier, *J. Mol. Catal.* **1991**, 65, L13–L19.
- [23] Widegren and Finke^[19] remarked that $\text{Hg}(0)$ -poisoning experiments are not universally applicable as $\text{Hg}(0)$ can cause side reactions and interact with some single-metal complexes: a) G. M. Whitesides, M. Hackett, R. L. Brainard, J. P. P. M. Lavalleye, A. F. Sowinski, A. N. Izumi, S. S. Moore, D. W. Brown, E. M. Staudt, *Organometallics* **1985**, 4, 1819–1830; b) R. A. Jones, F. M. Real, G. Wilkinson, A. M. R. Galas, M. B. Hursthouse, *J. Chem. Soc., Dalton Trans.* **1981**, 126–131; c) J. Stein, L. N. Lewis, Y. Gao, R. A. Scott, *J. Am. Chem. Soc.* **1999**, 121, 3693–3703; see also ref.^[22] While poisoning of the heterogeneous Pd -catalysts is well-documented,^[10] we could not find literature precedents of single-metal $\text{Pd}(0)$ -complexes that have been proven to induce a true homogeneous catalysis and be not affected by treatment with $\text{Hg}(0)$. For the recent discussions on $\text{Hg}(0)$ poisoning of Heck reaction see refs.^[9a,13a]
- [24] Metallic mercury was added to a reaction mixture at 37% completion. It was *vigorously* stirred for 1 h, then stirring stopped, the Hg -phase was allowed to completely settle to the bottom, the clear supernatant organic phase was transferred into the new vial, and the reaction kinetics was monitored further.
- [25] P. W. Collins, A. F. Gasielki, W. E. Perkins, G. W. Gullikson, R. G. Bianchi, S. W. Kramer, J. S. Ng, E. E. Yonan, L. Swenton, P. H. Jones, R. F. Bauer, *J. Med. Chem.* **1990**, 33, 2784–2793.
- [26] M. El Hattab, G. Culioli, A. Ortalo-Magne, L. Piovetti, S. E. Chitour, *J. Essential Oil Res.* **2002**, 14, 422–424.
- [27] S. Cacchi, G. Fabrizi, F. Gasparrini, C. Villani, *Synlett* **1999**, 345–347.
- [28] I. U. Khand, P. L. Pauson, M. J. A. Habib, *J. Chem. Res. Synop.* **1978**, 348–349.
- [29] E. A. Braude, W. F. Forbes, E. A. Evans, *J. Chem. Soc.* **1953**, 2202–2207.
- [30] The influence of anionic nonaflate on the catalytic activity would be masked by DMF and Et_3N which are more nucleophilic, stronger coordinating, and are present in the reaction mixture in greater excess. However, for the ligand-free Heck reactions of aryl halides, a kinetic model was suggested by Dupont and co-workers that accounts for the catalysis deactivation by formation of PdX_n^{m-} , see ref.^[9a] We thank one of the referees for the respective comment.