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Partial Hydrogenation of Alkynes to *cis*-Olefins by Using a Novel Pd^0–Polyethyleneimine Catalyst

Hironao Sajiki,*[a] Shigeki Mori,[a] Tomoyuki Ohkubo,[a] Takashi Ikawa,[a, b] Akira Kume,[a] Tomohiro Maegawa,[a] and Yasunari Monguchi[a]

The selective partial hydrogenation of alkynes to *cis*-alkenes represents an important class of chemical transformations that have found extensive use in the construction of an enormous variety of, for example, bioactive molecules, natural products, industrial materials.[1] The important transformation has mainly been accomplished under ordinary hydrogen pressure and at room temperature using heterogeneous Pd catalysts such as Lindlar catalyst ($Pd/CaCO_3$–Pb-$(OAc)_2$ in conjunction with quinoline)[2], Pdc[3] and Ni catalysts such as low-active Raney Ni[4], P-1 Ni[5], P-2 Ni[6], and Nic[7], and Au nanoparticles[8] and homogeneous Rh and Cr complexes[9] as a catalyst. In these cases except Lindlar catalyst, the narrow substrate-applicability, concomitant use with a basic additive, low *cis*/*trans* selectivity, pyrophoric property and/or operational complexity of the catalysts are undesirable as a general synthetic methodology and these are why such catalysts have never been a common selective catalyst for the partial hydrogenation of an alkyne to a *cis*-alkene. On the other hand, the Lindlar catalyst is widely applicable and used as such a selective catalyst although the pretreatment using environmentally harmful $Pb(OAc)_2$ and the simultaneous use with quinoline is necessary to achieve the chemoselective and geometrically selective partial hydrogenation. Furthermore, the smooth over-reduction to the corresponding alkanes efficiently proceeded under the Lindlar's hydrogenation conditions by the use of monosubstituted (terminal) alkynes as substrates. Therefore, the Lindlar's method is only applicable to the selective chemical transformation of disubstituted alkynes to *cis*-alkenes.[10] Thus, there is a need for the development of novel selective catalyst that can provide high yields and selectivity without any nucleophilic additives and the chemical pretreatment by an environmentally harmful materials. Recently, Alonso and Yus et al. reported an efficient method for the partial hydrogenation of both internal and terminal alkynes using Ni nanoparticles although the adjustment of the amount of the in situ generated molecular hydrogen source (Li powder and EtOH or *i*PrOH) is essential.[11] We now disclose a development of very practical catalyst and an efficient partial hydrogenation controlled by the catalyst activity that overcomes these serious and longstanding problems.

Recently, we have reported that a Pd/C catalyst formed an isolable complex with ethylenediamine (en) employed as the catalytic poison via one-on-one interaction between Pd metal and en, and the complex catalyst [Pd/C(en)] chemoselectively hydrogenated a variety of reducible functionalities in the presence of an *O*-benzyl, *O*-TES or *N*-Cbz protective group, benzyl alcohol or epoxide.[12] Besides, we also developed silk fibroin (Fib)-supported Pd^0 catalyst for the chemoselective hydrogenation of alkynes, alkenes and azides in the presence of other reducible functionalities.[13] During our effort to create a new Pd catalyst for hydrogenation possessing different chemoselectivity, we found that polyethyleneimine (PEI, branched polymer, average molecular weight approximately 25 000) supported Pd^0 catalyst selectively catalyzed hydrogenation of only alkynes including both mono- and disubstituted alkynes, without the reduction of other reducible functionalities.[14]

This paper describes the creation and application of a novel Pd^0–polyethyleneimine complex catalyst (Pd^0–PEI).

The 5% Pd^0–PEI catalyst was prepared by introduction of $Pd(OAc)_2$ directly in the MeOH solution of deaerated PEI under Ar atmosphere (Scheme 1). The resulting rust-colored solution was stirred under H_2 atmosphere at room temperature for 24 h and the solution changed gradually to black, in-

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[a] Prof. Dr. H. Sajiki, S. Mori, T. Ohkubo, Dr. T. Ikawa, A. Kume,
Dr. T. Maegawa, Dr. Y. Monguchi
Laboratory of Medicinal Chemistry, Gifu Pharmaceutical University
5-6-1 Mitahora-higashi, Gifu 502-8585 (Japan)
Fax: (+81) 58-237-5979
E-mail: sajiki@gifu-pu.ac.jp

[b] Dr. T. Ikawa
Current address: Laboratory of Synthetic Organic Chemistry
Department of Pharmaceutics, School of Pharmaceutical Sciences
University of Shizuoka, 52-1 Yada, Suruga-ku, Shizuoka, 422-8526
(Japan)

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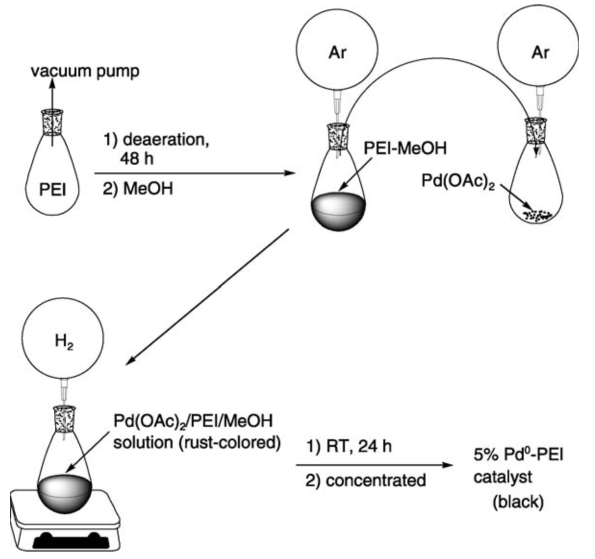
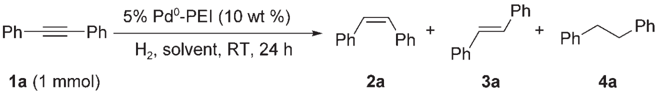


Scheme 1. Preparation of 5% Pd^0–PEI catalyst.

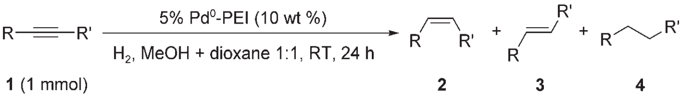
Table 1. Solvent effect of partial hydrogenation of diphenyl acetylene using Pd^0–PEI catalyst.

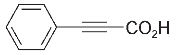
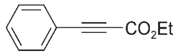
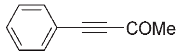
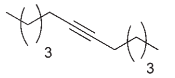
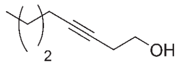
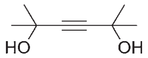


Entry	Solvent	**1a/2a/3a/4a**[a]
1	cyclohexane (2 mL)	100:0:0:0
2	AcOEt (2 mL)	100:0:0:0
3	dioxane (2 mL)	100:0:0:0
4	MeOH (2 mL)	0:68:2:30
5[b]	MeOH + dioxane	0:72:4:24
6[c]	MeOH + AcOEt	0:82:2:16
7	MeOH + AcOEt (1:1)	0:95:1:4
8	MeOH + dioxane (1:1)	0:97:1:2
9[d]	MeOH + dioxane (1:1)	0:95:1:4

[a] Determined by ^1H NMR spectroscopy. [b] MeOH (2 mL) and dioxane (0.5 mL) used as a solvent. [c] MeOH (2 mL) and AcOEt (0.5 mL) used as a solvent. [d] The reaction was performed for 12 h.

Table 2. Pd^0–PEI-catalyzed partial hydrogenation of disubstituted alkynes.



Entry	Substrate	**1/2/3/4**[a]
1[b]		0:96:4:0
2		0:94:0:6
3		0:36:58:6
4		0:100:0:0
5		0:100:0:0
6		0:100:0:0

[a] Determined by ^1H NMR spectroscopy. [b] K_2CO_3 (1 equiv) was used as an additive.

dicating the formation of the zero-valent Pd species. After concentration in vacuo, the obtained black gummy 5% Pd^0–PEI is stable for more than three years in a capped vial and is nonpyrophoric. The Pd deposition (5 weight%) into the PEI was based on the incipient ratio of $Pd(OAc)_2$ and PEI.

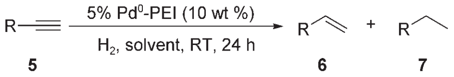
With 5% Pd^0–PEI in hand, its usefulness as catalyst by focusing on the chemoselective partial hydrogenation of alkynes was investigated. Reactions were typically carried out using 10 weight% versus substrate of 5% Pd^0–PEI in 2 mL solvent under H_2 atmosphere at room temperature. Although these preliminary studies were frustrated by no catalyst activity of 5% Pd^0–PEI in aprotic organic solvents (Table 1, entries 1–3), using MeOH as a solvent led to a dramatic increase in the hydrogenation catalyst activity toward diphenylacetylene (**1a**) giving *cis*-stilbene (**2a**) as a major product (68%) together with significant amount of diphenylethane (**4a**) by over-reduction. Mixing the more coordinating solvent such as dioxane and AcOEt led to a significant decrease in over-reduction (Table 1, entries 5–9). In MeOH/dioxane 1:1, the desired *cis*-stilbene (**2a**) was obtained in 97% selectivity and the ratio of products is not time-dependent (compare Table 1, entries 8 and 9).

To show the generality of the process, the use of various disubstituted alkynes was investigated (Table 2). The partial hydrogenation of aromatic disubstituted alkynes proceeded selectively at room temperature (Table 2, entries 1 and 2), as well as with aliphatic disubstituted alkynes (Table 2, entries 4–6). Even for the substrate bearing a conjugated ketone on the alkyne, the serious over-reduction was not observed while significant *cis*/*trans* isomerization of methyl styryl ketone accompanied the partial hydrogenation on the basis of keto–enol tautomerism (Table 2, entry 3).

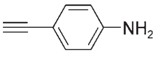
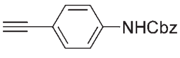
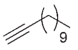
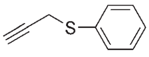
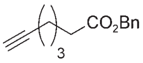
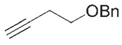
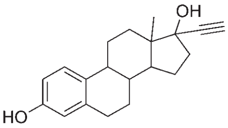
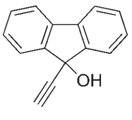
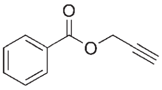
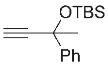
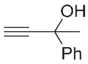
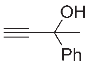
Amazingly, monosubstituted (terminal) alkynes (**5**) were found to be viable substrates (Table 3). Although the solvent tuning (addition or use of the more coordinating solvent dioxane) to obtain better selectivity is necessary (e.g., compare Table 3, entries 11 and 12), these results were well worth noting given the high propensity of both aromatic (Table 3, entries 1 and 2) and aliphatic (Table 3, entries 3–11) monosubstituted alkynes to undergo partial hydrogenation in good to excellent selectivities. Furthermore, other reducible functionalities such as *N*-Cbz protective group (Table 3, entry 3), benzyl ester (Table 3, entry 5), benzyl ether (Table 3, entry 6) and TBS ether (Table 3, entry 10) under the hydrogenation conditions could universally be tolerated.[15]

In summary, we have developed a new and selective catalyst, Pd^0–PEI, for the partial hydrogenation of disubstituted alkynes to *cis*-olefins. It is noteworthy that Pd^0–PEI catalyst is also applicable to the partial hydrogenation of monosubstituted (terminal) alkynes to monosubstituted olefins although such controlled reactions are usually impossible by the use of Lindlar catalyst.

Table 3. Pd^0–PEI-Catalyzed partial hydrogenation of monosubstituted alkynes.



5 6 7

Entry	Substrate	Solvent	5/6/7[a]
1		dioxane (2 mL)	11:85:4
2		MeOH (0.25 mL) + dioxane (1 mL)	0:93:7
3		dioxane (2 mL)	0:83:17
4		MeOH (1 mL) + AcOEt (1 mL)	0:98:2
5		MeOH (0.25 mL) + dioxane (1 mL)	0:100:0
6		MeOH (0.25 mL) + dioxane (1 mL)	0:96:4
7[b]		MeOH (2 mL) + dioxane (0.5 mL)	0:100:0
8		MeOH (0.5 mL) + dioxane (2 mL)	0:88:12
9		MeOH (1.5 equiv) + dioxane (2 mL)	0:83:17
10		MeOH (1 mL)	0:100:0
11		dioxane (2 mL)	0:88:12
12		MeOH (1 mL) + AcOEt (1 mL)	0:0:100

[a] Determined by ^1H NMR spectroscopy. [b] K_2CO_3 (1 equiv) was used as an additive.

Experimental Section

Preparation of 5% Pd^0–PEI catalyst: MeOH (100 mL, HPLC grade) was added to PEI (2.11 g, average M_w ~25000 by LS, average M_n ~10000 by GPC, high molecular weight, water free, purchased from Aldrich) deaerated for 48 h in vacuo. After PEI homogeneously solved, resulting solution was quickly poured into round-bottom flask measured $Pd(OAc)_2$ (225 mg, 1.00 mmol) under argon atmosphere. Next, the round-bottom flask was replaced with H_2 by three vacuum/H_2 (balloon) cycles after $Pd(OAc)_2$ completely solved in MeOH/PEI solution. The resulting solution was stirred for 24 h at room temperature and concentrated in vacuo.

General procedure for the partial hydrogenation of alkynes to olefins using Pd^0–PEI catalyst: In a test tube were placed substrate (1.00 mmol), 5% Pd^0–PEI (10 wt% of substrate), a stir bar, and solvent according to Table 3. The air inside the test tube was replaced with H_2 by three vacuum/H_2 (balloon) cycles, and the mixture was vigorously stirred at ambient temperature. After 24 h, the reaction mixture was partitioned between Et_2O (10 mL) and H_2O (10 mL) and the organic layer was washed with brine (10 mL), dried ($MgSO_4$), and filtered, and concentrated in vacuo. The product ratio was determined by ^1H NMR analysis.

Keywords: green chemistry · hydrogenation · palladium · partial hydrogenation · polyethyleneimine

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