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Deactivation of Heterogeneous Hydrogenation Catalysts by Alcoholic Solvents

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Abstract:

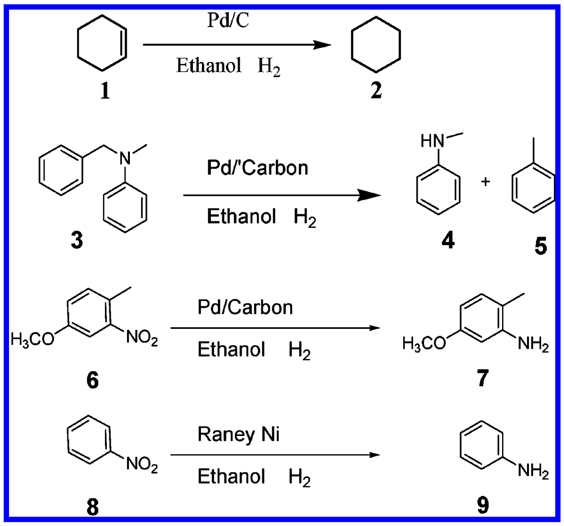
Hydrogenations using supported metal catalysts are ubiquitous in organic chemistry; yet often times there is a lack of knowledge of key subtle mechanistic features of these reactions that can spell the difference between success or failure in a given synthetic application. Herein we detail an unexpected deactivation of certain heterogeneous hydrogenation catalysts caused by the typical solvent of choice for such reactions, simple aliphatic alcohols. This phenomenon was found to be general for several classes of substrates using either Raney Ni or supported Pd-catalysts. The characteristics of this phenomenon, including the reversibility of the catalyst deactivation upon exposure to air, are consistent with literature reports of alcohol decomposition on metal surfaces forming adsorbed CO.

Alcohol Deactivation Effects

Heterogeneously catalyzed hydrogenations of olefins and polar functional groups are a standard reaction in every organic chemist's repertoire and play an important role in the synthesis of a number of pharmaceuticals and specialty chemicals.[1] Despite their prevalence, these catalysts are typically treated as a "black box", with limited understanding of the factors that influence reaction kinetics and selectivity. Although such an approach is sufficient for many applications, occasionally this can lead to problems since subtle variations in substrate, metal crystallite size, nature of support, and reaction conditions can dramatically affect reaction kinetics. Examples of such phenomena are commonplace in heterogeneous catalysis with documented reports of unusual rate behavior.[2]

We report here the unexpected observation of unusual rate behavior of heterogeneous hydrogenation catalysts under conditions likely to be encountered by the practicing organic chemist. We have found that typical hydrogenation catalysts are deactivated by prolonged contact with aliphatic alcoholic solvents. This phenomenon was found to be general for several classes of hydrogenation reactions (Scheme 1) using either Raney Ni or supported Pd-catalysts. Although anecdotal evidence for the adverse effects of alcoholic solvents on hydrogenation catalysts has been noted previously,[1a,b] this effect has not been widely recognized amongst practicing synthetic organic chemists.

Scheme 1



The effect of ethanol on reaction kinetics was studied by aging the Pd/C-catalyst in ethanol under nitrogen *after rigorous degassing* prior to charging cyclohexene and hydrogen to commence the reaction; the resulting reaction rate profiles are shown in Figure 1. The results indicate an approximate 5-fold suppression in reaction rate after aging the catalyst with ethanol for 8−20 h. A similar ethanol-

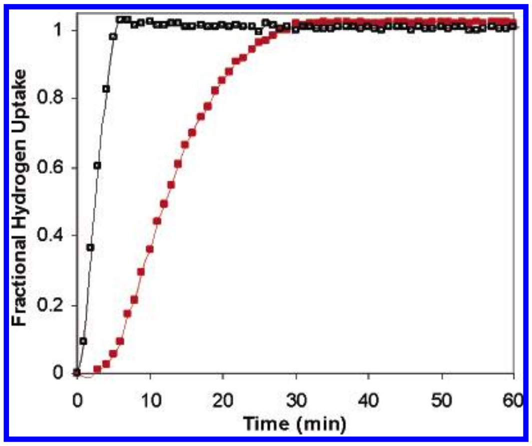


Figure 1. **Fractional hydrogen uptake profiles for the hydrogenation of 1 over Pd/C with no aging (black) and after 20 h of aging (red) in ethanol prior to the start of the reaction. Reaction conditions: 0.23 M 1, 4 wt % of 5% Pd/C, 30 °C, 40 psig.**

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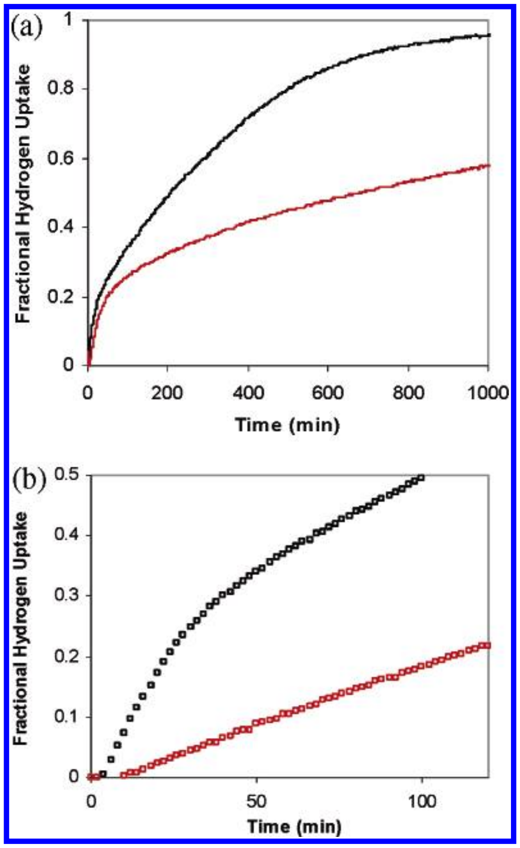

Figure 2. **Fractional hydrogen uptake profiles for hydrogenation of (a) 0.33 M 3 using 7 wt % of 5% Pd/C at 25 °C and 20 psig and (b) 0.11 M 6 using 5 wt % of 5% Pd/C at 25 °C, 20 psig. The black line represents hydrogenation without aging the catalyst in ethanol, and the red line represents hydrogenation after aging the catalyst in ethanol for 20 h under nitrogen.**

induced deactivation phenomenon was also observed during debenzylation of **3** and nitro reduction of **6** on Pd/C as shown in Figure 2.[3] The generality of this behavior is further demonstrated in the Raney Ni catalyzed reduction of nitrobenzene as shown in Figure 3.[4]

Surface science studies on single-crystal group 8 metals indicate that ethanol readily undergoes dissociative adsorption on the metal surface to form a metal alkoxide which then decomposes to a [RCH_xO] precursor followed by formation of CO and carbonaceous species. These transformations are known to occur on Pd surfaces at temperatures less than 25 °C.[5] A similar decomposition of allylic alcohols and α,β-unsaturated aldehydes under synthetically relevant hydrogenation conditions over supported metal catalysts was shown to form adsorbed CO that poisoned the catalyst surface. The catalytic activity in that case was regenerated by brief exposure of the catalyst to air to oxidize the adsorbed CO to CO_2.[2d,6] In accord with this precedent, the ethanol-induced catalyst deactivation of Pd/C in the present study was also reversed by brief oxygen exposure of the catalyst to air as shown in Figure 4A for hydrogenation of **1**. The H_2 uptake profile for a reaction with a catalyst that was aged in ethanol for 20 h prior to the reaction exhibited a suppressed reaction rate; the activity was restored after a brief air exposure. A similar effect of air exposure in restoring catalytic activity was also noted for the case of Raney Ni catalyzed hydrogenation of **8** (Figure 4B).

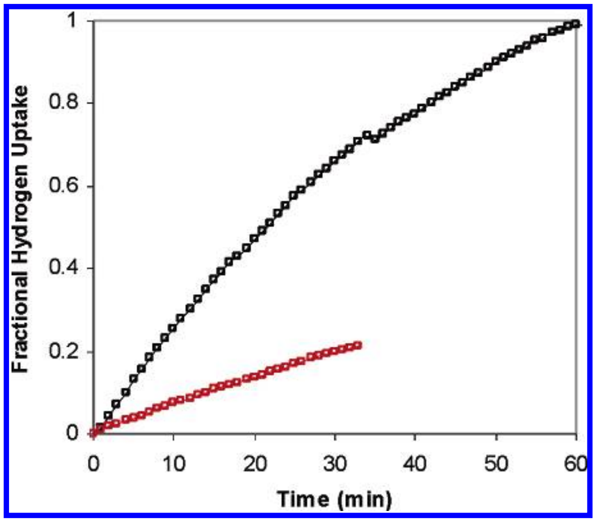

Figure 3. **Effect of aging the Raney Ni in ethanol for 18 h prior to hydrogenation of 8. Reaction conditions: 0.16 M 8, 100 wt % Raney Ni, 25 °C, 30 psig. The black line represents hydrogenation without aging the catalyst in ethanol, and the red line represents hydrogenation after aging the catalyst in ethanol for 20 h under nitrogen**

In a series of control experiments, direct exposure of hydrogenation reaction mixtures utilizing Pd/C or Raney Ni as catalyst to gaseous CO led to partial or complete suppression of the reaction, as expected (Figure 5). In accord with literature observations, brief exposure of CO-poisoned reaction mixtures to air restored some or all of the catalyst activity.

The behavior reported in Figures 1−4 was also observed with other alcoholic solvents including methanol, 1-propanol, and 2-propanol. While the details of the deactivation pathway may differ among the different alcohols, the poisoning of the catalyst surface and subsequent regeneration with air exposure are common to all of the alcohols studied. It should be noted that, in contrast to the catalyst poisoning in the presence of alcoholic solvents, no deactivation was observed with ethyl acetate as solvent.

Different supports, i.e., $SiO_2-Al_2O_3$ and various carbon sources, metal precursors, and the starting oxidation state[7] of the catalyst were tested, and the ethanol poisoning effect was shown to be general over a wide range of supported Pd catalysts as reported in Table 1. There were a subset of

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(3) Figure 2b only shows the results for the first 2 h of reaction to magnify the initial reaction rate differences. The experiment with no ethanol age went to complete conversion in 10 h.

(4) After 30 min, both hydrogenations in Figure 3 were stopped, the headspace was purged with nitrogen, and 20 psig air was injected. There was no effect of air exposure on the reaction rate in the absence of the ethanol age. The complete data set, in the form of a reaction rate profile, including the effect of air exposure is shown in Figure 4B with an explanation in the text.

(5) (a) Shekhar, R.; Barteau, M. *Catal. Lett.* **1995**, *31*, 221−237. (b) Davis, J. L.; Barteau, M. *Surf. Sci.* **1987**, *187*, 387−406. (c) Davis, J. L.; Barteau, M. *Surf. Sci.* **1990**, 235−248. (d) Shekhar, R.; Barteau, M.; Plank, R.; Vohs, J. *J. Phys. Chem.* **1997**, *101*, 7939−7951. (e) Gates, S. M.; Russell, J. N.; Yates, J. T., Jr. *Surf. Sci.* **1984**, *146*, 199−210.

(6) (a) English, M.; Ranade, V. S.; Lercher, J. A. *Appl. Catal. A: Gen.* **1997**, *163*, 111−122. (b) Singh, U. K.; Vannice, M. A. *J. Catal.* **2000**, *199*, 73−84.

(7) Oxidized supported Pd catalysts are presumably present as $Pd(OH)_2$ which may be reduced in situ with alcoholic solvents. See: Kanie, O.; Grotenberg, G.; Wong, C.-H. *Angew. Chem., Int. Ed.* **2000**, *39*, 4545−4547.

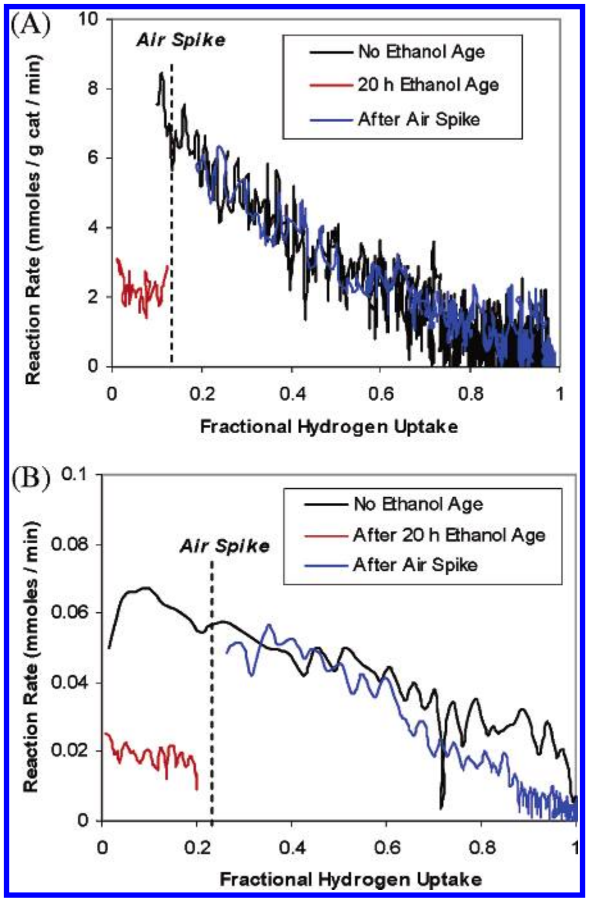


Figure 4. **Reaction rate profile for (A) hydrogenation of 0.4 M 1 using 1 wt % of 5% Pd/C at 30 °C, and 40 psig and (B) 0.16 M 8 using 100 wt % of Raney Ni at 25 °C and 30 psig. In both cases the reaction rate profile in the absence of aging with ethanol (black line) is compared to the reaction rate profile when the catalyst was aged in ethanol for 20 h prior to starting the reaction (red line). The deactivated catalyst was regenerated during the course of the reaction after 20% of the hydrogen uptake was observed by treating the catalyst to a headspace of air prior to restarting the reaction (blue line).**

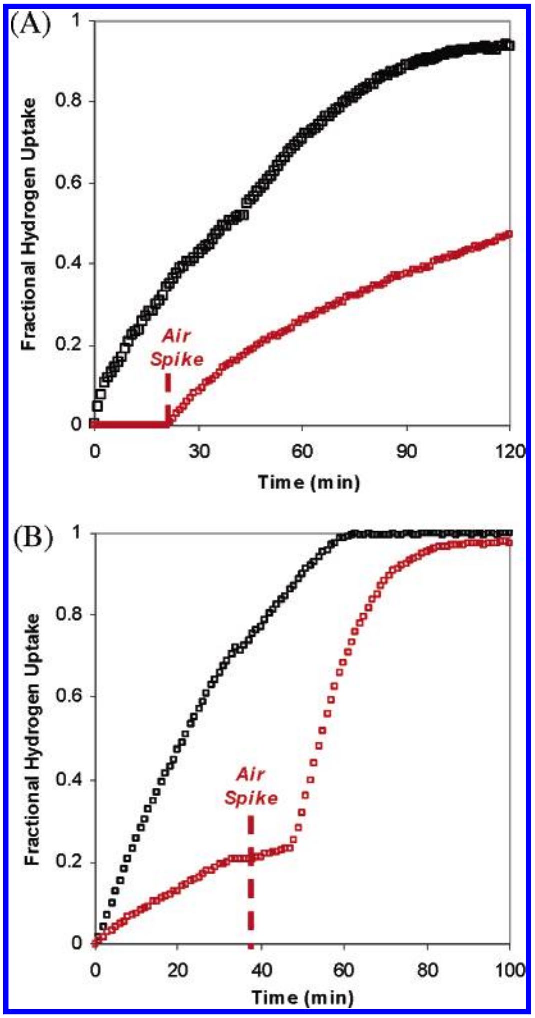


Figure 5. **Effect of CO preadsorption on hydrogenation activity of (A) 0.4 M 1 using 1.5 wt % of 5% Pd/C at 30 °C, 40 psig and (B) 0.16 M 8 using 100 wt % Raney Ni at 25 °C, 30 psig. The red line represents a reaction wherein the catalyst, in an inert reactor, was exposed to 10 psig CO prior to charging the substrate and commencing the reaction. The air spike was conducted by exposing the reaction mixture to 20 psig air for 30 min at 25 °C before restarting the reaction. The black line represents a reaction in which the catalyst was not prepoisoned with CO.**

catalysts that are shaded in gray in the table that did not exhibit this behavior, and the role of support, metal precursor, and pretreatment conditions in ethanol decomposition is under further investigation; however preliminary trends indicate that the acidity of the support may be at least partially responsible for the observed behavior.

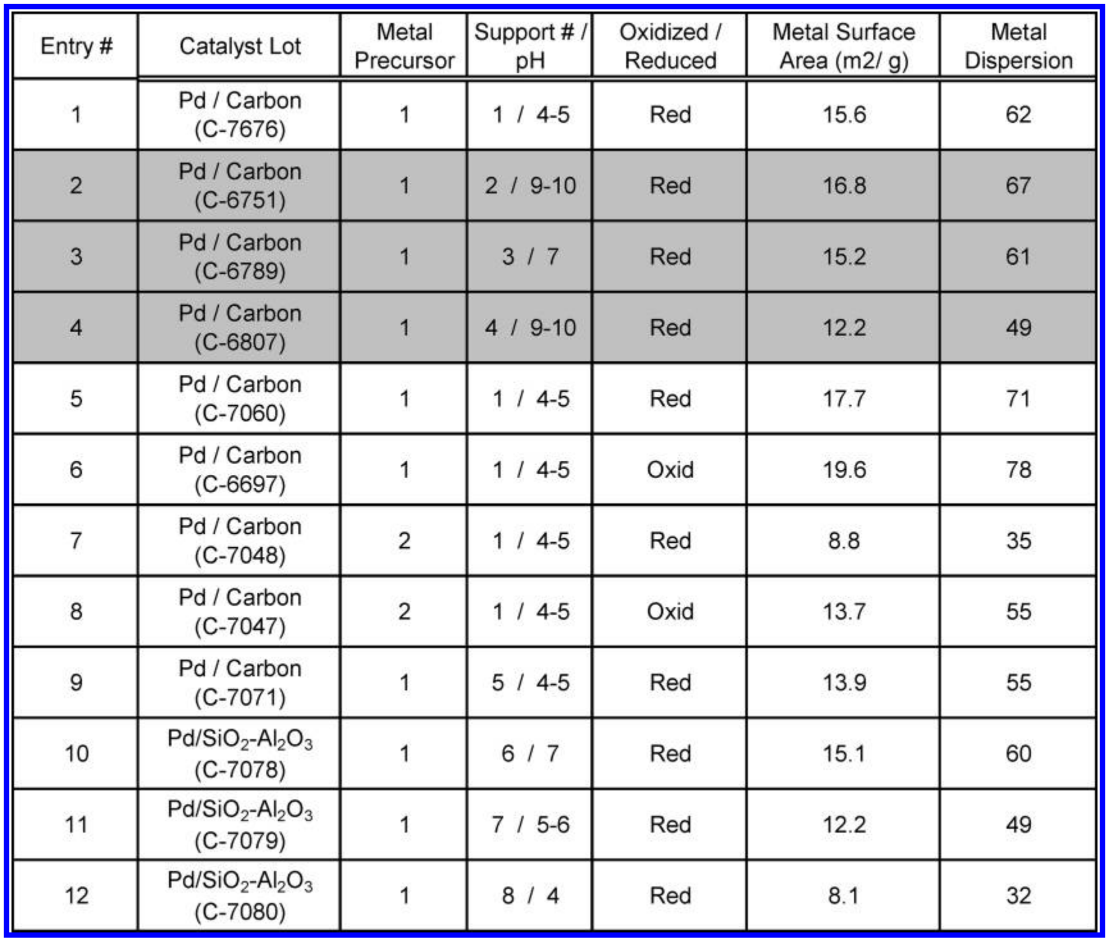
Finally, it should be stressed that while the observations highlighted in the present work are consistent with the cause of the catalyst deactivation being alcohol decomposition on the catalyst surface to form adsorbed CO, other possibilities such as the role of impurities in the solvent and/or the effect of the metal oxidation state under reaction conditions cannot be discounted.

The practical impact of these observations to the synthetic organic chemist will depend on a number of factors, key among them the age time of the catalyst with solvent prior to introduction of hydrogen and the effectiveness of inertion of the catalyst/solvent mixture prior to reaction. For bench-scale reactions, the age time may be short enough, and the inertion, poor to nonexistent, and this deactivation phenomenon may not be evident. Upon scale-up, however, this deactivation behavior could lead to irreproducibility in reaction rates and/or stalled reactions.

Conclusions

Heterogeneously catalyzed hydrogenation reactions are ubiquitous in organic synthesis, with ethanol and methanol being the most common solvents employed. The results presented herein indicate a general phenomenon of catalyst poisoning due to the use of these solvents. This poisoning effect was shown to be relevant over a number of different alcoholic solvents and classes of substrates using either Raney Ni or supported Pd catalysts. The poisoning effect can be reversed in some cases by brief exposure of the catalyst to air. Although the source of the alcohol poisoning effects was not definitively identified, the experimental observations were consistent with literature reports of alcohol decomposition on catalyst surfaces leading to adsorbed CO.

Table 1. **Physical Properties of Catalyst Tested for Ethanol-Induced Catalyst Deactivation During Pd/C-Catalyzed Hydrogenation of 1**[a]



Entry #	Catalyst Lot	Metal Precursor	Support # / pH	Oxidized / Reduced	Metal Surface Area (m2/ g)	Metal Dispersion
1	Pd / Carbon (C-7676)	1	1 / 4-5	Red	15.6	62
2	Pd / Carbon (C-6751)	1	2 / 9-10	Red	16.8	67
3	Pd / Carbon (C-6789)	1	3 / 7	Red	15.2	61
4	Pd / Carbon (C-6807)	1	4 / 9-10	Red	12.2	49
5	Pd / Carbon (C-7060)	1	1 / 4-5	Red	17.7	71
6	Pd / Carbon (C-6697)	1	1 / 4-5	Oxid	19.6	78
7	Pd / Carbon (C-7048)	2	1 / 4-5	Red	8.8	35
8	Pd / Carbon (C-7047)	2	1 / 4-5	Oxid	13.7	55
9	Pd / Carbon (C-7071)	1	5 / 4-5	Red	13.9	55
10	Pd/SiO_2-Al_2O_3 (C-7078)	1	6 / 7	Red	15.1	60
11	Pd/SiO_2-Al_2O_3 (C-7079)	1	7 / 5-6	Red	12.2	49
12	Pd/SiO_2-Al_2O_3 (C-7080)	1	8 / 4	Red	8.1	32

[a] Entries 1−9 are Pd/C-catalysts, while entries 10−12 are Pd/SiO_2−Al_2O_3 catalysts. All catalysts exhibited ethanol-induced catalyst deactivation except those shaded in gray.

Experimental Section

Solvents and reagents were used as received from commercial vendors. All Pd/C catalysts used in this study were obtained from Johnson Matthey and used as is without additional pretreatment. The Raney Ni catalysts used in this study were from Grace Davison (Raney 6800).

General Hydrogenation Procedure. All experiments were conducted in an Argonaut Endeavor reactor system with eight parallel glass-lined reactors and polypropylene agitators; the reaction progress was monitored by hydrogen uptake measurements. A 5% Pd/C catalyst (or water wet Raney Ni) was charged to the reactor followed by the substrate in ethanol. The reactor was purged with nitrogen prior to introducing hydrogen, leak tested for 5 min, and the reaction commenced by starting agitation. To examine the effect of ethanol on catalyst deactivation, ethanol and catalyst were charged to an inerted reactor, and the contents were rigorously degassed with nitrogen pressure purges prior to aging under nitrogen for an extended period of time (8−20 h). The degassed substrate solution was then charged prior to commencing the hydrogenation. The reaction progress was monitored by H_2 uptake measurements. The effect of an air spike was studied by shutting down the hydrogenation during the course of the reaction, replacing the headspace with nitrogen, and aging the catalyst under 20 psig air at 25 °C for 30 min. Hydrogenation was commenced by replacing the head space with first nitrogen then hydrogen prior to commencing hydrogenation and monitoring the reaction progress via hydrogen uptake measurements.

Hydrogenation of 1: 0.23 M **1**, 4 wt % of 5% Pd/C, 30 °C, 40 psig.

Hydrogenation of 3: 0.33 M **3**, 7 wt % of 5% Pd/C, 25 °C, 20 psig. The reaction progress was confirmed by LC measurements on an end of reaction sample using a Zorbax SB-C18 column.

Hydrogenation of 6: 0.11 M **6**, 5 wt % of 5% Pd/C, 25 °C, 20 psig. The reaction progress was confirmed by LC measurements on an end of reaction sample using a Zorbax SB-C18 column.

Hydrogenation of 8: 0.16 M *8*, 100 wt % Raney Ni, 25 °C, 30 psig.

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