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Synthesis of Alcohols *via* a Rhodium-Catalyzed Hydroformylation–Reduction Sequence using Tertiary Bidentate Amine Ligands

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Abstract: The synthesis of alcohols from aromatic olefins is described using a rhodium-catalyzed hydroformylation–reduction sequence with the assistance of a tertiary diamine ligand. The alcohols are produced in excellent branched to linear ratios and in good to excellent isolated yields. In all cases no aldehyde product, from hydroformylation, or alkyl product, from olefin reduction, was detected.

Keywords: alcohols; carbonylation; diamine; hydroformylation; reduction

Introduction

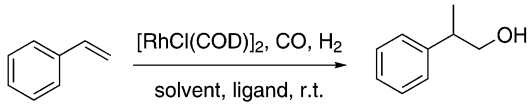
The direct synthesis of alcohols from olefins using syngas (carbon monoxide and hydrogen) through a two-step hydroformylation–reduction sequence remains a challenge. There have been many transition metal catalyst systems that have been developed to make alcohols from olefins, including Pd,[1] Ru,[2] Rh,[3] and Co.[4] Rhodium-catalyzed systems remain the most popular because of their high catalytic activity. A major problem in producing alcohols from olefins is the lack of reaction selectivity, many side products being produced including reduced olefins, *n* and *i* aldehydes/alcohols and mixtures of all components. The industrial process for making alcohols from olefins is currently a two-step process, whereby the aldehyde product is first isolated from the hydroformylation reaction. A separate second step is needed to reduce the aldehyde to the alcohol product. A one-pot sequence would be much more attractive because it would streamline the process to yield alcohols by hopefully lowering the reaction time, labour and overall cost.

In general there are many more rhodium/phosphine catalyst systems that produce aldehydes through hydroformylation,[5] as opposed to catalytic systems that yield alcohols from aldehyde reduction. Aldehyde products that result from hydroformylation are quite often the desired products, however other types of compounds can be made by reacting the *in-situ* prepared aldehyde; products such as amines,[6] indoles,[7] or other nitrogen heterocycles[8] that result from reacting the intermediate aldehyde[9] are often the goal of the research rather than the aldehyde itself. The use of nitrogen ligands in hydroformylation reactions is rather uncommon,[10] however it has been shown that they can facilitate the formation of alcohols.[11] Beyond simply mono-substituted olefin hydrocarbons, there have not been many applications of nitrogen coordinating ligands for the synthesis of alcohols from olefins using a hydroformylation–reduction sequence.[11] We now report a highly selective alcohol synthesis from olefins using a rhodium-catalyzed process that employs a tertiary diamine ligand.

Results and Discussion

Our initial testing began using 1.0 mmol of styrene and the following conditions: 2.5 mol% RhCl[COD] dimer, 10 mol% *N,N,N′,N′*-tetramethyl-1,4-diaminobutane, H_2 and CO gas (1.38 MPa each), and 3 mL of THF as the solvent, at room temperature. These conditions furnished the branched alcohol exclusively but only in 6% yield. In addition there were no signs of any olefin reduction product or hydroformylation aldehyde product. Additional screening ensued which consisted of using NEt_3 as a ligand in various solvents (Table 1, entries 2–4). In all cases significant starting material was recovered from the reaction. Increasing the pressure of syngas only helped marginally (Table 1, entries 5 and 6).

Table 1. Optimization of alcohol synthesis at room temperature; varying gas pressure, solvents and ligands.



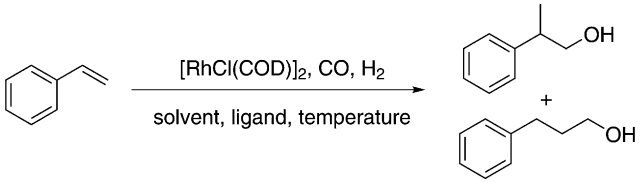
Entry	Ligand	Solvent	Pressure[b]	Yield[c] [%]
1	$Me_2N(CH_2)_4NMe_2$	THF	2.76	6
2	NEt_3	PhMe	2.76	9
3	NEt_3	THF	2.76	–[d]
4	NEt_3	DCM	2.76	8
5	$Me_2N(CH_2)_4NMe_2$	PhMe	4.14	8
6	$Me_2N(CH_2)_4NMe_2$	THF	4.14	9

[a] All reactions were performed in a glass liner inside a metal autoclave using 0.96 mmol of styrene, 2.5 mol% rhodium dimer complex, 10 mol% diamine ligand and 3 mL of solvent.
[b] Combined pressures in MPa of the reagent gases (CO and H_2), the pressure of each gas was equal for all reactions.
[c] Isolated yield of branched alcohols.
[d] Decomposition.

The next step in reaction optimization consisted of increasing the reaction temperature beyond room temperature (Table 2). Running the reaction at 38 °C gave the desired product(s) with a branched to linear ratio of 12.4, but only in 36% isolated yield. Increasing the reaction temperature to 48 °C diminished the branched to linear ratio slightly to 12.2 but increased the isolated yield significantly to 53%. Finally an 82% isolated yield was achieved by increasing the temperature another 10 °C to 60 °C, however, the branched to linear ratio fell to 9.6. Additional ligands, solvents and syngas pressures were screened to see if the branched to linear ratio could be increased. In all cases there was a lower branched to linear ratio and isolated yield with the exception of using MeCN as the solvent (entry 10), whereby the ratio of 11.9 was attained in 59% yield.

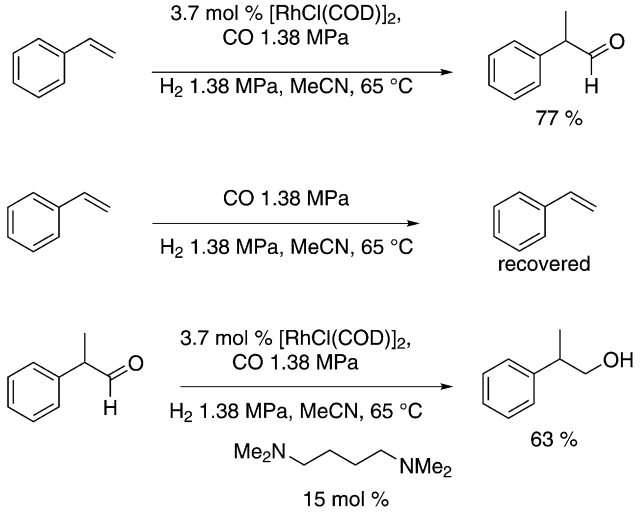
Three background reactions were run to gain insight into the reaction mechanism (Scheme 1). The first background reaction subjected styrene to the hydroformylation–reduction sequence reaction conditions in the absence of the tertiary diamine ligand. This resulted in the production of the branched aldehyde, crude ^{1}H NMR showed that there wasn't any branched alcohol, linear alcohol or linear aldehyde produced. The second background reaction consisted of subjecting styrene to a syngas atmosphere without any rhodium catalyst, which resulted in recovered styrene. The final background reaction had the branched aldehyde subjected to the hydroformylation–reduction sequence reaction conditions, which resulted in the production of the branched alcohol.

Table 2. Optimization of alcohol synthesis by reductive hydroformylation; varying solvents, temperature and ligands.



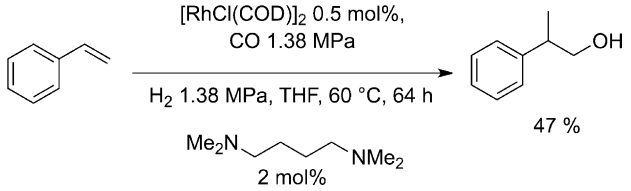
Entry	Ligand	Solvent	b:l[d]	Yield[e] [%]
1[b]	$Me_2N(CH_2)_4NMe_2$	THF	12.4	36
2[c]	$Me_2N(CH_2)_4NMe_2$	THF	12.2	53
3	$Me_2N(CH_2)_4NMe_2$	THF	9.6	82
4	NEt_3	THF	5.0	31
5	$Me_2N(CH_2)_6NMe_2$	THF	7.9	48
6	$Me_2N(CH_2)_2NMe_2$	THF	6.1	57
7	$Me_2N(CH_2)_4NMe_2$	PhMe	6.8	40
8	$Me_2N(CH_2)_4NMe_2$	THF	6.9	54[f]
9	$MeHN(CH_2)_2NHMe$	THF	–	–
10	$Me_2N(CH_2)_4NMe_2$	MeCN	11.9	59

[a] All reactions were performed in a glass liner inside a metal autoclave at 1.38 MPa each of CO and H_2, 0.96 mmol of styrene, 2.5 mol% rhodium dimer complex, 10 mol% diamine ligand, 60 °C reaction temperature (unless otherwise stated) and 3 mL of solvent.
[b] The reaction temperature was 38 °C.
[c] The reaction temperature was 48 °C.
[d] Branched to linear ratio determined by crude ^{1}H NMR.
[e] Isolated yield of branched and linear alcohols.
[f] Yield for the reductive hydroformylation of styrene by using 0.69 MPa each of CO and H_2.



Scheme 1. Background reactions run to gain an understanding of the reaction mechanism.

The reaction conditions were optimized to use 3.75 mol% of the rhodium dimer complex. However, the loading of the rhodium catalyst can be reduced if desired. As shown in Scheme 2, a 0.5 mol% loading of the rhodium dimer complex can achieve a reasona-



Scheme 2. Hydroformylation–reduction sequence reaction after a reaction time of 64 h with 0.5 mol% dimer complex loading.

ble 47% isolated yield of the branched alcohol in 64 h. The catalyst has a rather low turnover frequency but it appears to proceed in relatively large turnover numbers.

With optimized conditions in hand we evaluated the scope of the reaction (Figure 1). The reaction yields a number of branched alcohols in very good yields for a variety of substituted benzene ring systems. In all cases there were no traces of the olefin reduction product or the aldehyde product. The presence of halogens does not effect the reaction, regardless of whether it is a bromine or chlorine atom or whether the position is *ortho* or *para*. Methoxy ether groups do not affect the reaction in the *meta* or *para* position. However, the starting material 1-methoxy-2-propylenebenzene did not afford any product; only starting material was recovered. This observation suggests that coordination by *ortho* substituent groups can interfere with the reaction. It is conceivable that these coordinating groups can compete against the olefin for a coordination sphere within the rhodium complex thereby disrupting the hydroformylation step. Extended aromatic groups also work well, such as the *para*-phenylstyrene (**1c**) and the naphthalene ring system (**1j**). Disubstituted olefins also work, however the yield is typically lower than for monosubstituted olefins. Indene afforded the alcohol (**1g**) in 62% yield and 1-[(*E*)-prop-1-enyl]benzene gave the linear product (**1k**) in 44% yield. 1,2-Dihydronaphthalene also worked, but gave the alcohol (**1l**) in modest yield (35%) and with a branched to linear regioselectivity of 3.7.

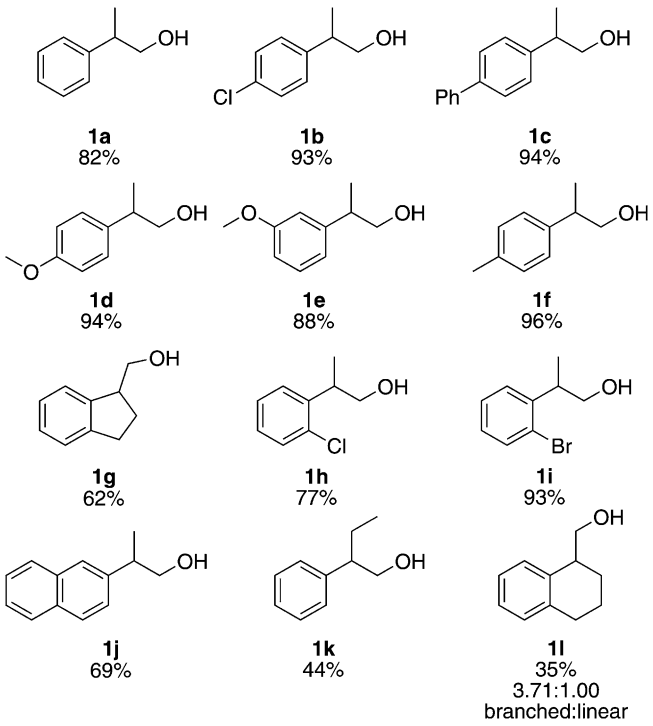


Figure 1. Substrate scope of rhodium-catalyzed hydroformylation–reduction sequence with different aromatic olefins. *Reaction conditions:* 0.72 mmol of aromatic olefin, 3.75 mol% of $[RhCl(COD)]_2$, 15 mol% diamine ligand (*N,N,N′,N′*-tetramethyl-1,4-diaminobutane), 1.38 MPa CO and 1.38 MPa H_2 gas, 3 mL of MeCN, 60 °C reaction temperature, 22 hour reaction time.

Conclusions

In summary, tertiary diamine ligands in conjunction with RhCl[COD] dimer is an effective catalytic system to directly prepare alcohols in good branched to linear ratio, from aromatic styrene and related compounds. Selectivity to alcohol products is excellent.

Experimental Section

General Procedure

The glass liner that was used was charged with a stir bar, flame-dried and allowed to cool. The cooled glass liner was charged with 13.3 mg of $[RhCl(COD)]_2$ (0.054 mmol). In a 1 dram vial was weighed the olefin (0.722 mmol) and 15.6 mg of *N*, *N*, *N′*, *N′*-tetramethylbutane-1,4-diamine (0.108 mmol); 1 mL of freshly distilled MeCN was added and the solution was charged into the glass liner containing the rhodium complex. An additional 2 mL of freshly distilled MeCN were used to rinse out the 1 dram vial holding the olefin solution. The glass liner was placed into the autoclave and screw capped with the metal cover and a pressure gauge was attached. The contents of the autoclave were purged five times with CO gas to 1.38 MPa each time and pressurized to a final pressure of 1.38 MPa. The autoclave valve was then closed to prevent any gas from being released. The CO gas line was cleared of CO gas and disconnected from the autoclave; an H_2 gas line was then connected to the autoclave. The H_2 gas line was purged 5 times and then the H_2 gas valve was placed on the "LOAD" position. The valve to the autoclave was slowly opened and the pressure on the autoclave was allowed to climb to 2.76 MPa from 1.38 MPa, the autoclave valve was then closed. The H_2 gas line was cleared of H_2 gas and disconnected from the autoclave; the autoclave was then placed in a 60 °C preheated oil bath, heated by a hotplate stirrer, and hooked up to

a vent line. The contents of the autoclave were allowed to stir in the oil bath overnight. After stirring for 21 h in the heated oil bath the autoclave was removed from the oil bath and allowed to cool for 30 min. After cooling the autoclave was depressurized, the vent line was removed and the crude reaction mixture was poured into a single-neck round-bottom flask, the glass liner was rinse with dichloromethane and the crude reaction mixture was concentrated and then subjected to silica gel chromatography.

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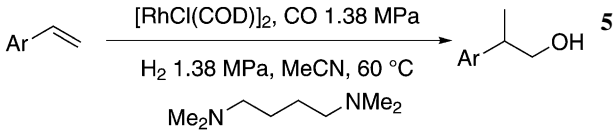

5

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