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Asymmetric Reductive Ring-Opening of Bicyclic Olefins Catalyzed by Palladium and Nickel Complexes

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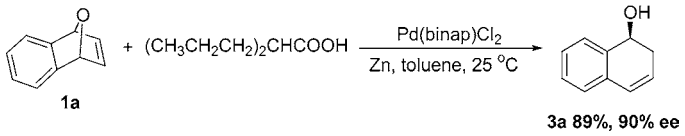
ABSTRACT



Asymmetric reductive ring opening of oxa- and azabenzonorbornadienes with organic acids and zinc powder under mild conditions catalyzed by Ni(binap)Cl_2 or Pd(binap)I_2 produces the corresponding 1,2-dihydronaphth-1-ols in good to excellent yields with high enantioselectivity.

Transition metal-catalyzed ring-opening reaction of oxabicyclic compounds is very useful in the synthesis of cyclic and acyclic compounds with multiple stereocenters.[1] Nucleophilic ring opening of oxabicyclic alkene using organomagnesium, organolithium, organozinc reagents, organoboronic acids, alcohols, and carboxylates has been extensively studied.[2−6] Our long interest in the chemistry of oxa- and aza-bicyclic olefins[7−12] has led to the development of palladium and nickel-catalyzed ring-opening addition of these alkenes with organic iodides[10,11] and more recently with terminal acetylenes.[12] Lautens et al. have demonstrated the reductive ring opening of oxabicyclic alkenes via the palladium-catalyzed hydrostannation and nickel-catalyzed hydroalumination reaction.[13] In addition, a nickel-catalyzed hydride (DIBAL-H) reductive ring opening of oxabicyclic alkenes to give ring-opening products with excellent enantioselectivity was reported.[14] However, to date, no report on organic acid-promoted (asymmetric) reductive ring opening of oxabicyclic alkenes has been given. In this letter, we describe a palladium and nickel-catalyzed reductive ring

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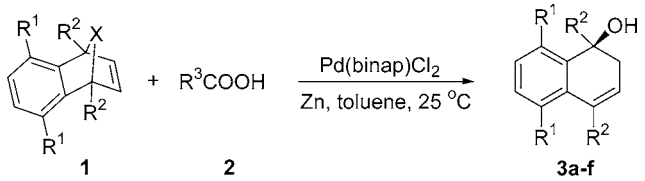
opening of oxabenzonorbornadienes with organic acids to furnish 1,2-hydronaphth-1-ols in good yields and high enantiomeric excess (ee) (Scheme 1). This nickel and palladium-

Scheme 1



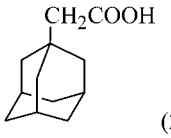
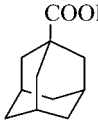
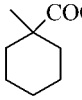
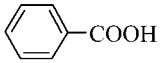
1a $R^1 = R^2 = H$, X = O
1b $R^1 = CH_3$, $R^2 = H$, X = O
1c $R^1 = H$, $R^2 = CH_3$, X = O
1d $R^1 = R^2 = H$, $X = NCO_2CH_3$
1e $R^1 = R^2 = CH_3$, $X = NCO_2CH_3$
1f $R^1 = R^2 = H$, $X = NSO_2C_6H_4CH_3$

catalyzed asymmetric reductive ring opening offers a convenient and mild method for the construction of enantiomerically enriched 1,2-dihydronaphth-1-ol in one pot from easily accessible starting material. Moreover, the enantiopure 1,2-dihydronaphth-1-ol is an important precursor for the synthesis of sertraline, an antidepressant agent.[15,16]

7-Oxabenzonorbornadiene (**1a**) undergoes reductive ring opening readily in the presence of an organic carboxylic acid, zinc metal, and a nickel or palladium phosphine complex. For example, treatment of **1a** (0.50 mmol), acetic acid (**2c**) (1.5 mmol), zinc (2.5 mmol), and 5 mol % Ni(dppe)I_2 in THF at 20 °C for 3 h afforded 1,2-dihydronaphth-1-ol in 94% yield. Control experiments indicate that no reaction occurs in the absence of zinc powder, acetic acid, or metal (Ni or Pd) catalyst. Since a bidentate ligand was used in the catalytic reaction, we also tested the asymmetric version of the present catalytic reaction by employing bidentate chiral ligands for the catalysts. Thus, the reaction of **1a**, acetic acid (1.5 mmol), zinc (2.5 mmol), and 5 mol % Pd((*R*)-binap)Cl_2 as the catalyst in toluene afforded (*S*)-1,2-dihydronaphth-1-ol in 90% yield with an ee of 77% (entry 3, Table 1). On the other hand, the same reaction using Ni[(*S*)-binap]I_2 in acetonitrile at 25 °C for 1 h afforded (*R*)-1,2-dihydronaphth-1-ol in 87% yield with an ee of 58%. Other nickel complexes using chiral ligands, (*S*,*S*)-chiraphos and (*R*)-prophos, gave similar yields but with very low ee values for product **3a**.

To understand the nature of the present asymmetric reductive ring opening and to optimize the reaction conditions, several different organic acids were tested for the ring opening of **1a** using Pd(binap)Cl_2 as the catalyst. The results in Table 1 show that the organic acid used influences

Table 1. Effect of Various Organic Acids on the Reductive Ring Opening of 7-Oxabenzonorbornadiene **1a**[a]

entry	acid	time (h)	yield (%)[b]	ee (%)
1	$(CH_3CH_2CH_2)_2CHCOOH$ (**2a**)	2	87	83
2	$(CH_3)_3CCH_2COOH$ (**2b**)	2	89	82
3	CH_3COOH (**2c**)	2	90	77
4	$CH_3(CH_2)_6COOH$ (**2d**)	3	69	73
5	 (**2e**)	3	87	79
6	 (**2f**)	2	86	30
7	 (**2g**)	2	84	62
8	 (**2h**)	2	81	70

[a] Unless stated otherwise, each reaction was carried out using 7-oxabenzonorbornadiene (**1a**) (0.50 mmol), acid **2** (1.50 mmol), Pd(binap)Cl_2 (5.0 mol %), and Zn (2.50 mmol) in toluene (3.0 mL) at 25 °C under N_2 for the reaction time mentioned in the table. [b] Isolated yields.

drastically both the yield and the ee value of product 1,2-dihydronaphth-1-ol. Acetic acid (**2c**), 1-adamantane acetic acid (**2d**), 1-adamantane carboxylic acid (**2e**), 1-methyl-1-cyclohexanecarboxylic acid (**2f**), octanoic acid (**2g**), and benzoic acid (**2h**) afforded **3a** in moderate to good yields but in moderate enantioselectivities (Table 1, entries 3−8). Valproic acid (**2a**) and *tert*-butyl acetic acid (**2b**) appear to be the best two among the acids tested, giving **3a** in 87 and 89% yields and in ees of 83 and 82%, respectively (entries 1 and 2).

The effect of solvents for the formation of enantiopure 1,2-dihydronaphth-1-ol (**3a**) was briefly investigated. Reaction conditions similar to those shown in Table 1 using **1a** and valproic acid (**2a**) at 25 °C with a reaction time of 2 h were used. Among the solvents tested (toluene, acetonitrile, and THF), toluene gave the best yield (87%) and ee value (83%) of **3a**. In acetonitrile, the yield and ee were 72 and 78%, respectively, while in THF the corresponding values were 86 and 72%. The ee value also depends substantially on the reaction temperature. When the reaction was carried out at 0 °C, **3a** was obtained in 80% yield with ee of 89%, but the reaction needed 12 h for completion. However, further decrease of the reaction temperature led to incompletion of the reaction with little improvement of the ee value. Similar effects of solvent and organic acid were also observed for the Ni[(*S*)-binap]I_2-catalyzed reductive ring opening of **1a**.

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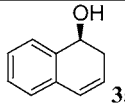
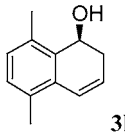
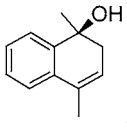
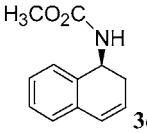
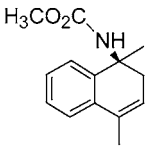
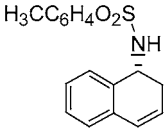
The amount of catalyst and zinc used also affected the yield and ee value of the present asymmetric catalytic reaction. The reaction of **1a** with **2a** in the presence of 1.0 mol % Pd(binap)Cl_2 instead of the standard 5.0 mol % catalyst afforded **3a** in 78% yield and 80% ee, but longer reaction time (12 h) was required for the completion of the reaction. Increasing the amount of zinc to 5.0 mmol afforded a higher yield of 92% without affecting the ee (83%). Similarly, an increase in the amount of acid to 2.5 mmol increased the yield from 87 to 90% with no change in the ee value. If acid **2a** was stirred with the Pd catalyst and Zn for 1 h and followed by addition of **1a**, the catalytic reaction gave excellent yield (89%) and enantiomeric excess (90%) (entry 1, Table 2). Slow addition of the acid over a period of time did not improve either the yield or the ee.

The reductive ring opening can be extended to other oxa- and azabenzonorbornadienes. Table 2 summarizes the results of these palladium and nickel-catalyzed reactions. The reaction of 7-oxabenzonorbornadiene **1a** with acid **2b** in the presence of 5 mol % Ni(binap)I_2 and zinc in acetonitrile at 25 °C for 2 h afforded 1,2-dihydronaphth-1-ol in 89% yield and 77% ee (Table 2, entry 2). In a similar way, substituted 7-oxabenzonorbornadienes **1b** having two methyl groups on its aromatic ring reacts with **2b** in the presence of Pd catalyst to afford the ring-opening product **3b** in 77% yield and an ee of 40%, whereas the nickel catalyst provided **3b** in the excellent yield of 86% and an ee of 71% (entries 3 and 4). It was quite surprising that Pd catalyst did not afford any desired product for the ring-opening reaction of **1c** (entry 5), whereas Ni catalyst generated **3c** in a good yield of 83% but in very low enantiomeric excess (entry 6). Similar to 7-oxabenzonorbornadienes, azabicyclic alkenes also undergo reductive ring opening under the standard catalytic conditions. Thus, the reaction of 7-azabenzonorbornadiene **1d** with **2a** in the presence of Pd(binap)Cl_2 in toluene at 25 °C for 3 h produced 1,2-dihydronaphthalenyl carbamate **3d** in 84% yield and 80% ee (entry 7). The nickel catalyst system also gave results similar in yield and ee (see entry 8). The results in Table 2 show that in most reactions the nickel catalyst gives a better yield but in lower enantiomeric excess compared to the palladium complex. The reductive ring opening also proceeded smoothly with substituted 7-azabenzonorbornadiene **1e** having two methyl groups on the bridgeheads to give product **3e** in 79% yield and 27% ee (entry 9). Similarly, **1f** also reacts with acid in the presence of Pd catalyst to afford the 1,2-dihydronaphthalenyl carbamate derivative **3f** in good yield and enantiomeric excess (entry 10).

The reductive ring-opening strategy can be further applied to nonaromatic bicyclic systems. Reaction of bicyclic alkene **4** with **2b** in the presence of Ni(binap)I_2 afforded a highly substituted cyclohexenol derivative **5** in 63% yield and 43% enantioselectivity. Interestingly, for the reaction of **6**, an exo isomer of **4**, with **2b** under similar conditions, no anticipated reductive ring-opening product was obtained but a bicyclic-[3.2.1]lactone **7** was obtained instead in 85% yield and 53% ee (Scheme 2). Product **7** is likely formed via reductive ring opening of **6**, followed by selective lactonization of the

Table 2: Results of Palladium and Nickel-Catalyzed Reductive Ring Opening of 7-Oxabenzonorbornadienes **1a**[a]

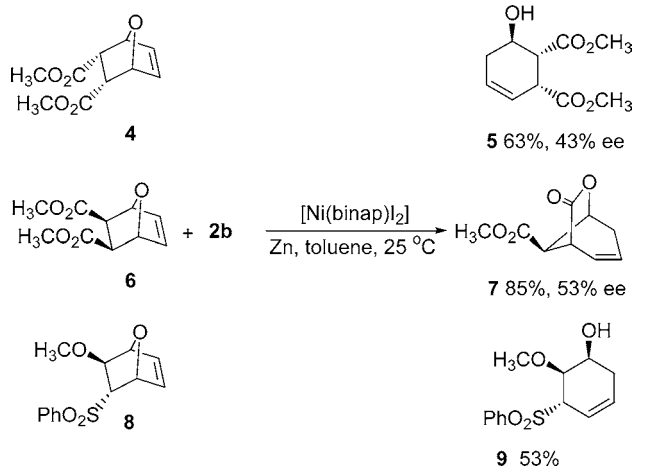
entry	1		time	product	yield (%)[b]	ee (%)
1[c]	**1a**	Pd	2 h	 **3a**	89	90
2[d]	**1a**	Ni	2 h	**3a**	89	77
3[c]	**1b**	Pd	7h	 **3b**	77	40
4[d]	**1b**	Ni	4 h	**3b**	86	71
5[c]	**1c**	Pd	48 h	 **3c**	-	-
6[d]	**1c**	Ni	12 h	**3c**	83	10
7[c]	**1d**	Pd	3 h	 **3d**	84	80
8[d]	**1d**	Ni	3 h	**3d**	86	75
9[c]	**1e**	Pd	12 h	 **3e**	79	27
10[c]	**1f**	Pd	12 h	 **3f**	82	71

[a] Unless stated otherwise, all reactions were carried out using 7-oxabenzonorbornadiene **1a** (0.50 mmol), acid **2** (1.50 mmol), catalyst (5.0 mol %), Zn (2.50 mmol), and solvent (3.0 mL) at 25 °C under N_2 for the period of time indicated. [b] Isolated yields. [c] Pd = [Pd((*R*)-binap)Cl_2] catalyst (5.0 mol %) and toluene (3 mL) were used. [d] Ni = [Ni((*S*)-binap)I_2] catalyst (5.0 mol %) and acetonitrile (3 mL) were used. [e] For entries 1, 2, 5−7, 9, and 10, valproic acid was used. [f] For entries 3, 4, and 8, *tert*-butyl acetic acid was used. For a detailed procedure, see Supporting Information.

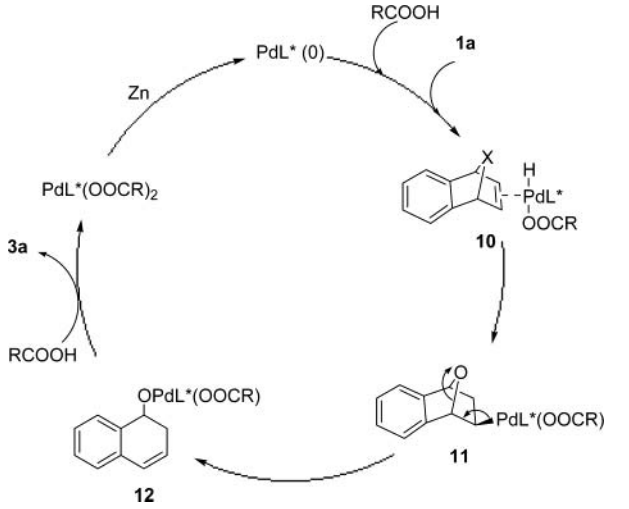
intermediate. The reductive ring opening of unsymmetrical bicyclic alkene **8** proceeded smoothly with remarkable regioselectivity. Only product **9** with the hydroxy group next to the methoxy moiety was obtained. The crystal structure of **9** was determined by X-ray diffraction. The methoxy group appears to show a strong directing effect on the regioselectivity during the catalytic reductive ring opening of **8** to give **9**. There was no enantioselectivity for the catalytic reaction, and only racemic product was observed.

It is interesting to compare the present results with those from rhodium-catalyzed ring-opening reaction of carboxylic acids with oxabicyclic alkenes reported by Lautens recently.[5c] In this rhodium-catalyzed reaction, a carboxylate group acts as a nucleophile and adds to the olefinic carbon of **1a**. In

Scheme 2



Scheme 3



our case, the carboxylic acid acts as the hydrogen source. The carboxylate group does not add to the alkene carbon of **1a** but does influence the ee value of the catalytic reaction.

While the detailed pathway[17] is not clear, on the basis of the above results and the requirement of organic acid, the key steps are proposed as shown in Scheme 3. The reduction of Pd(II) to Pd(0) by zinc initiates the catalytic reaction.[18] Oxidative addition of organic acid to Pd(0) leads to the generation of Pd(II) hydride species.[19] Coordination of the carbon−carbon double bond of 7-oxabenzonorbornadiene via the exo face to the Pd center and insertion of the double bond to the Pd-hydride results in the formation of intermediate **11**. Subsequent β-heteroatom elimination leading to intermediate **12**, followed by protonation, affords the final product **3a** and palladium(II) species. The latter is then reduced to Pd(0) by zinc. This proposed mechanism is similar to that for the palladium or nickel-catalyzed addition of aryl halide to 7-oxa- or azabicyclic alkenes.[10,11]

In conclusion, we have developed a novel palladium and nickel-catalyzed asymmetric ring-opening reaction of oxa- and azabicyclic compounds with organic acids to afford ring-opening products in good to excellent yields with high enantioselectivity. This reaction offers a very convenient and mild method for the synthesis of enantiopure 1,2-dihydronaphthalene derivatives. Studies on further expansion of the scope of this Pd and Ni-catalyzed reaction are in progress.

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Supporting Information Available: An experimental procedure and spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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