Nickel-Catalyzed Highly Stereoselective Ring Opening of 7-Oxa- and Azanorbornenes with Organic Halides

Chiou-Chii Feng, Malay Nandi, Thota Sambaiah, and Chien-Hong Cheng*

Department of Chemistry, National Tsing Hua University, Hsinchu 30043, Taiwan

Received November 24, 1998

Nickel-catalyzed ring-opening reactions of 7-heteroatom norbornadienes and norbornenes with various organic halides to give products with multiple stereocenters are described. Treatment of 7-oxabenzonorbornadiene (**1a**) and 7-carbomethoxy-7-azabenzonorbornadiene (**1b**) with aryl iodides (ArI) in the presence of $NiCl_2(PPh_3)_2$ and Zn powder gave the corresponding ring-opening addition products *cis*-1,2-dihydro-2-aryl-1-naphthol (**2a**−**m**) and methyl *N*-[*cis*-1,2-dihydro-2-aryl-1-naphthyl]-carbamate (**3a**−**e**) completely stereoselectively in 40−99% yields. The nickel system also catalyzes the reaction of highly substituted oxabicyclic [2.2.1] compounds (**1c**−**e**) with organic halides (PhI, $PhCH_2Br$, PhCHCHBr, and $PhCBrCH_2$) to give the corresponding ring-opening products (**4a**−**d**, **5**, **6a**,**b**) that consist of four fixed stereocenters. Studies on the effect of solvent on the reaction of **1a** with PhI show that CH_3CN gives the highest yield of product **2a**; no product **2a** is observed when toluene, dichloromethane, methanol, DMF, or DMSO is used as solvent. Addition of extra PPh_3 to the reaction mixture reduced the yield of **2a**. A mechanism is proposed to account for the formation of these nickel-catalyzed ring-opening addition products.

Introduction

Ring opening of oxabicyclic and azabicyclic compounds is an exceedingly important method in the synthesis of cyclic and acyclic compounds with multiple stereocenters.[1,2] A general strategy is to construct highly substituted rings with the required stereocenters, which are then cleaved to give chemically complex acyclic molecules. Nucleophilic ring opening of oxabicyclic alkenes using nucleophiles such as organocuprates, organolithium reagents, organomagnesium compounds, diphenylphosphide, and Lewis acidic anhydrides has been extensively studied.[3,4] Recently, Lautens et al. have reported nickel-catalyzed regio- and enantioselective nucleophilic ring opening of oxabicyclic alkenes with DIBAL-H and Grignard reagents.[5]

Previously, we successfully applied electrophilic reagents such as aryl halides, alkenyl halides, and alkyl halides in the presence of a palladium complex, zinc powder, and zinc chloride in the ring opening of 7-heteroatom-norbornene derivatives.[6] Interesting observations by Lautens et al. regarding the nucleophilic ring opening of oxabicyclic alkenes catalyzed by nickel complexes and the success of the palladium-catalyzed ring opening of 7-heteroatom-norbornadiene derivatives with organic halides prompted us to investigate the catalytic activity of Ni systems in the addition of organic halides to various oxa- and azabicyclic alkenes. The results show that nickel phosphine complexes are more reactive than palladium complexes in these ring-opening addition reactions. Nickel complexes catalyze the ring-opening addition of various organic halides to not only 7-heteroatom-benzonorbornadiene but also highly substituted 7-oxanorbornenes to yield products with multiple stereocenters (eq 1−3). Moreover, the mechanism for this nickel-catalyzed reaction appears different from that for nickel-catalyzed nucleophilic ring opening of oxabicyclic alkenes reported by Lautens.[5] Here, we report the scope and mechanism of this facile one-pot transformation.

(1) (a) Masamune, S.; Kim, C. U.; Wilson, K. E.; Spessard, G. O.; Georghiou, P. E.; Bates, G. S. *J. Am. Chem. Soc.* **1975**, *97*, 3512. (b) Nakano, A.; Takimoto, S.; Inanaga, J.; Katsuki, T.; Ouchida, S.; Inoue, K.; Aiga, M.; Okukado, N.; Yamaguchi, M. *Chem. Lett.* **1979**, *1019*, 1021. (c) Grieco, P. A.; Ohfune, Y.; Yokoyama, Y.; Owens, W. *J. Am. Chem. Soc.* **1979**, *101*, 4749. (d) White, J. D.; Fukuyama, Y. *J. Am. Chem. Soc.* **1979**, *101*, 226. (e) For an interesting discussion of this approach, see: White, J. D. *Strategies and Tactics in Organic Synthesis*; Lindberg, T., Ed.; Academic Press: New York, 1984; Chapter 13.

(2) Oxabicyclic compounds as valuable intermediates, selected reviews, see: (a) Lipshutz, B. H. *Chem. Rev.* **1986**, *86*, 795. (b) Vogel, P.; Fattori, D.; Gasparini, F.; Le Drian, C. *Synlett* **1990**, 173. (c) Lautens, M. *Synlett* **1993**, 177. For leading ref, see: (d) Arjona, O.; Dios de, A.; Fernandez de la Pradilla, R.; Plumet, J.; Viso, A. *J. Org. Chem.* **1994**, *59*, 3906 and references therein. Oxanorbornenic derivative used for the synthesis of macrocyclic ring systems, see: (e) Ashton, P. R.; Brown, G. R.; Isaacs, N. S.; Giuffrida, D.; Kohnke, F. H.; Mathias, J. P.; Slawin, A. M. Z.; Smith, D. R.; Stoddart, J. F.; Williams, D. J. *J. Am. Chem. Soc.* **1992**, *114*, 6330. (f) Ashton, P. R.; Girreser, U.; Giuffrida, D.; Kohnke, F. H.; Mathias, J. P.; Raymo, F. M.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. *J. Am. Chem. Soc.* **1993**, *115*, 5422.

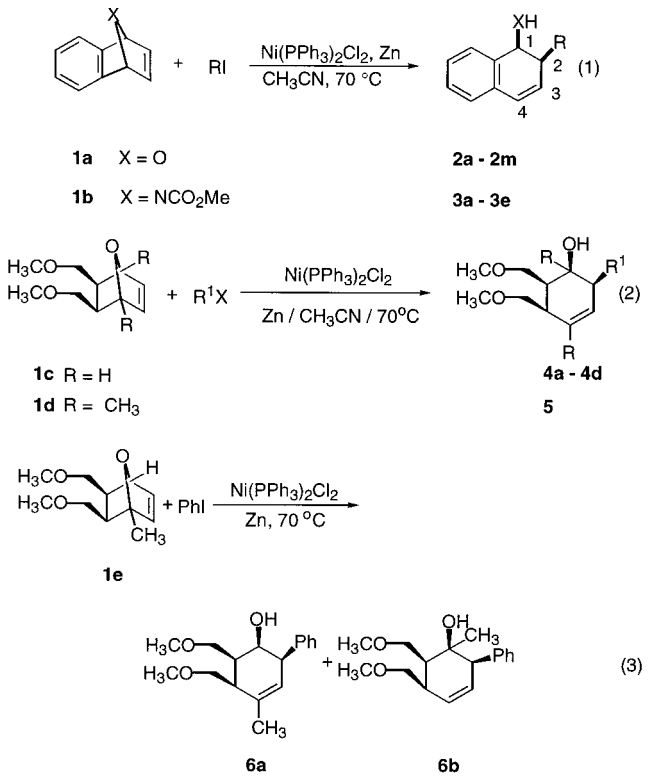
(3) (a) Woo, S.; Keay, B. A. *Synthesis* **1996**, 669. (b) Lautens, M. *Synlett* **1993**, 177. (c) Lautens, M. *Pure Appl. Chem.* **1992**, *64*, 1873. (d) Vogel, P. *Bull. Soc. Chim. Belg.* **1990**, *99*, 395. (e) Lautens, M.; Ma, S. *Tetrahedron Lett.* **1996**, *37*, 1727. (f) Arjona, O.; Conde, S.; Plumet, J.; Viso, A. *Tetrahedron Lett.* **1995**, *36*, 6157. (g) Arjona, O.; Fernandez de la Pradilla, R.; Garcia, E.; Martin-Domenech, A.; Plumet, J. *Tetrahedron Lett.* **1989**, *30*, 6437. (h) Lautens, M.; Abd-El-Aziz, A. S.; Lough, A. *J. Org. Chem.* **1990**, *55*, 5305. (i) Arjona, O.; Fernandez de la Pradilla, R.; Mallo, A.; Plumet, J.; Viso, A. *Tetrahedron Lett.* **1990**, *31*, 1475. (j) Lautens, M.; Fillion, E.; Sampat, M. *J. Org. Chem.* **1997**, *62*, 7080.

(4) (a) Gillespie, D. G.; Walker, B. J.; Stevens, D.; McAuliffe, C. A. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1697. (b) Cuny, G. D.; Buchwald, S. L. *Organometallics* **1991**, *10*, 363.

(5) (a) Lautens, M.; Chiu, P.; Ma, S.; Rovis, T. *J. Am. Chem. Soc.* **1995**, *117*, 532. (b) Lautens, M.; Ma, S. *J. Org. Chem.* **1996**, *61*, 7246. (c) Lautens, M.; Rovis, T. *J. Org. Chem.* **1997**, *62*, 5246. (d) Lautens, M.; Rovis, T. *Tetrahedron* **1998**, *54*, 1107.

(6) (a) Duan, J.-P.; Cheng, C.-H. *Tetrahedron Lett.* **1993**, *34*, 4019. (b) Duan, J.-P.; Cheng, C.-H. *Organometallics* **1995**, *14*, 1608.

10.1021/jo982312e CCC: $18.00
Published on Web 04/27/1999



Results and Discussion

Treatment of 7-oxabenzonorbornadiene (**1a**) with an aryl iodide in the presence of $NiCl_2(PPh_3)_2$ (5 mol %) and zinc (10 equiv) in acetonitrile at 70 °C afforded the corresponding ring-opening product 2-substituted *cis*-1,2-dihydro-1-naphthol **2** (eq 1 and Table 1). The net result of this nickel-promoted reaction may be considered to be an exo 1,4-C-H addition of an arene to compound **1a**. There was no trans isomer detected by ^{1}H NMR spectra or GC analysis, indicating that the reactions were completely stereoselective. A large number of aryl iodides were found to undergo this ring opening, and the results are shown in Table 1. However, aryl iodides with $COCH_3$, NO_2, OH, and NH_2 substituents decreased the catalytic activities and yields (Table 1, entries 10−13). No addition product was detected from the reaction of chlorobenzene with **1a** (entry 17), and a poor yield (entry 16) of the ring-opening product was obtained for bromobenzene. The use of KI along with bromobenzene failed to improve the yield (entry 16).[7] Alkyl iodides such as ethyl iodide and *n*-propyl iodide did not react with **1a** under the reaction conditions for addition of aryl iodide to **1a**, but methyl iodide added to **1a** slowly gave the corresponding 2-substituted *cis*-1,2-dihydro-1-naphthol **2m** in 40% yield.

Products **2** were fully characterized by spectral methods. For example, in the ^{1}H NMR spectrum of **2a**, signals for the olefinic protons appear at 6.12 (H-3) and 6.69 (H-4) ppm, whereas the protons (H-1 and H-2) bonded to the carbons at which hydroxyl and phenyl groups are attached show signals at 4.92 and 3.86 ppm, respectively. The cis stereochemistry of the hydroxyl and aryl groups was established on the basis of the ^{1}H NMR coupling constant (J_{H1-H2} = 6 Hz) and earlier precedents.[6] ^{13}C NMR spectral and mass data are also consistent with the proposed structure.

Similarly to substrate **1a**, 7-carbomethoxy-7-azabenzonorbornadiene (**1b**) reacted with various organic iodides in the presence of $NiCl_2(PPh_3)_2$ and zinc in acetonitrile to afford ring-opening products 2-substituted methyl *N*-[*cis*-1,2-dihydro-1-naphthyl]carbamates (**3**) in good to excellent yields (Table 1, entries 19−24). These catalytic reactions also yield completely stereoselective products. Products **3** were characterized by ^{1}H and ^{13}C NMR, IR, and mass spectral data. Most of these reactions show trends similar to those with **1a** as substrate. The reaction of 4-iodoacetophenone with **1b** (Table 1, entry 24) yields no expected product similar to **2j**; for comparison, the reaction of 4-iodoacetophenone with **1a** (entry 10) afforded product **2j** in 55% yield.

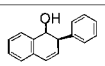
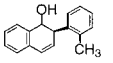
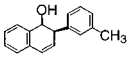
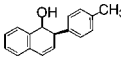
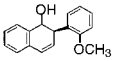
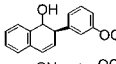
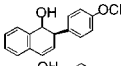
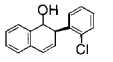
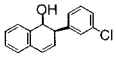
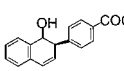
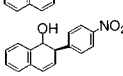
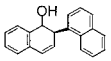
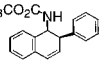
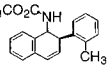
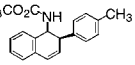
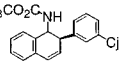
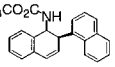
The catalytic reaction is successfully extended to highly substituted 7-oxanorbornenes (**1c**−**e**) as bicyclic alkenes. The addition reaction between iodobenzene and compound **1c** (Table 2, entry 1) in acetonitrile in the presence of $Ni(PPh_3)_2Cl_2$[8] (5 mol %) and zinc (3 equiv) occurs at 70 °C, affording completely stereoselective ring-opening product **4a**. Compound **4a** is fully characterized by spectral methods. Benzyl bromide and α- and *β*-bromostyrenes also give ring-opening products in good yields (Table 2, entries 2−4). The styryl group in compound **4c** was found to be trans, although a mixture of both cis and trans *β*-bromo styrene was used for the addition reaction. 3-Iodopentenone and methallyl bromide (Table 2, entries 5 and 6) failed to give the corresponding ring-opening product. Compound **1d** with two methyl groups attached to bridgehead carbons of the 7-oxanorbornene moiety also undergoes electrophilic ring opening to give stereoselective product **5** (Table 2, entry 7) in moderate yield. For the unsymmetrical 7-oxanorbornene **1e**, the addition reaction in acetonitrile gave two regioisomers **6a** and **6b** in a 2:1 ratio in 72% total yield. The major product **6a** was from addition of the phenyl group to the olefin carbon distal to the bridgehead methyl group. For this nickel-catalyzed ring opening of bicyclic alkenes **1c**−**e**, four fixed stereocenters are readily constructed. It is interesting to note that in the nickel-catalyzed nucleophilic ring opening of bicyclic alkenes involving organomagnesium reagents,[5b] the products observed also possess four stereocenters, but the stereochemistry is different from that observed in eqs 2 and 3.

We showed previously that $PdCl_2(PPh_3)_2$ catalyzed the ring opening of **1a** and **1b**.[6] Because the reaction conditions for nickel and palladium systems are substantially different, it is difficult to compare their catalytic activities. In general, the palladium-catalyzed ring-opening reactions were carried out in THF at 60 °C in the presence of Zn, $ZnCl_2$, and Et_3N, whereas the nickel-catalyzed reactions were performed in acetonitrile in the presence of Zn at 70 °C. The time required for completion of reaction is ca. 2−3 times shorter for the nickel system than for the palladium system. A major difference between these two metal catalysts is that the palladium system does not effectively catalyze ring opening of norbornene derivatives **1c**−**e** with aryl iodides.

(7) (a) Chao, C. S.; Cheng, C.-H.; Chang, C. T. *J. Org. Chem.* **1983**, *48*, 4904. (b) Yang, S. H.; Li, C. S.; Cheng, C.-H. *J. Org. Chem.* **1987**, *52*, 691.

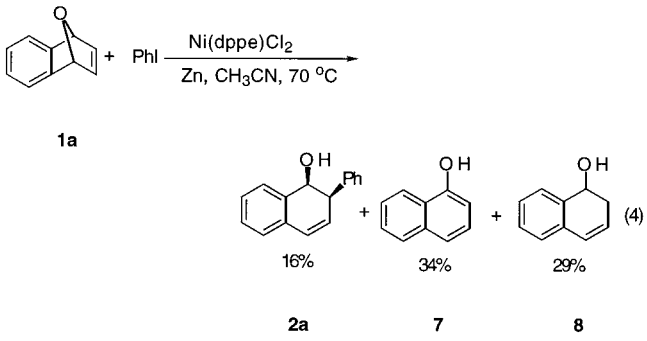
(8) Ni-catalyzed Felkin-type coupling, see: (a) Felkin, H.; Swierczewski, G. *Tetrahedron* **1975**, *31*, 2735. (b) Consiglio, G.; Morandini, F.; Piccolo, O. *Helv. Chim. Acta* **1980**, *63*, 987. (c) Consiglio, G.; Waymouth, R. M. *Chem. Rev.* **1989**, *89*, 257. (d) Wenkert, E.; Fernandes, J. B.; Michelotti, E. L.; Swindell, C. S. *Synthesis* **1983**, 701. (e) Didiuk, M. T.; Morken, J. P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1995**, *117*, 7273. (f) Consiglio, G.; Morandini, F.; Piccolo, O. *J. Am. Chem. Soc.* **1981**, *103*, 1846. (g) Felkin, H.; Joly-Goudket, M.; Davies, S. G. *Tetrahedron Lett.* **1981**, *22*, 1157.

Table 1. Addition Reaction of Organic Iodides with 1a and 1b in the Presence of $NiCl_2(PPh_3)_2$/Zn

Entry	Substrate	RX	Reaction Time (h)	Product		Yield[c] (%)
1	**1a**	C_6H_5I	1.2		**2a**	80 (77)
2	**1a**	*o*-$CH_3C_6H_4I$	2.5		**2b**	70
3	**1a**	*m*-$CH_3C_6H_4I$	1.2		**2c**	83 (78)
4	**1a**	*p*-$CH_3C_6H_4I$	1.2		**2d**	88
5	**1a**	*o*-$CH_3OC_6H_4I$	2.5		**2e**	78 (76)
6	**1a**	*m*-$CH_3OC_6H_4I$	1.2		**2f**	88 (83)
7	**1a**	*p*-$CH_3OC_6H_4I$	2.5		**2g**	72
8	**1a**	*o*-ClC_6H_4I	2.0		**2h**	66 (62)
9	**1a**	*m*-ClC_6H_4I	1.5		**2i**	99
10	**1a**	*p*-$CH_3COC_6H_4I$	8		**2j**	55 (50)
11	**1a**	*p*-$NO_2C_6H_4I$	8		**2k**	trace
12	**1a**	*p*-HOC_6H_4I	2.0	--		--
13[a]	**1a**	*o*-$NH_2C_6H_4I$	2.2	--		--
14	**1a**	*o*-$C_{10}H_7I$	2.0		**2l**	94
15	**1a**	C_6H_5Br	5		**2a**	18
16	**1a**	C_6H_5Br[b]	5		**2a**	17
17[a]	**1a**	C_6H_5Cl	2.2	--		--
18	**1a**	CH_3I	11		**2m**	40
19	**1b**	C_6H_5I	1.4		**3a**	78 (72)
20	**1b**	*o*-$CH_3C_6H_4I$	2.0		**3b**	78
21	**1b**	*p*-$CH_3C_6H_4I$	3.0		**3c**	97
22	**1b**	*m*-ClC_6H_4I	1.5		**3d**	85 (76)
23	**1b**	*o*-$C_{10}H_7I$	12		**3e**	83
24[a]	**1b**	*p*-$CH_3COC_6H_4I$	24	--		--

[a] Starting material was recovered. [b] Reaction was carried out with 4 equiv of KI. [c] Reactions were carried out at 70 °C in CH_3CN, and yields were obtained from NMR spectra using an internal standard (1,3,5-trimethylbenzene); isolated yields are shown in parentheses.

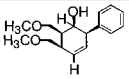
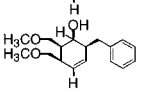
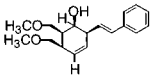
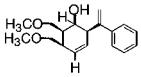
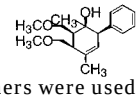
In most cases, addition reaction of aryl iodides to **1a** and **1b** in the presence of $NiCl_2(PPh_3)_2$/Zn produces small amounts of 1-naphthol **7** and 1,2-dihydro-1-naphthol **8**[9,10] (combined yields are less than 10%). Compound **8** became a major product when the catalyst was changed from $NiCl_2(PPh_3)_2$ to $NiCl_2$(dppe) (eq 4). Addition of water (0.5



equiv) increased the yield of 1,2-dihydro-1-naphthol to 44% yield (**8**:**2a** = 7:1). If MeOH was employed as solvent, product **8** was isolated in 81% yield.

Effect of Reaction Conditions on Ring Opening of 1a with Iodobenzene. To understand the effect of reaction conditions on the present catalytic reactions, we carried out the reaction of iodobenzene with **1a** in the presence of $NiCl_2(PPh_3)_2$ and Zn metal in various solvents at different temperatures. To our surprise, of the several tested solvents including toluene, dichloromethane, methanol, DMF, DMSO, and THF, only acetonitrile appears effective for the catalytic reaction, giving 83% yield of addition product **2a** in 1.2 h at 70 °C and 14% yield at room temperature in 24 h. In THF the reaction produced **2a** in 10% yield at 60 °C in 24 h. In other solvents such as toluene, dichloromethane, methanol, DMF, and DMSO, the reaction yielded no **2a**. The lack of catalytic activity in toluene and dichloromethane is likely due to ready decomposition of the Ni(0) catalyst in these essentially noncoordinating solvents. This is evidenced by the observation that in these two cases, the dissolved catalyst lost color rapidly to give a clear solution and precipitate of nickel metal. The absence of product **2a** in MeOH results from the fact that the Ni(0) catalyst is protonated by methanol to yield side product **8**. In strongly coordinating solvents such as DMF and DMSO, **1a** competes ineffectively with solvent molecules for coordination to the nickel center, precluding the addition reaction. It is interesting to note that for the same addition reaction catalyzed by $PdCl_2(PPh_3)_2$ and zinc metal, THF was the best solvent.[6]

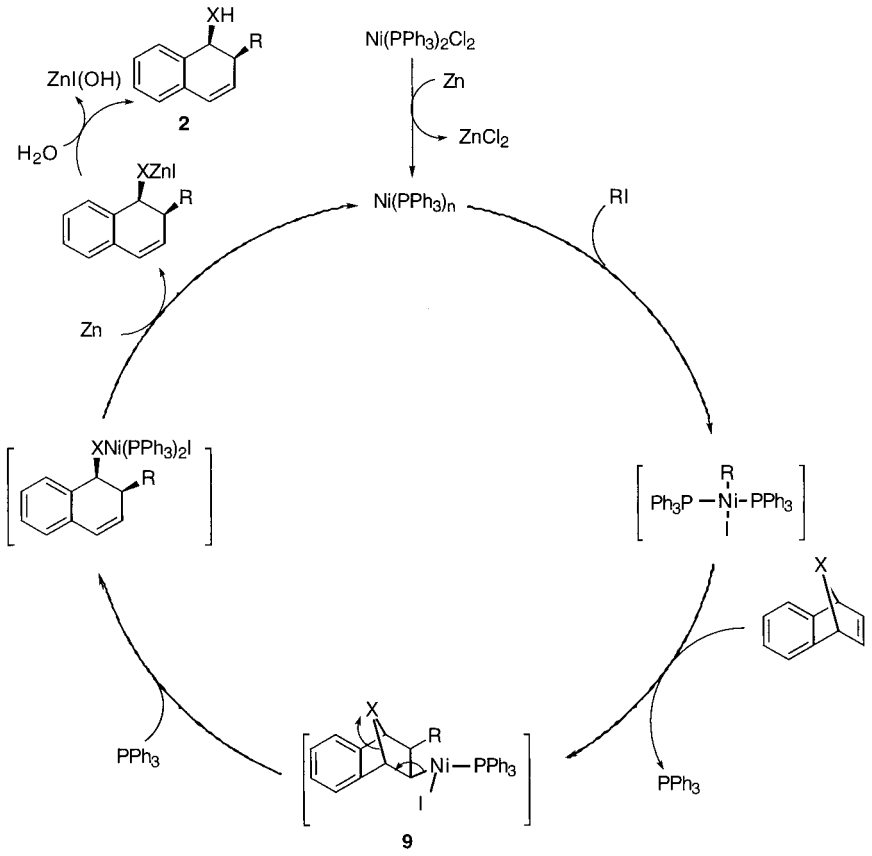
Table 2. Addition Reaction of RX with 1c−e in the Presence of $NiCl_2(PPh_3)_2$/Zn

Entry	Substrate	RX	Reaction Time (h)	Product		Yield[b]
1	**1c**	C_6H_5I	2		**4a**	83
2	**1c**	$C_6H_5CH_2Br$	1		**4b**	85
3	**1c**	$C_6H_5CHCHBr$[a]	1.5		**4c**	71
4	**1c**	$C_6H_5C(Br)CH_2$	1.5		**4d**	79
5	**1c**	C_5H_7IO	3	--		--
6	**1c**	C_4H_7Br	3	--		--
7	**1d**	C_6H_5I	3.5		**5**	52[c]

[a] A mixture of cis and trans isomers were used for the reaction. [b] Isolated yields. [c] Starting material (15%) was recovered.

(9) Brown, H. C.; Prasad, J. V. N. V. *J. Org. Chem.* **1985**, *50*, 3002.
(10) (a) Jeffrey, A. M.; Jerina, D. M. *J. Am. Chem. Soc.* **1972**, *94*, 4048. (b) Agarwal, R.; Boyd, D. R.; McMordie, R. A. S.; O'Kane, G. A.; Porter, P.; Sharma, N. D.; Dalton, H.; Gray, D. J. *J. Chem. Soc., Chem. Commun.* **1990**, 1711 and references therein.

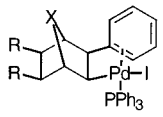
Scheme 1



Excess PPh_3 in the reaction inhibits the catalytic activity. For example, on addition of 2, 8, and 16 equivs of PPh_3 to the reaction of **1a** with iodobenzene, yields of **2a** decreased to 75%, 67%, and 64%, respectively. Apparently, PPh_3 competes effectively with **1a** for coordination to the nickel center and hence inhibits the product formation.

Reaction Mechanism. On the basis of the known chemistry of oxidative addition of aryl halides to Ni(0) complexes and insertion of norbornadiene and its derivatives into metal−carbon bonds, a mechanism shown in Scheme 1 is proposed to account for the present nickel-catalyzed reactions. The first step of the reaction involves the reduction of Ni(II) to Ni(0) by zinc.[11] This is followed by oxidative addition of RX to Ni(0) species to form Ni-$(PPh_3)_2$RI.[12] Exo addition of Ni−R in Ni$(PPh_3)_2$RI to substrate **1** affords intermediate **9**. β-Heteroatom elimination of **9** followed by reduction with zinc metal gives a zinc salt of **2** and regenerates the nickel(0) catalyst, which then reacts with RI to continue the catalytic cycle. Hydrolysis of the zinc salt affords the final product **2**.

To show that Ni$(PPh_3)_2$ArX is an intermediate in the catalytic ring opening, we synthesized NiPh$(PPh_3)_2$Br from the reaction of PhBr with Ni$(PPh_3)_4$.[13] It is noteworthy that the attempt to prepare the corresponding iodide complex NiPh$(PPh_3)_2$I from the reaction of iodobenzene with Ni$(PPh_3)_4$ failed because this complex is thermally unstable. Treatment of NiPh$(PPh_3)_2$Br with **1a** at 60 °C in acetonitrile for 1 h afforded **2a** in essentially quantitative yield. These observations firmly suggest that NiR$(PPh_3)_2$X is an important intermediate for the catalytic ring-opening reaction. The proposed exo addition of an organic group in NiR$(PPh_3)_2$X to **1a** to yield **9** gains strong support from the observed cis stereochemistry of products **2** and the observation that reaction of Pd$(PPh_3)_2$-ArI with norbornadiene or its derivatives yielded Pd complexes **10** in which the aryl group and the Pd center are all at an exo position.[14] Both Pd$(PPh_3)_2$ArI and **10** are active catalytic intermediates in addition reactions of aryl halides to **1a** to give **2** in the presence of the $PdCl_2$-$(PPh_3)_2/ZnCl_2/Zn/NEt_3$ system.



10

R = H, CO_2Me
X = CH_2, O

The observed retardation of the reaction rate by excess PPh_3 indicates that dissociation of PPh_3[15] from Ni$(PPh_3)_2$-ArI to create a vacant coordination site so as to accommodate the incoming substrate 7-heteroatom norbornadiene in the proposed catalytic cycle (Scheme 1) is a rate-limiting step. Further evidence for dissociation of PPh_3 from Ni$(PPh_3)_2$ArI[16] arises from the observation that replacement of Ni$(PPh_3)_2Cl_2$ by Ni(dppe)Cl_2 as the cata-

(11) (a) Kende, A. S.; Liebeskind, L. S.; Braitsch, D. M. *Tetrahedron Lett.* **1975**, 3375. (b) Zembayashi, M.; Tamao, K.; Yoshida, J.; Kumada, M. *Tetrahedron Lett.* **1977**, 4089. (c) Takagi, K.; Hayama, N. *Chem. Lett.* **1983**, 637. (d) Takagi, K.; Hayama, N.; Inokawa, S. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 3691.

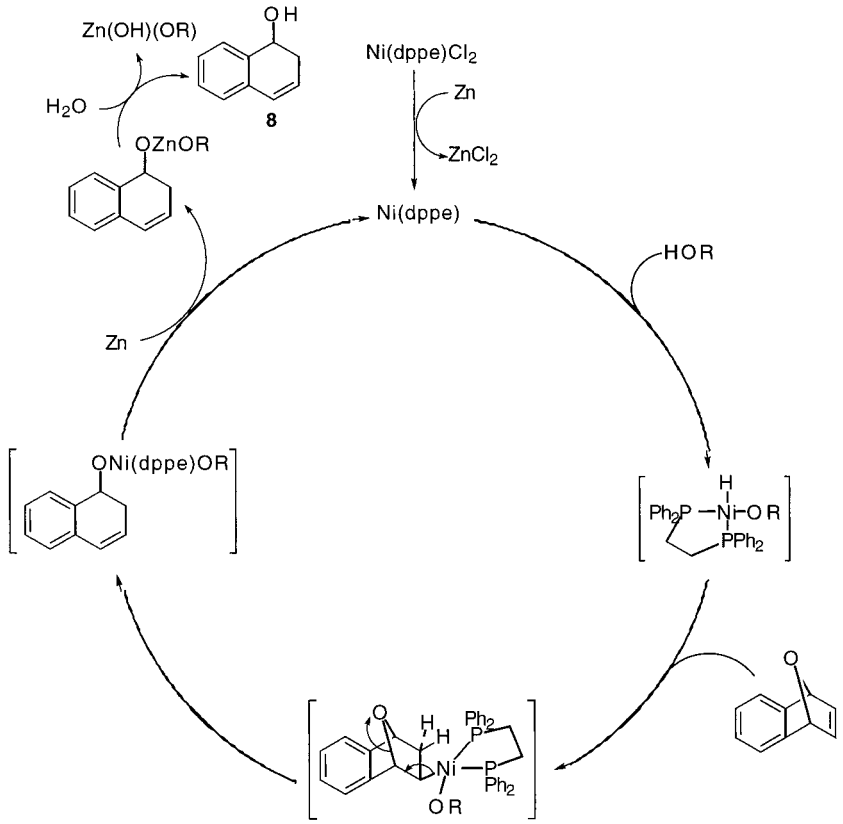
(12) (a) Amatore, C.; Jutand, A. *Organometallics* **1988**, *7*, 2203. (b) Morrell, D. G.; Kochi, J. K. *J. Am. Chem. Soc.* **1975**, *97*, 7262.

(13) Hidai, M.; Kashiwagi, T.; Ikeuchi, T.; Uchida, Y. *J. Organomet. Chem.* **1971**, *30*, 279.

(14) Duan, J. P.; Cheng, C.-H. *J. Chin. Chem. Soc.* **1994**, *41*, 749.

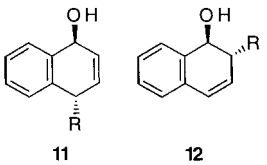
(15) (a) Brumbaugh, J. S.; Whittle, R. R.; Parvez, M.; Sen, A. *Organometallics* **1990**, *9*, 1735. (b) Samsel, E. G.; Norton, J. R. *J. Am. Chem. Soc.* **1984**, *106*, 5505.

Scheme 2



lyst for addition of iodobenzene with **1a** sharply decreased the yield of **2a**. The bidentate dppe ligand is expected to be much less favored for dissociation. The solvent dependence of the present addition may be understood on the basis of the dissociation of PPh_3 from $Ni(PPh_3)_2ArI$ and competition of substrate **1a** with solvent molecules for the vacant site. In the strongly coordinating solvents dimethylformamide and dimethyl sulfoxide, the vacant site generated is completely occupied by a solvent molecule, leading to complete deactivation of the catalyst.

Another possible mechanism for the present nickel-catalyzed ring-opening reaction involves a nickel π-allyl complex as suggested by Lautens et al.[5b] Oxidative addition of compound **1** to Ni(0) forms a π-allyl complex. Reaction of the latter with RZnX generated from the reaction of organic halide (RX) with zinc metal followed by hydrolysis gives compound **2**. To explore the possibility of this mechanism, several experiments were carried out, leading to the following observations. First, the reaction of PhZnCl and **1a** in the presence of $Ni(PPh_3)_2Cl_2$ in acetonitrile at 70 °C yields no **2a**, but produces the biphenyl in 78% yield. Second, a control reaction indicates that there is no reaction of iodobenzene with the zinc metal powder we used in THF or acetonitrile at 60−70 °C. Third, for all reactions shown in eq 1, there are no ring-opening products **11** and **12**, which were observed for the ring-opening reaction involving a nickel π-allyl complex as catalyst intermediate. On the basis of the above observations, a nickel π-allyl mechanism is unlikely.



11 **12**

An acid-catalyzed aromatization of **1a** likely accounts for formation of side product **7**.[6] This is evidenced by the observation that heating **1a** in the presence of zinc halide, which is produced in the catalytic reaction, in acetonitrile leads to formation of **7** in quantitative yield. For the formation of product **8** (Scheme 2), the reaction pathway likely involves a Ni(II) hydride, generated in situ by reducing NiL_2Cl_2 with zinc metal followed by oxidative addition of a water or alcohol molecule. Subsequent insertion of **1a** into the Ni(II)−hydride bond and β-heteroatom elimination followed by reduction with zinc metal gives a zinc metal salt and regenerates the nickel(0) catalyst. Hydrolysis of the zinc salt affords product **8**. Pentacoordinated Ni(II) hydride[17] is probably a reactive intermediate as $Ni(dppe)Cl_2$ showed greater selectivity for product **8** than did $Ni(PPh_3)_2Cl_2$.

Conclusion

We have developed a nickel-catalyzed stereoselective ring opening of oxa- and azabicyclic alkenes with various organic halides. This methodology is successfully extended to highly substituted 7-oxanorbornenes to give products with multiple stereocenters. The nickel catalyst is more active than the previously reported palladium analogue; the latter is unable to promote ring opening of oxabicyclic [2.2.1] compounds. The mechanism for the present catalytic reaction, involving oxidative addition of an organic halide to a nickel(0) species as a key step,

(16) Ozawa, F.; Kubo, A.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 1417.

(17) Rajanbabu, T. V.; Casalnuovo, A. L. *J. Am. Chem. Soc.* **1996**, *118*, 6325.

differs completely from that proposed by Lautens et al. for nucleophilic ring openings of oxabicyclic compounds catalyzed by nickel complexes.

Experimental Section

All reactions were conducted under a nitrogen atmosphere on a dual-manifold Schlenk line using purified deoxygenated solvents and standard inert atmosphere techniques, unless otherwise stated. Reaction chemicals were used as purchased without further purification. The catalysts $NiCl_2(PPh_3)$[2,18] and $NiCl_2$(dppe),[18] 3-iodocyclopentenone, and *N*-carbomethoxy-7-azabenzonorbornadiene[19] were synthesized according to reported procedures.

General Reaction Procedure for the Reaction of Organic Iodides with 7-Oxa-, 7-Azanorbornadienes or 7-Oxanorbornenes (1a−e). A round-bottom sidearm flask (50 mL) was charged with $NiCl_2(PPh_3)_2$ (0.016 g, 0.025 mmol), zinc powder (0.315 g, 5 mmol), a 7-heteroatom norbornene derivative (0.500 mmol), and a magnetic stirring bar. After the flask was sealed with a rubber septum, the system was evacuated and purged with nitrogen gas three times. A mixture of freshly distilled acetonitrile (3.0 mL) and organic halide (1.00 mmol) was added via a syringe through the rubber septum into the flask. The mixture was heated with stirring at 70 °C until the 7-heteroatom norbornene derivative was consumed as indicated by TLC analysis of the solution. During the reaction, the color of the mixture gradually changed from green to yellow-green and remained the same color for the rest of reaction period. The reaction mixture was then cooled and stirred under air for 20 min at room temperature. After filtration through Celite, the solution was concentrated on a rotary evaporator and separated on a silica gel column using a mixture of ethyl acetate/hexane as eluent to give the pure addition product.

Products **2a**−**m**, **3a**−**e**, **4a**−**d**, and **5** were obtained with this procedure. Compounds **2a**−**d**, **2f**−**g**, **2i**−**l**, **3a**,**c**, and **4a**,**b** were characterized by comparing their spectral data with those reported earlier. Important spectral data for products **2e**,**h**,**m**, **3b**,**e**, **4c**,**d**, and **5** follow.

***cis*-1,2-Dihydro-2-(2-methoxyphenyl)-1-naphthol (2e):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.02 (d, J = 5.31 Hz, OH, 1H), 3.86 (s, OCH_3, 3H), 4.42 (ddd, J = 5.55 Hz, J = 2.85 Hz, J = 2.84 Hz, 1H), 4.91 (t, J = 5.28 Hz, 1H), 6.05 (dd, J = 9.67 Hz, J = 3.50 Hz, 1H), 6.72 (dd, J = 9.66 Hz, J = 2.46 Hz, 1H), 6.94 (m, 2 H), 7.12−7.37 (m, 6H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 40.29, 55.44, 69.94, 110.48, 120.82, 126.32, 126.82, 127.46, 127.72, 128.01, 128.21, 128.26, 129.77, 130.07, 132.35, 135.72, 157.23; IR (neat) 3526, 3456, 3034, 2930 cm^{-1}; HRMS calcd for $C_{17}H_{16}O_2$ 252.1150, found 252.1140.

***cis*-1,2-Dihydro-2-(2-chlorophenyl)-1-naphthol (2h):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.56 (d, J = 6.21 Hz, OH, 1H), 4.49 (m, 1H), 4.89 (t, J = 5.43 Hz, 1H), 6.04 (dd, J = 9.50 Hz, J = 2.84 Hz, 1H), 6.74 (dd, J = 6.74 Hz, J = 2.78 Hz, 1H), 7.19−7.48 (m, 8H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 43.98, 69.17, 126.68, 126.93, 127.95, 128.05, 128.28, 128.40, 128.77, 128.99, 129.52, 130.95, 132.06, 134.13, 136.85; IR (neat) 3389, 3048, 2913 cm^{-1}; HRMS calcd for $C_{16}H_{13}OCl$ 256.0655, found 256.0641.

***cis*-1,2-Dihydro-2-methyl-1-naphthol (2m):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (d, J = 7.60 Hz, CH_3, 3H), 1.55 (s, OH, 1H), 2.61−2.69 (m, 1H), 4.58 (d, J = 4.40 Hz, 1H), 5.80 (dd, J = 9.50 Hz, J = 3.00 Hz, 1H), 6.51 (dd, J = 9.50 Hz, J = 2.40 Hz, 1H), 7.11 (dd, J = 6.80 Hz, J = 1.60 Hz, 1H), 7.22−7.30 (m, 2H), 7.36 (dd, J = 6.80 Hz, J = 1.2 Hz, 1H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 13.86, 35.10, 71.43, 126.26, 126.41, 127.12, 127.47, 128.22, 132.26, 132.41, 136.55; IR (neat) 3262, 2965 cm^{-1}; HRMS calcd for $C_{11}H_{12}O$ 160.0888, found 160.0889.

Methyl *N*-[*cis*-1,2-Dihydro-2-(2-methylphenyl)-1-naphthyl]carbamate (3b): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.39 (s, CH_3, 3H), 3.52 (s, OCH_3, 3H), 4.20 (br s, 1H), 4.79 (br d, J = 9.58 Hz, NH, 1H), 5.26 (br t, J = 8.17 Hz, 1H), 6.05 (dd, J = 9.65 Hz, J = 4.22 Hz, 1H), 6.68 (dd, J = 9.58 Hz, J = 2.06 Hz, 1H), 7.03−7.31 (m, 8H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 19.61, 40.53, 51.57, 52.07, 126.08, 126.29, 126.45, 127.12, 128.00, 128.13, 128.25, 128.52, 130.51, 130.66, 132.82, 134.46, 136.40, 136.58, 156.44; IR (neat) 3367, 3038, 2944, 1714 cm^{-1}; HRMS calcd for $C_{19}H_{19}NO_2$ 293.1416, found 293.1417.

Methyl *N*-[*cis*-1,2-Dihydro-2-(3-chlorophenyl)-1-naphthyl]carbamate (3d): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.64 (s, OCH_3, 3H), 3.84 (br t, J = 5.22, 1H), 4.74 (br d, J = 9.99 Hz, NH, 1H), 5.32 (br t, J = 8.46 Hz, 1H), 6.09 (dd, J = 9.69 Hz, J = 4.86 Hz, 1H), 6.72 (dd, J = 9.63 Hz, J = 1.65 Hz, 1H), 6.99−7.31 (m, 8H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 44.65, 52.26, 52.71, 125.55, 126.61, 127.15, 127.56, 128.05, 128.36, 128.84, 129.07, 129.29, 129.70, 132.85, 134.12, 134.25, 139.75, 156.51; IR (neat) 3419, 3319, 3039, 2953, 2843, 1713 cm^{-1}; HRMS calcd for $C_{18}H_{16}N_2OCl$ 313.0870, found 313.0856.

Methyl *N*-(*cis*-1,2-Dihydro-2-naphthyl-1-naphthyl)carbamate (3e): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.44 (s, OCH_3, 3H), 4.77 (br d, J = 9.21 Hz, NH, 1H), 4.88 (br t, J = 9.99 Hz; 1H), 5.45 (br t, J = 8.37 Hz, 1H), 6.20 (dd, J = 9.65 Hz, J = 4.28 Hz, 1H), 6.77 (dd, J = 9.63 Hz, J = 1.95 Hz, 1H), 7.17−7.55 (m, 8H), 7.74 (t, J = 4.68 Hz, 1H), 7.86 (d, J = 7.83 Hz, 1H), 8.16 (d, J = 8.25 Hz, 1H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 39.30, 51.96, 52.58, 123.04, 125.32, 125.58, 126.09, 126.32, 126.59, 127.73, 127.94, 128.08, 128.20, 128.35, 128.77, 129.04, 130.67, 132.30, 132.95, 133.82, 133.94, 134.46, 156.50; IR (neat) 3416, 3320, 3046, 2953, 1712 cm^{-1}; HRMS calcd for $C_{22}H_{19}NO_2$ 329.1418, found 329.1416.

(1*R,2*R**,5*R**,6*R**)-5,6-Bis(methoxymethyl)-2-(*β*-styryl)-cyclohex-3-en-1-ol (4c):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (ddd, J = 8 Hz, J = 7 Hz, J = 2 Hz, 1H), 2.57 (m, 1H), 3.1 (m, 1H), 3.38 (s, 3H), 3.4 (s, 3H), 3.46 (d, J = 10 Hz, 2H), 3.55 (d, J = 8 Hz, 2H), 3.86 (dd, J = 10 Hz, J = 2 Hz, 1H), 4.16 (d, J = 10 Hz, 1H), 5.63 (dd, J = 10 Hz, J = 1 Hz, 1H), 5.71 (dd, J = 10 Hz, J = 3 Hz, 1H), 6.43 (dd, J = 16 Hz, J = 7 Hz, 2H), 7.16 (d, J = 7 Hz, 1H), 7.24 (d, J = 8 Hz, 2H), 7.36 (d, J = 8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 36.14, 41.18, 45.88, 58.84, 67.78, 71.33, 72.74, 126.18, 126.97, 128.35, 128.82, 130.67, 131.31, 137.63; IR (neat) 3384, 3024, 2885, 2242 cm^{-1}; HRMS calcd for $C_{18}H_{24}O_3$ 288.1725, found 288.1719.

(1*R,2*R**,5*R**,6*R**)-5,6-Bis(methoxymethyl)-2-(α-styryl)-cyclohex-3-en-1-ol (4d):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (q, J = 8 Hz, 6 Hz, 1H), 2.57 (m, 1H), 3.29 (s, 3H), 3.34 (s, 3H) 3.46 (m, 4H), 3.54 (dd, J = 10 Hz, J = 2 Hz, 1H), 3.75 (d, J = 9 Hz, 1H), 5.11 (s, 1H), 5.38 (s, 1H), 5.82 (m, 1H), 7.28 (m, 5H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 36.13, 41.46, 46.87, 58.74, 58.8, 64.07, 71.48, 73.04, 114.65, 126.74, 127.3, 128.17, 128.26, 129.06, 142.02, 149.13; IR (neat) 3408, 2894 cm^{-1}; HRMS calcd for $C_{18}H_{24}O_3$ 288.1725, found 288.1716.

(1*R,2*R**,5*R**,6*R**)-5,6-Bis(methoxymethyl)-4-methyl-2-phenyl-cyclohex-3-en-1-ol (5):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 (s, 3H), 1.70 (s, 3H), 2.34 (m, 1H), 2.48 (m, 1H), 3.34 (s, 3H), 3.39 (s, 3H), 3.48 (d, J = 10 Hz, 1H), 3.59 (d, J = 10 Hz, 1H), 3.71 (dd, J = 15 Hz, J = 6 Hz, 2H), 3.78 (dd, J = 15 Hz, J = 6 Hz, 2H), 4.69 (s, 1H), 5.37 (s, 1H), 7.23 (m, 5H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 21.76, 24.94, 40.39, 46.32, 54.29, 58.70, 58.89, 67.79, 68.50, 70.47, 126.20, 126.86, 127.36, 130.68, 132.97, 141.78; IR (neat) 3424, 2905 cm^{-1}; HRMS calcd for $C_{18}H_{24}O_2$ (M^+ − O) 272.1776, found 272.1760.

Acknowledgment. We thank the National Science Council of the Republic of China for financial support (Grant NSC85-2113-M-007-004) of this work, and M.N. and T.S. thank NSC for postdoctoral fellowships.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra for **2e**,**h**, **3b**,**d**−**e**, **4c**−**d**, and **5** are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

JO982312E

(18) (a) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation*; Plenum Press: New York, 1991. (b) Colquhoun, H. M.; Holton, J.; Thompson, D. J.; Twigg, M. V. *New Pathways For Organic Synthesis−Practical Applications of Transition Metals*; Plenum Press: New York, 1988.

(19) Cragg, G. M. L.; Giles, R. G. F.; Roos, G. H. P. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1339.