ORGANIC LETTERS

2008
Vol. 10, No. 17
3689−3692

Asymmetric Ring-Opening Reaction of Oxabicyclic Alkenes with Aryl Boronic Acids Catalyzed by P-Containing Palladacycles

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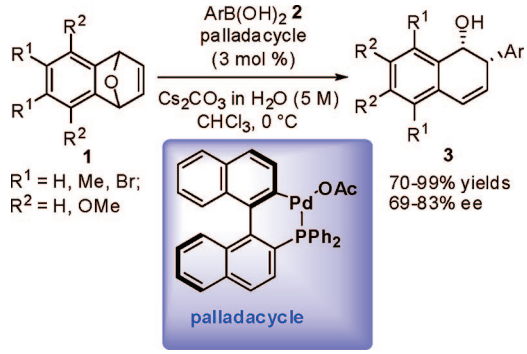
Received June 9, 2008

ABSTRACT



The chiral phosphine-containing palladacycle, synthesized easily from H-MOP, showed its high catalytic activity as well as asymmetric induction ability in ring-opening reaction of oxabicyclic alkenes with arylboronic acids, providing corresponding products in high yields and high ee.

Palladacycles represent an important class of catalyst in organic synthesis because of their easy availability, extra stability toward air and moisture, versatile frameworks, and high catalytic activity.[1] Since Herrmann and Beller reported the first example using the highly active cyclopalladated tri-*o*-tolylphosphine as a catalyst in Heck reaction,[2] many kinds of palladacycles have been synthesized and applied in a variety of reactions and a high turnover number (TON) was achieved in some reactions.[3] Although palladacycles have shown many advantages in catalysis, they are mainly used in Heck-type reactions and coupling reactions,[1,2,4,5] and mechanistic studies showed that they served as catalyst precursors in these kinds of reactions.[1d,4m,5e,6] Asymmetric induction has been realized in some examples;[7] however, chiral palladacycles served as Lewis acids in most cases. Also, racemic products were given in some other examples despite chiral palladacycles being used.[5f,8] To explore the applications of palladacycles as real transition metal catalysts in asymmetric catalysis is still a challenge.

In our previous work,[8,9] we developed several benzylic substituted palladacycles and demonstrated their highly

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10.1021/ol801294b CCC: $40.75
Published on Web 08/07/2008

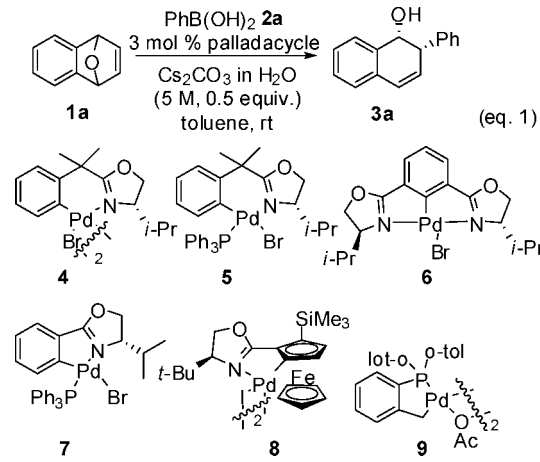
catalytic activity in the hydrophenylation of norbornenes and in the ring-opening reaction of oxabicyclic alkenes with organozinc halides prepared in situ. The ^{31}P NMR studies of ring-opening reaction implied that the palladacycle was the real catalyst in the reactions. However, racemic products were separated though the palladacycle was optically active. After testing several reagents, it was found that optically active product was obtained when phenylboronic acid was used as reagent, although the ee was lower. Further study showed that the ee value greatly increased when phosphorus-containing palladacycle was used.[5g,h,10] In this letter, we report our preliminary results in the asymmetric ring-opening reaction of oxabicyclic alkenes with arylboronic acids catalyzed by palladacycles.

At the beginning of our study, we tested the palladacycles **4**−**9** in the ring opening of 7-oxabicycle alkene **1a** with phenyl boronic acid **2a** (eq 1, Table 1). The results showed that all N-containing palladacycles **4**−**8** gave product in lower yields (entries 1−2 and 4−6), though pincer complex **6** and Overman's palladacycle **8** provided product in 57% ee (entries 4 and 6). Pd black also appeared using palladacycle dimer **4**. When the reaction proceeded at 60 °C using benzylic substituted palladacycle **5**, a 92% yield of product in 18% ee was obtained (entry 3). However, palladacycle **9** with phosphorus as the coordination atom showed its highly catalytic activity in the reaction, providing product **3a** in 95% yield (entry 7).

Table 1. Optimization of Palladacycle-Catalyzed Ring Opening of **1a** with $PhB(OH)_2$ **2a**[a]

entry	palladacycle	solvent	yield %[b]	ee %[c]
1	**4**	toluene	trace	−
2	**5**	toluene	trace	−
3[d]	**5**	toluene	92	18
4	**6**	toluene	17	57[e]
5	**7**	toluene	45	4
6	**8**	toluene	10	57[e]
7	**9**	toluene	95	−
8	**11**	toluene	95	64
9	**11**	THF	86	65
10	**11**	MeOH	94	65
11	**11**	Et_2O	86	65
12	**11**	CCl_4	90	58
13	**11**	DMF	80	55
14	**11**	CH_3CN	73	60
15	**11**	CH_2Cl_2	96	76
16	**11**	$CHCl_3$	95	78
17[f]	**11**	$CHCl_3$	95	79

[a] Reaction conditions: **1a**:$PhB(OH)_2$:palladacycle:Cs_2CO_3 = 1:1.2:0.03:0.5. [b] Isolated yield. [c] Determined by chiral HPLC. [d] Run at 60 °C. [e] Opposite enantiomer observed (HPLC). [f] Run at 0 °C.



The above results indicate that the catalytic activity of P-palladacycles is higher than N-palladacycles. This suggested that chiral P-palladacycles should be synthesized and tested. H-MOP was used as starting material because it has demonstrated its excellent asymmetric induction ability in many reactions.[11] Reaction of (*S*)-H-MOP and $Pd(OAc)_2$ in the ratio 1:1 in toluene at 50 °C led to the formation of the axial−chiral palladacycle **11** in 65% yield, which is air,

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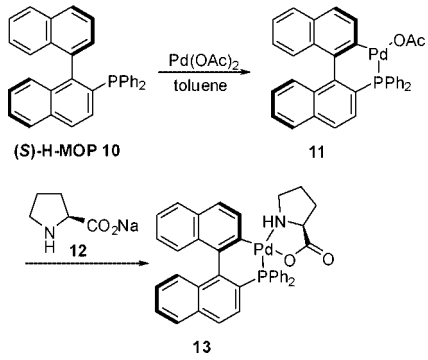
Scheme 1. Synthesis of P-Containing Palladacycles **11** and **13**

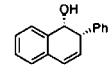
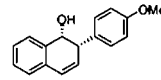
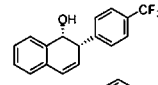
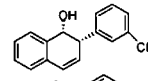
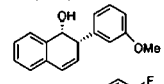
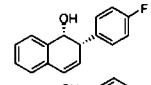
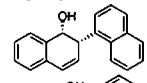
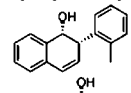
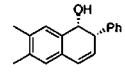
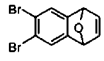
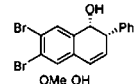
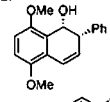
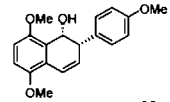
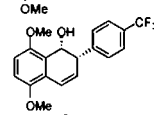
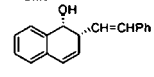


moisture, and thermally stable. It was converted to P-palladacycle **13** by treatment with proline sodium salt (Scheme 1). The structure of **13** was confirmed by X-ray diffraction analysis (see Supporting Information), from which we can see that Pd connects with C2′ of H-MOP.[12]

With chiral P-containing palladacycle **11** in hand, it was applied in the ring-opening reaction of oxabicycles with aryl boronic acids. The results are listed in Table 1.

From Table 1, we can see that the reaction proceeded smoothly in most solvents to give the product in excellent yields (entries 8−17). The best result was obtained when chloroform was used as solvent, when the ee value of the product **3a** was 78% and the yield was 95% (entry 16). The ee value for **3a** was 79% when the reaction was run at 0 °C (entry 17). When other bases, such as potassium fluoride, potassium orthophosphate, and potassium carbonate were

Table 2. Asymmetric Ring Opening of Oxabicyclic Alkenes with Aryl Boronic Acids[a]

entry	substrate **1**		**2**, Ar	product, **3**		yield%[b]	ee%[c]
1		**a**	phenyl		**a**	95	79
2		**a**	4-MeOC$_6$H$_4$		**b**	94	79
3		**a**	4-CF$_3$C$_6$H$_4$		**c**	95	73
4		**a**	3-ClC$_6$H$_4$		**d**	92	74
5		**a**	3-MeOC$_6$H$_4$		**e**	91	73
6		**a**	4-FC$_6$H$_4$		**f**	95	72
7		**a**	1-naphthyl		**g**	70	19
8		**a**	2-MeC$_6$H$_4$		**h**	85	30
9		**b**	phenyl		**i**	96	73
10		**c**	phenyl		**j**	90	83
11		**d**	phenyl		**k**	99	68
12		**d**	4-MeOC$_6$H$_4$		**l**	99	71
13		**d**	4-CF$_3$C$_6$H$_4$		**m**	71	70
14		**a**	PhCH=CH		**n**	76	79

[a] Reaction conditions: **1**:**2**:**11**:Cs_2CO_3 = 1:1.2:0.03:0.5. [b] Isolated yield. [c] Determined by chiral HPLC.

used, almost the same yields of product but lower ee values were obtained (not shown in the table).

Under the optimized conditions, the substrate scope of the oxabicyclic alkenes and aryl boronic acids was evaluated (eq 2, Table 2). Phenylboronic acid (entries 1 and 9−11) and most of the aryl boronic acids with electon-donating groups (entries 2, 5, and 12) and electron-withdrawing groups (entries 3, 4, 6, and 13) reacted with different substituted oxabicyclic alkenes **1** smoothly to provide corresponding ring-opening products in good to excellent yields. The ee values were from 68% to 83%, except for 2-methylphenyl and naphthylboronic acids, which gave products in good yield but lower ee (entry 7 and entry 8). Substituents on the oxabicyclic alkene have some effect on the reaction. For example, the ee value of the product increased to 83% when an electron-withdrawing group Br was present in **1** (entry 10), while the presence of electron-donating Me and MeO groups in **1** lowered the ee value of the products (entry 9 and entry 11). The substituents did not, however, influence the yields. Cinnamyl boronic acid was also a suitable reagent for the reaction, providing the product in 76% yield and in 79% ee (entry 14). The absolute configuration of product **3a** was assigned as (1*R*, 2*S*) by comparison its HPLC trace with that of an authentic sample.[13]

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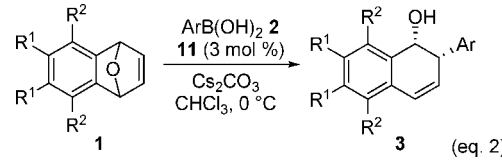
In conclusion, a highly efficient ring-opening reaction has been realized using chiral palladacycle as the catalyst, which represents an example of a palladacycle as a transition metal catalyst in asymmetric catalysis. Further investigations on the applications of palladacycles in asymmetric reactions are in progress.



(eq. 2)

Acknowledgment. Financially supported by the Major Basic Research Development Program (2006CB806100), National Natural Sciences Foundation of China (20532050, 20672130), Chinese Academy of Science, Croucher Foundation of Hong Kong, and Shanghai Committee of Science and Technology. T.K.Z. gratefully thanks the Croucher Foundation of Hong Kong for a studentship. This paper is dedicated to Professor Xiyan Lu on the occasion of his 80th birthday.

Supporting Information Available: Synthesis of palladacycles **11** and **13** and CIF file for **13**. Experimental procedure for ring opening-reaction, ^{1}H and ^{13}C NMR spectra, as well as HPLC data for products **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL801294B