Metal Promoted Synthesis of Heterocycles from Heteroacyclic Compounds

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New synthetic methods, based upon metal mediated or catalyzed C-C/C-O/C-N bond formation, for heterocycles and their application to natural product syntheis are described.

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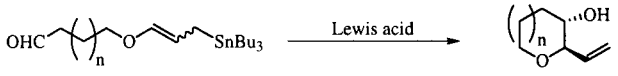
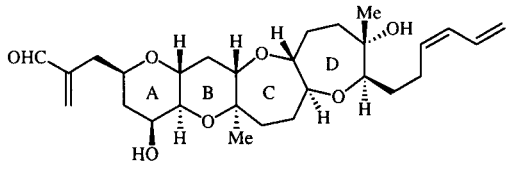
(1) Synthesis of Cyclic Ethers through Allylic Tin-Aldehyde Condensation. Synthesis of Marine Natural Products.

For many years, we have been investigating inter- and intra-molecular allylic tin-aldehyde condensation reactions [1]. The Lewis acid mediated intramolecular reaction of allylic tin having aldehyde at the terminus of the carbon chain gave the corresponding ß-hydroxy cyclic ethers stereoselectively in high yields. This reaction was applied to the stereocontrolled total synthesis of hemibrevetoxin B [2].





Hemibrevetoxin B

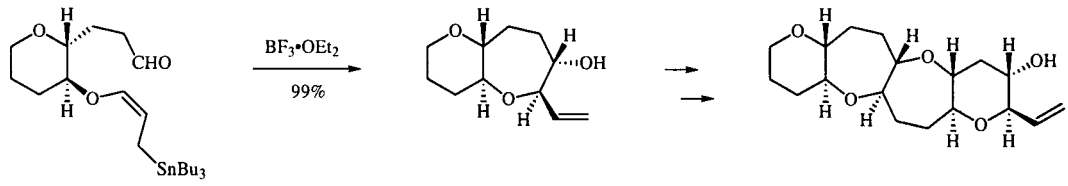
Hemibrevetoxin B (**1**), which has a 6,6,7,7-tetracyclic ether skeleton including 10 stereocenters, an α-vinyl aldehyde and a (*Z*)-diene moiety, was isolated from the cultured cells of the red tide organism *Gymnodinium breve* by Shimizu in 1989 [3]. The unique structural features have attracted the attention of synthetic chemists, and a number of strategies have been investigated. The first total synthesis of hemibrevetoxin B (**1**) was accomplished by Nicolaou in 1992 and the second was achieved by us in 1995. More recently, the Nakata and Mori groups have also reported the total and formal total syntheses of **1**, respectively. The serious drawback of our previous synthesis was that the conversion of allyl ether to γ-alkoxyallylstannane in a certain stage resulted in only 16% yield (*vide post* **30**), although good yields were obtained in the other steps. Now, we have found a new method for the synthesis of γ-alkoxyallylstannanes, and by using this method the problem has been solved.

Strategy and Retrosynthetic Analysis.

The allylic tin-aldehyde condensation is recognized to be one of the most powerful methods for the synthesis of oxepane derivatives [4]. For example, the reaction of monocyclic ether **2** with BF_3•OEt_2 gave quantitatively the cyclic ether **3** as the sole product (Scheme 1). The characteristic features of this reaction are not only the high yield and high stereoselectivity, but also the presence of a hydroxy and a vinyl group attached to the newly formed cyclic ether skeleton. Further manipulation based on these two functional groups can lead to aldehyde and γ-alkoxyallylstannane side chains, thus the repeated use of the cyclization produced the 6,7,7,6-tetracyclic ether **4** which is a part of brevetoxin B. Encouraged by these successful results, we examined the retrosynthetic analysis of hemibrevetoxin B (**1**) as illustrated in Scheme 2.

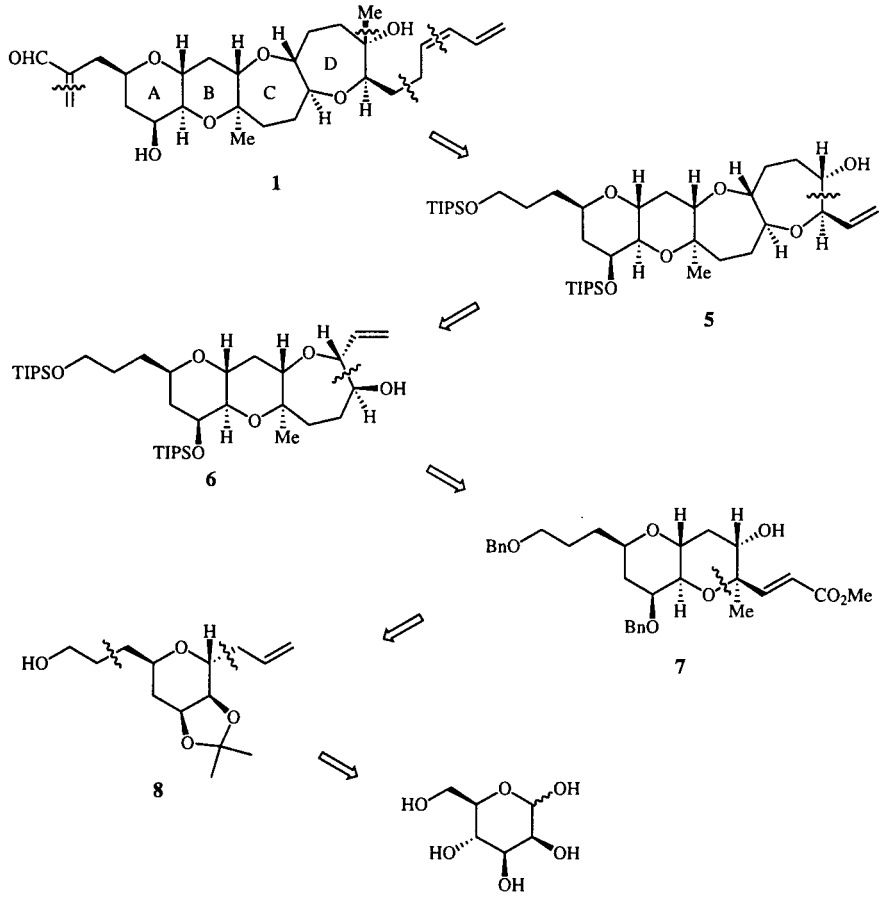
Since constructions of the α-vinyl aldehyde and (*Z*)-diene moieties have been developed by Nicolaou, we focused our efforts on the synthesis of the potential precursor **5**. Sequential retrosynthetic disassembly of the bis-oxepane ring system of **5** based on the allylic tin methodology mentioned above allowed the generation of the intermediate **7** *via* **6**. The B ring of **7** was then retrosynthetially bro-

Scheme 1



2 **3** **4**

Scheme 2
Retrosynthetic Analysis of Hemibrevetoxin B (1)



ken by an epoxide opening-ring closure reaction leading to the known starting material **8**, which can be derived from D-mannose.

Synthesis of the AB Ring System.

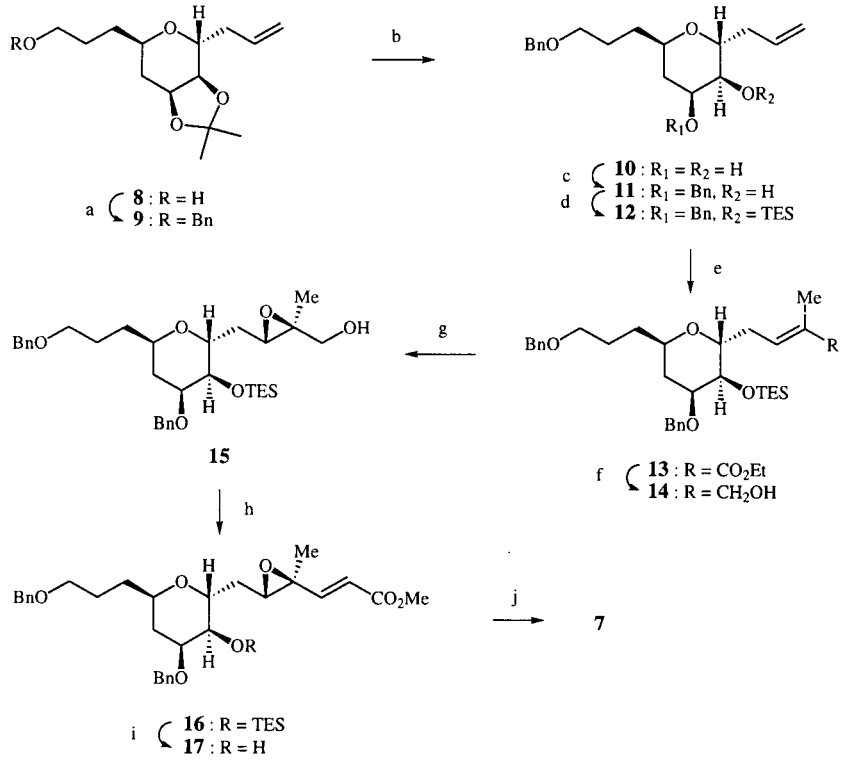
The preparation of AB ring system was carried out primarily based on a modification of Nicolaou's method (Scheme 3). Thus, protection of the primary alcohol of **8** as a benzyl ether led to **9**, followed by methanolysis of the acetonide group to give the diol **10** quantitatively. Allylic alcohol **14** was produced in five steps as shown in Scheme 3. Sharpless asymmetric epoxidation of **14** using (+)-diethyl tartrate (DET) as a chiral auxiliary gave the epoxide **15**, which was converted to ester **17** as illustrated in Scheme 3. Cyclization of the hydroxy epoxide **17** with camphorsulfonic acid gave **7** to complete synthesis of the AB ring system.

Construction of the C Ring.

The stereocontrolled synthesis of the C ring is shown in Scheme 4. The secondary hydroxy group of **7** was protected as an acetate to give **18**, debenzylation and hydrogenation of which afforded the diol **19** in high yield. The free OH groups were protected with triisopropylsilyl triflate to give the bis-silyl ether **20** quantitatively. Reduction of **20** with $LiAlH_4$ afforded the diol **21** in 100% yield. Selective protection of the primary alcohol followed by allylation of the secondary alcohol and selective cleavage of the TES ether under mild acidic conditions gave the allyl ether **22**. Generation of the corresponding allylic anion by using excess *sec*-BuLi/TMEDA followed by trapping with *n*-Bu_3SnCl afforded **23**, which was oxidized to produce the cyclization precursor **24**.

Aldehyde **24** was then subjected to the cyclization by treatment with $BF_3{\cdot}OEt_2$ at -78° to give the desired tricyclic ether **6** in 94% yield with high stereoselectivity. Although the stereochemistry of **6** was not confirmed at this stage, we presumed it from the preliminary study described in Scheme 1. The observed high stereoselectivity can be explained by the well-accepted acyclic transition state model (Figure 1) [5].

Scheme 3 [a]



[a] (a) BnBr, KH, THF, room temperature, 98%; (b) HCl, MeOH, room temperature, 100%; (c) (i) Bu_2SnO, MeOH, reflux; (ii) BnBr, CsF, DMF, room temperature, 94%; (d) Chloromethylsilane (TESCl), imidazole, DMF, room temperature, 99%; (e) (i) O_3, CH_2Cl_2, -78°, then Ph_3P, room temperature; (ii) $Ph_3P{=}C(Me)CO_2Et$, benzene, reflux, 91%; (f) Diisobutyaluminum hydride (DIBALH), CH_2Cl_2, -78°, 87%; (g) (+)-DET, Ti(O-*i*-Pr)$_4$, *t*-BuOOH, 4A molecular sieves, CH_2Cl_2, -20°; (h) (i) SO_3•py, DMSO, Et_3N, CH_2Cl_2, room temperature; (ii) $Ph_3P{=}CHCO_2Me$, benzene, reflux, 82% from **14**; (i) Tetrabutylammonium fluoride (TBAF), THF, room temperature, 100%; (j) Camphorsulfonic acid (CSA), CH_2Cl_2, room temperature, 81%.

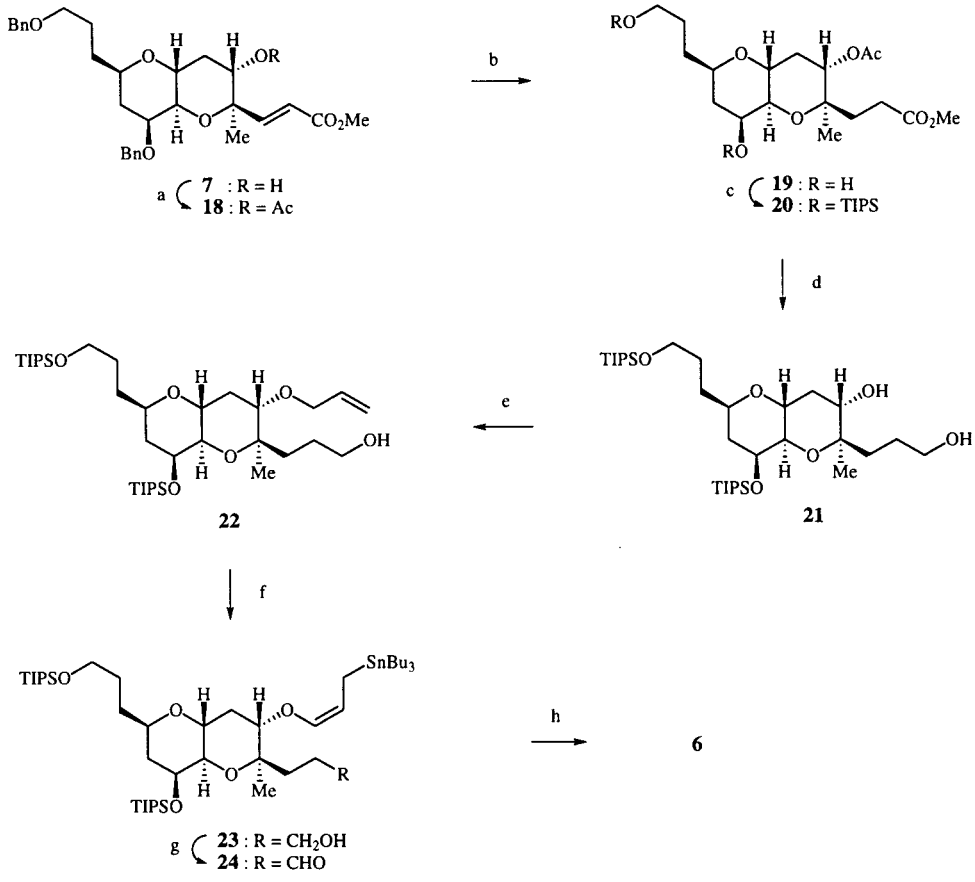
To avoid the 1,3-diaxial repulsion, the allylic stannane moiety and the carbonyl oxygen of the substrate are oriented to a *pseudo*-equatorial position (**24A**) leading to **6**. All the other transition state structures (**24B**, **C**, and **D**) do not contribute to the reaction because of the significant steric repulsion of the axially oriented groups, as depicted in Figure 1 [6].

Synthesis of the D Ring and Completion of the Total Synthesis.

Acetylation of **6** followed by ozonolysis and Wittig reaction afforded α,β-unsaturated ester **26** *via* **25**, quantitatively (Scheme 5). Further elaboration of **26** was carried out using the similar methodology as shown in Scheme 4 to provide **29**. In contrast to earlier results in the synthesis of compound **23**, the usual allylic anion formation followed by trapping with *n*-Bu_3SnCl afforded **30** in only 16% yield along with the recovered starting material. Deprotonation of the sterically bulky allylic ether **29** would possibly be quite slow and the decomposition of the resulting allylic anion would compete if a prolonged reaction time was employed. This problem prompted us to develop a new synthesis of γ-alkoxyallylstannanes.

Scheme 6 shows the general synthetic sequence for the γ-alkoxyallylstannanes *via* an acetal cleavage. We have found that the combined use of trimethylsilyl iodide (TMSI) and hexamethyldisilazane (HMDS) is the best choice for the cleavage of mixed acetals having the tributylstannyl group. The acetals are easily prepared by acid catalyzed reaction of the corresponding alcohols and γ-methoxyallylstannane **31**. As demonstrated in Table 1, the reaction of secondary alcohol **32**, prepared quantitatively by selective protection of the primary hydroxy group of **21** with pivaloyl chloride (PvCl)/pyridine, with **31** in the presence of a catalytic amount of CSA proceeded smoothly to give the mixed acetal **33** as a 1:1 diastereomeric mixture. It should be noted that the use of an excess of **31** is required to obtain the mixed acetals in high yield, otherwise a significant amount of symmetric acetal is formed as a by-product. Treatment of **33** with TMSI and HMDS afforded the desired enol ether **34** in 83% yield. Interestingly, only (Z)-allylic stannane was produced, perhaps due to the coordination of ether oxygen to a tin atom. Encouraged by this success, the acetal methodology was used to introduce the allylic stannane moiety efficiently into tricyclic ether **35** (Table 1). It is

Scheme 4 [a]



[a] (a) Ac_2O, pyridine, DMAP, CH_2Cl_2, room temperature, 97%; (b) H_2, $Pd(OH)_2$-C, MeOH, room temperature, 99%; (c) Triisopropylsilyl trifluoromethanesulfonate (TIPSOTf), 2,6-lutidine, DMF, room temperature to 70°, 100%; (d) $LiAlH_4$, ether, 0°, 100%; (e) (i) TESCl, Et_3N, CH_2Cl_2, -15°; (ii) allyl bromide, KH, THF, room temperature; (iii) Amberlyst-15, EtOH, room temperature, 96%; (f) *s*-BuLi, *N,N,N',N'*-methylethylenediamine (TMEDA), THF, -78°, then *n*-Bu_3SnCl, -78° to room temperature, 69%; (g) SO_3•py, DMSO, Et_3N, CH_2Cl_2, room temperature, 90%; (h) BF_3•OEt_2, CH_2Cl_2, -78°, 94%.

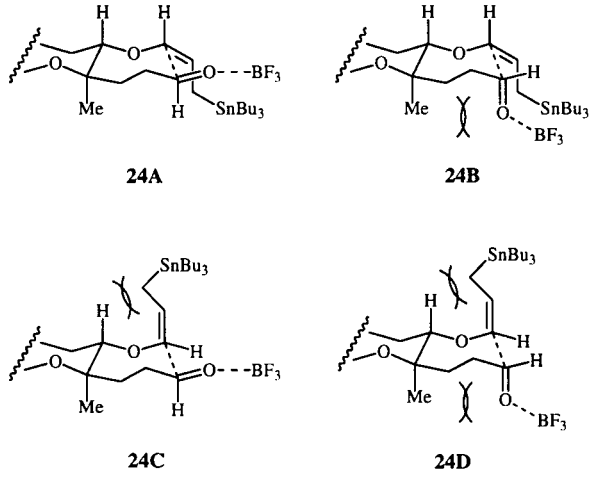
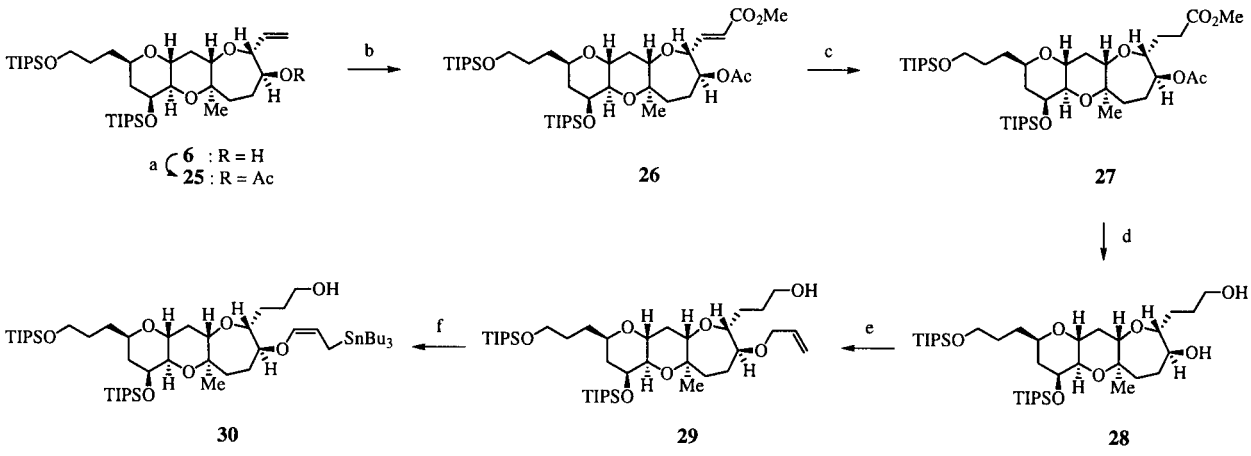


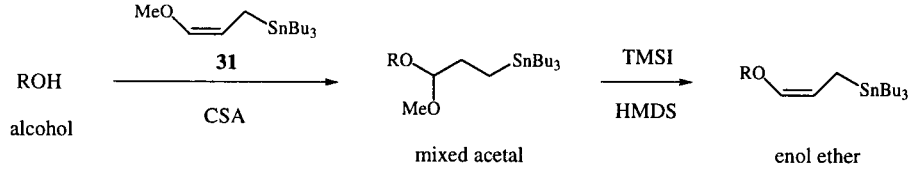
Figure 1. Presumed transition states of the cyclization of **24**.

Scheme 5 [a]



[a] (a) Ac_2O, pyridine, DMAP, CH_2Cl_2, room temperature, 100%; (b) (i) O_3, CH_2Cl_2, -78°, then Ph_3P, -78° to room temperature; (ii) $Ph_3P{=}CHCO_2Me$, CH_2Cl_2, 0° to room temperature, 99%; (c) (i) H_2, 10% Pd-C, EtOAc, room temperature; (d) $LiAlH_4$, ether, 0°, 98%; (e) (i) TESCl, Et_3N, CH_2Cl_2, -15°; (ii) allyl bromide, KH, THF, room temperature; (iii) Amberlyst-15, EtOH, room temperature, 94%; (f) *s*-BuLi, TMEDA, THF, -78°, then *n*-Bu_3SnCl, -78° to room temperature, 16%.

Scheme 6



notable that both of acetal formation and cleavage were not affected by the bulkiness of the substrates.

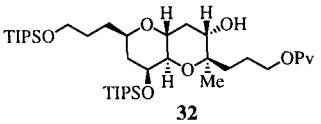
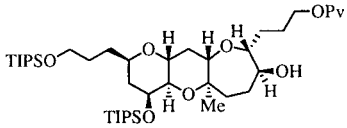
The final sequence of the synthesis is shown in Scheme 7. Removal of the pivalate protecting group with DIBALH led to **30**, which was oxidized to furnish the aldehyde **38**. The $BF_3{\bullet}OEt_2$ mediated cyclization of **38** afforded the tetracyclic ether **5** as a sole product in 98% yield. Again, perfect stereoselectivity was observed in the cyclization step. The introduction of a methyl group at the D ring was performed using Murai protocol. Thus, Swern oxidation of **5** followed by treatment with MeMgBr in toluene at -78° gave an 86:14 mixture of the desired isomer **39** and its epimer **40**. As reported by Nicolaou, the reaction carried out in ether gave poor selectivity (*ca.* 1:1). The major product **39** was isolated by chromatography, and the tertiary alcohol was protected with *tert*-butyldimethylsilyl triflate (TBSOTf)/2,6-lutidine to give **41**. Ozonolysis of **41** followed by Wittig reaction gave **42**, hydrogenation of which followed by $LiAlH_4$ reduction afforded **44** *via* **43**. Dess-Martin oxidation of **44** followed by treatment with the ylide derived from $PhSe(CH_2)_3P^+Ph_3\ Br^-$ and *n*-BuLi, and oxidation-*syn*-elimination using H_2O_2 and $NaHCO_3$ afforded diene **45**, selective desilylation of which gave **46**. Dess-Martin oxidation followed by treatment with Eschenmoser's salt afforded **47**, which was converted to hemibrevetoxin B (**1**) by removal of the silyl protecting groups using SiF_4. Synthetic hemibrevetoxin B (**1**) exhibited physical and spectroscopic data ($[\alpha]_D$, ir, ^1H and ^{13}C nmr) identical with those of the natural product.

(2) Synthesis of Nitrogen and Oxygen Heterocycles *via* Palladium Catalyzed Reactions.

(a) A New Method for the Synthesis of Nitrogen Heterocycles *via* Palladium Catalyzed Intramolecular Hydroamination of Allenes.

Transition metal catalyzed addition reactions of nitrogen nucleophiles to olefinic double bonds have been regarded as one of the most useful and straightforward

Table 1
Synthesis of the γ-Alkoxyallylstannanes *via* an Acetal Cleavage

Alcohol	Mixed Acetal [a]	Enol Ether [b]
 **32**	**33:** 85%	**34:** 83%
 **35**	**36:** 93%	**37:** 85%

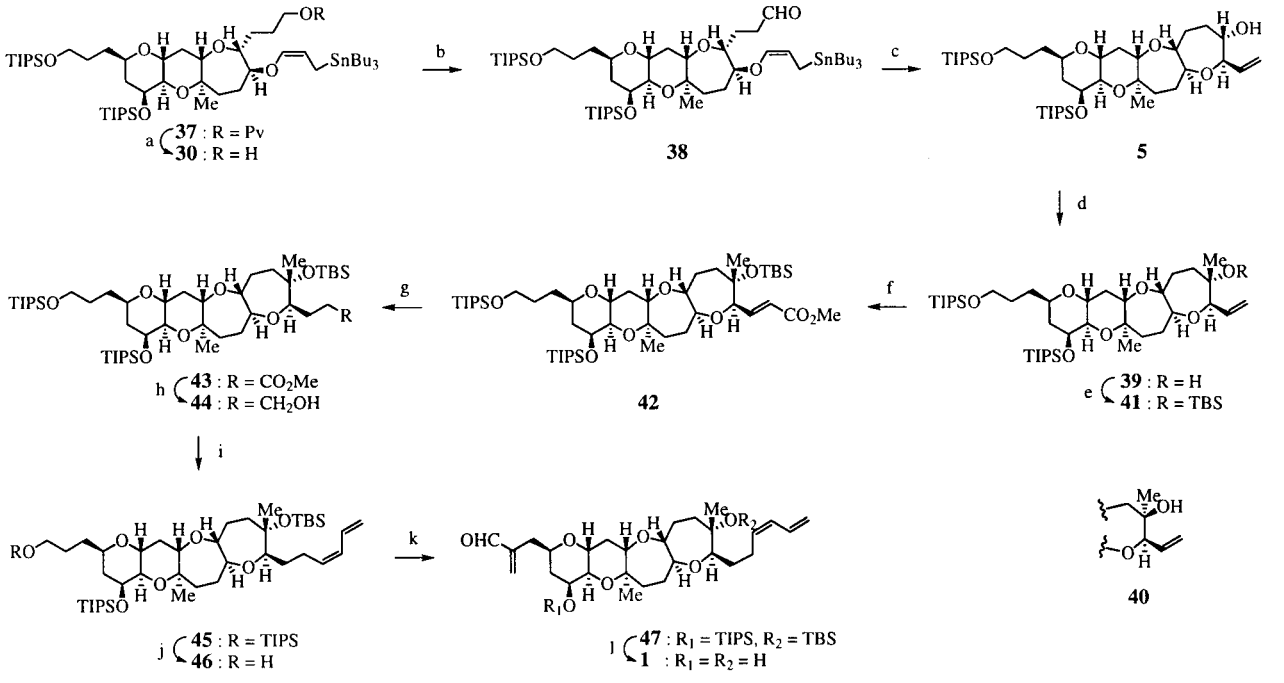
[a] 3.0 equivalents of **31**, 0.2 equivalent of CSA, CH_2Cl_2, room temperature; [b] 5.0 equivalents of TMSI, 7.0 equivalents of HMDS, CH_2Cl_2, -15°.

methods for C-N bond formation. It has been found that certain amines and amides undergo the addition reaction to unactivated C-C multiple bonds in the presence of transition metal catalysts; this is the so-called "hydroamination". Most of the amination reactions are based on nucleophilic addition to the metal-activated olefins (Figure 2, Type I) [7]. Recently, Marks and his co-workers reported a different type of hydroamination reaction catalyzed by organolanthanoid complexes [8], in which the amination reaction proceeded through the insertion of the N-M bond (M = lanthanoid metals) into a carbon-carbon multiple bond (Figure 2, Type II).

Type I M = Pd^{2+}, Ag^+, Hg^{2+}, ... Type II M = organolanthanoids

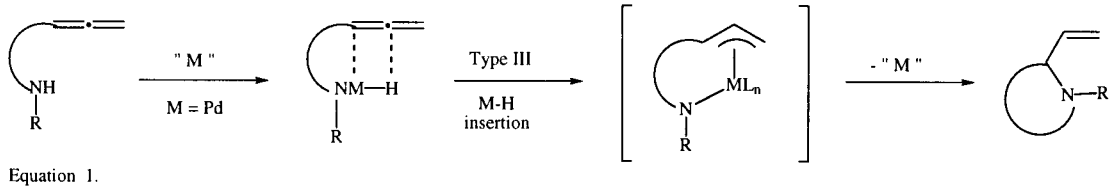
Figure 2. Previous intramolecular hydroamination reaction.

Scheme 7 [a]



[a] (a) DIBALH, CH_2Cl_2, -78°, 96%; (b) SO_3•py, DMSO, Et_3N, CH_2Cl_2, room temperature, 79%; (c) BF_3•OEt_2, CH_2Cl_2, -78°, 98%; (d) (i) $(COCl)_2$, DMSO, CH_2Cl_2, then Et_3N, -78° to room temperature; (ii) MeMgBr, toluene, -78° to room temperature, 83% (**39**:**40** = 86:14); (e) TBSOTf, 2,6-lutidine, CH_2Cl_2, room temperature, 85%; (f) (i) O_3, CH_2Cl_2, -78°, then Ph_3P, -78° to room temperature; (ii) Ph_3P=$CHCO_2Me$, CH_2Cl_2, room temperature, 82%; (g) H_2, 10% Pd-C, EtOAc, room temperature, 94%; (h) $LiAlH_4$, ether, 0°, 93%; (i) (i) Dess-Martin periodinane, CH_2Cl_2, room temperature; (ii) $PhSe(CH_2)_3P^+Ph_3$ Br^-, *n*-BuLi, HMPA, -78° to room temperature; (iii) H_2O_2, $NaHCO_3$, THF, room temperature, 74%; (j) TBAF, THF, room temperature, 91%; (k) (i) Dess-Martin periodinane, CH_2Cl_2, room temperature; (ii) $Me_2(CH_2)N^+I^-$, Et_3N, CH_2Cl_2, room temperature, 89%; (l) SiF_4, CH_2Cl_2-CH_3CN (1:1), room temperature, 76%.

We report an entirely new type of the hydroamination reaction (Type III) which proceeds through the insertion of M-H bond (M = Pd) to allenic double bond [9]. Amines or sulfonyl amides, bearing an allene group at the terminus of the carbon chain, undergo facile intramolecular hydroamination reaction in the presence of a catalytic amount of $[(\eta^3\text{-}C_3H_5)PdCl]_2$-dppf-$CH_3CO_2H$, giving the corresponding pyrrolidines and piperidines in good to high yields (Equation 1). The results are summarized in Table 2.

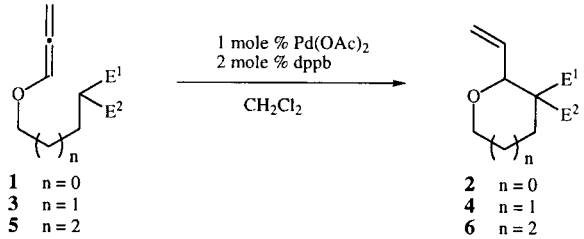


Equation 1.

The following mechanistic rationale may account for the present Pd-catalyzed cyclization of amines and amides although it is speculative. Initially, Pd(0) catalyst would add oxidatively to acetic acid to give hydridopalladium(II) intermediate H-PdOAcL_2. The ligand exchange between OAc of the Pd species and allenic amine derivative HNR_2 would produce another hydridopalladium species (H-PdNR_2L_2) and acetic acid. The π-allylpalladium complex would be formed through intramolecular hydropalladation of H-PdNR_2L_2, and subsequent reductive elimination would furnish the cyclized product.

(b) Synthesis of Cyclic Ethers *via* the Palladium Catalyzed Intramolecular Hydrocarbonation of Alkoxyallenes

Although many useful methodologies have been developed to construct cyclic ethers, a new flexible procedure which tolerates the introduction of a wide variety of functional groups is still needed. We previously found that certain activated methylene and methine compounds (carbon pronucleophiles, H-Nu) add to the double-bond of allenes ($RCH{=}C{=}CH_2$) in the presence of palladium catalysts to give the corresponding addition products ($RCH{=}CHCH_2Nu$) in good to high yields [10]. This direct addition reaction of carbon pronucleophiles, the so called hydrocarbonation reaction, is one of the ideal C-C bond forming procedures for a concise synthesis of molecules having multi-functional groups. We now report that the cyclization of alkoxyallenes **1**, **3** and **5** proceeds smoothly in the presence of catalytic amounts of $Pd(OAc)_2$-dppb complex, affording the corresponding 5- to 7-membered cyclic ethers **2**, **4** and **6**, respectively, in good to high yields (Equation 2) [11]. The results are summarized in Table 3.

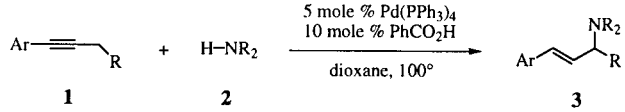


Equation 2.

A proposed mechanism for the palladium catalyzed cyclization is shown in Scheme 8. Pd(0) catalytic species would be generated *in situ* and would add oxidatively to the C-H bond of the pronuleophiles to form a hydridopalladium(II) intermediate **A**. Both hydropalladation and carbopalladation could account for the formation of the cyclic ether, however, our previous study on the construction of carbocycles suggests that the cyclization reaction proceeds through hydropalladation to the coordinated allene to form π-allylpalladium intermediate **B**. Reductive elimination would afford a desired cyclic ether and Pd(0) catalytic species. Although further investigation is needed to settle the precise mechanism, the present cyclization reaction provides a new procedure for constructing 5- to 7-membered cyclic ethers under extremely mild and neutral conditions.

(c) Palladium/Benzoic Acid Catalyzed Hydroamination of Alkynes.

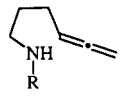
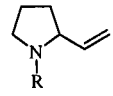
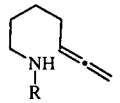
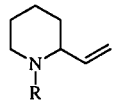
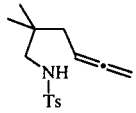
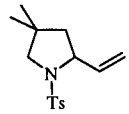
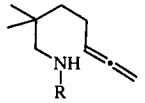
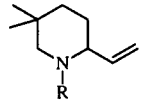
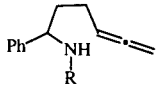
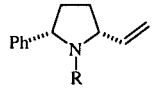
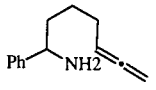
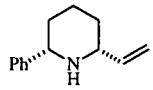
Recently, we reported that certain alkynes react with carbon pronucleophiles in the presence of palladium/-acetic acid catalyst to give the corresponding allylation products (formal hydrocarbonation based on the rearrangement of an alkyne to an allene) [12]. It occurred to us that the formal hydrocarbonation may be extended to the formal hydroamination to provide a new atom-economical procedure for the synthesis of amines from alkynes. Actually, the reaction of certain aromatic acetylenes **1** with amines **2** in the presence of 5 mole % $Pd(PPh_3)_4$ and 10 mole % $PhCO_2H$ in dioxane at 100° gave the corresponding allylic amines **3** in very high to good yields (Equation 3) [13].



1 2 3

Equation 3.

Table 2
Palladium Catalyzed Intramolecular Hydroamination of Allenes [a]

Entry	Allene	Reaction time, hours	Product	Yield,% [b]
				
1 [c]	**1a** R = Ts	30	**2a** R = Ts	58
2	**1a**	6	**2a**	87
3 [d]	**1a**	10	**2a**	80
4	**1b** R = Tf	2	**2b** R = Tf	90
5 [e]	**1c** R = Bn	4	**2c** R = Bn	60
				
6	**3a** R = Ts	10	**4a** R = Ts	41
7	**3b** R = Tf	4	**4b** R = Tf	58
				
8	**5**	5	**6**	78
				
9	**7a** R = Ts	6	**8a** R = Ts	60
10	**7b** R = Tf	1.5	**8b** R = Tf	84
				
11 [e]	**9a** R = H	3	**10a** R = H	41 [f] (50:50)
12	**9b** R = Tf	2	**10b** R = Tf	80 (94:6)
				
13 [e]	**11**	4	**12**	52 (>95:<5)

[a] The reactions were carried out in dilute THF solution (0.025 *M* for the allene) in the presence of 5 mole % $[(\eta^3\text{-}C_3H_5)PdCl]_2$, 10 mole % 1,1'-bis(diphenylphosphino)ferrocenee (dppf), 100 mole % acetic acid, except where otherwise indicated; [b] Isolated yield; [c] In the absence of acetic acid; [d] 25 mole % of acetic acid was used; [e] 15 mole % of acetic acid was used; [f] **10a** was relatively unstable and therefore it was converted to the tosyl amide derivative. The yield refers to the isolated tosyl amides.

In an initial experiment, 1-phenyl-1-propyne (**1a**) was treated with 1 equivalent of dibenzylamine (**2a**), $Pd(PPh_3)_4$ (5 mole %), and benzoic acid (10 mole %) in dioxane at 100° to give the allylic amine **3a** as a sole product in 98% yield (Table 4, entry 1). Similarly, the reactions of **1a** with secondary amines **2b-d** gave the allylic amines **3b-d**, respectively, in good to high yields (entries 2-4). In all cases, no regio- or stereoisomers were obtained. No reaction took place in the absence of benzoic acid. Other examples with various alkynes are summarized in Table 4.

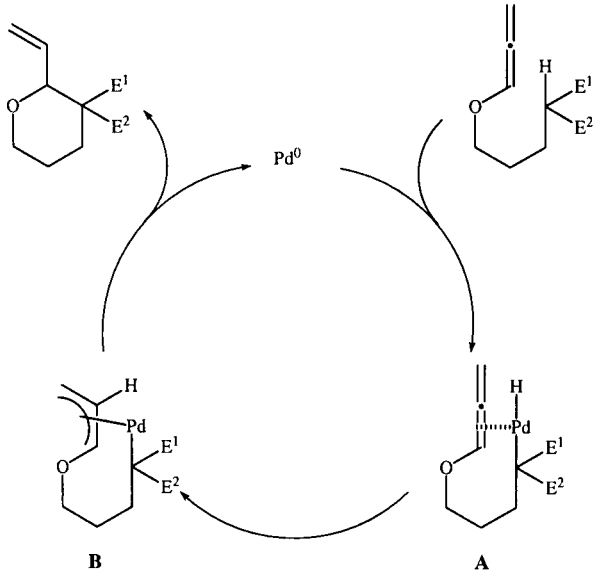
The usefulness of this transformation is demonstrated by the intramolecular version of the hydroamination reac-

Table 3
Palladium Catalyzed Intramolecular Hydrocarbonation of Alkoxyallenes [a]

Entry	n	Alkoxyallene E^1	Alkoxyallene E^2		Reaction time, (Hours)	Product	Yield, % [b] (Diastereomeric Ratio)
1	0	CN	CN	**1**	0.5	**2**	79
2	1	CN	CN	**3a**	0.25	**4a**	86
3 [c]	1	CN	CN	**3a**	0.5	**4a**	82
4	1	CN	SO_2Ph	**3b**	3.5	**4b**	88 (94:6)
5	1	SO_2Ph	SO_2Ph	**3c**	1.5	**4c**	92
6	1	CN	CO_2Me	**3d**	1	**4d**	77 (80:20)
7 [d]	1	SO_2Ph	CO_2Me	**3e**	2	**4e**	70 (81:19)
8 [d]	1	CO_2Me	CO_2Me	**3f**	6	**4f**	0 [e]
9 [f]	2	CN	CN	**5**	1	**6**	88

[a] The reaction was conducted in the presence of 1 mole % $Pd(OAc)_2$/2 mole % 1,4-bis(diphenylphosphino)butane (dppb) in CH_2Cl_2 (1.0 *M*) at room temperature unless otherwise indicated; [b] Isolated yield, the ratio of the stereoisomers was determined by ^1H nmr; [c] 0.1 mole % $Pd(OAc)_2$/0.2 mole % dppb was used as a catalyst system; [d] The reaction was conducted at 50°; [e] A significant amount of the allene was recovered; [f] The reaction was conducted in 0.1 *M* CH_2Cl_2 solution.

Scheme 8
Proposed Mechanism for the Intramolecular Hydrocarbonation of Alkoxyallenes



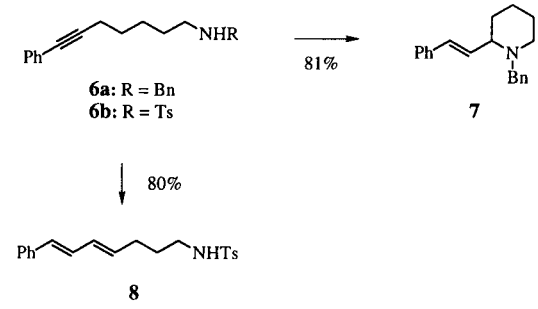
tion. The reaction of the alkynes **4a** and **4b**, having a mono-protected amino group at the terminus of the carbon chain, under the standard conditions mentioned above gave the pyrrolidine derivatives **5a** and **5b**, respectively, in good yields (Equation 4).

4a: R = Bn
4b: R = Ts

5a: R = Bn (70%)
5b: R = Ts (82%)

Equation 4.

Similarly, the benzylamine derivative **6a** cyclized to produce piperidine **7** in 81% yield (Equation 5). Interestingly, the tosylamide counterpart **6b** gave the linear diene **8** in 80% yield. Perhaps, the tosyl group would decrease the nucleophilicity of the nitrogen atom, hampering the cyclization. The diene **8** would be produced from the corresponding π-allylpalladium species *via* β-elimination.



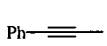
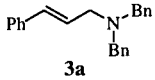
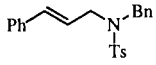
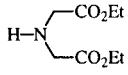
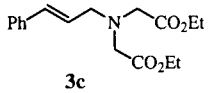
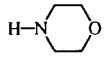
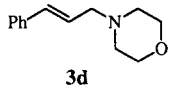
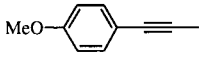
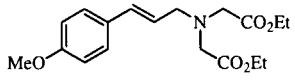
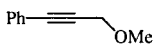
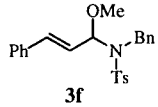
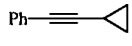
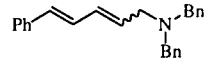
6a: R = Bn
6b: R = Ts

7

8

Equation 5.

Table 4
Palladium/Benzoic Acid Catalyzed Hydroamination of Alkynes

Entry	Alkyne	Amine	Product	Yield (%) [a]
1	 **1a**	 **2a**	 **3a**	98
2	**1a**	 **2b**	 **3b**	98
3	**1a**	 **2c**	 **3c**	77
4	**1a**	 **2d**	 **3d**	94
5	 **1b**	**2c**	 **3e**	82
6	 **1c**	**2b**	 **3f**	61
7	 **1d**	**2a**	 **3g** (*E* :*Z* = 85:15)	72 [b]

[a] Isolated yield; [b] Inseparable mixture of the stereoisomers. The ratio was determined by ^{1}H nmr analysis.

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