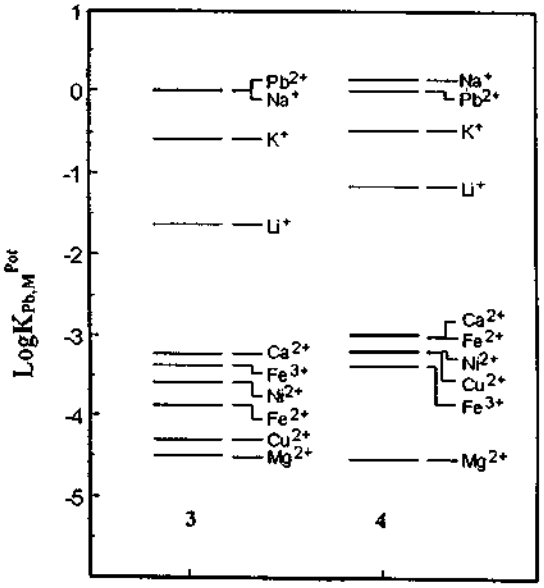

Figure 1. Potentiometric Selectivity of Compound **3** and **4** for Pb^{2+} over Other Metal Ions.

amide end-groups were successfully accomplished with quantitative yields. Complexation abilities of ligands **3** and **4** by ISE system show an excellent selectivity for Pb^{2+} over Cu^{2+}. To further investigate the influence of lipophilicity which decreases the Pb^{2+}/Cu^{2+} selectivity in this study, syntheses of novel acyclic polyether diamides in which the length of lipophilic tail and the number of ethylene glycol units are varied and their complexation studies in ISEs are in progress and the results will be reported.

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Conformational Effects on the Palladium-Mediated Tandem Alkene Insertion Reactions

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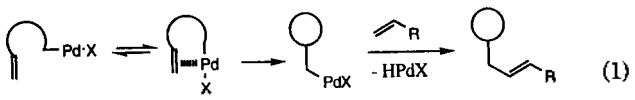
Organopalladium chemistry has evolved as a powerful technique in organic synthesis.[1] Among them, palladium-promoted intramolecular[2] or intermolecular[3] sequential alkene insertion reaction has recently attracted wide attention, because it constitutes a strong tool to form a series of C-C bonds in a single step. One of the strategies to achieve the Pd(0)-catalyzed tandem reaction is the intramolecular cycli-

zation followed by the intermolecular alkene insertion process. Mechanistically, the reaction is initiated by the coordination of the palladium(II) species to π-electron of the alkene to generate cyclized organopalladium intermediate, which undergoes Heck-type reaction (eq. 1).



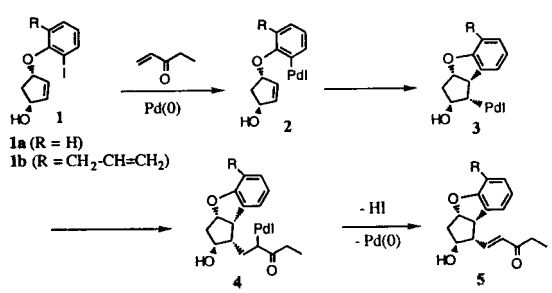
(1)

Therefore, obtaining the intramolecular proximity between the C=C bond and Pd(II) is of great importance to achieve the efficient tandem insertions. Even though much synthetic efforts have been made in this area, the conformational effect of the organopalladium substrate is not well reported.[4] In this paper, we want to describe the experimental observations and computational analysis on this topic.

As a part of our synthetic efforts on prostaglandin analogues,[3,5] we designed the sequential alkene addition process catalyzed by Pd(0) complexes (Scheme 1). The organopalladium intermediate **2** was expected to undergo intramolecular carbopalladation, followed by intermolecular alkene insertion and HPdI elimination to give the desired product **5**. We examined the feasiblity of the proposed procedure with iodoarene **1a**[6] in the presence of ethyl vinyl ketone as an external olefin.

Upon subjection of **1a** to the Pd(0)-catalyzed reaction conditions, to our disappointment, intermolecular Heck-type product **6a** was obtained as a major product in 42% yield (Scheme 2). Most of the side products obtained were identified to be the allylic cleavage one from the substrate **1a**. Even though the reaction was tried with different reaction conditions,[7] no desired product **5a** was identified. We figured this observation asumming that, in the case of **1a**, the rotamer **1-anti** would be present as the predominant isomer due to steric preference. Failure of the requisite proximity between π-electron of cyclopentene and the pd(II) in **1-anti** led to the intermolecular Heck-type addition favorable over the cyclization. Therefore, shift of the conformational equilibrium to the rotamer **1-syn** will clearly increase the chance of cyclization to give the tandem insertion product **5**, which can be accomplished by the introduction of a bulky group at the R position in the compound **1**.

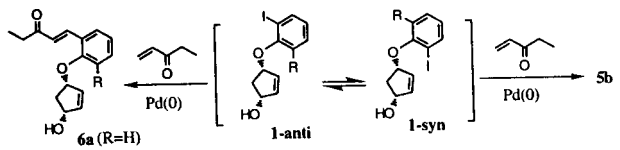
To examine this hypothesis, the substituted aryl iodide **1b**[6] was prepared and subjected to the same reaction condition employed above. As expected, the desired product **5b** was obtained in 44% yield. The rest of the starting material was found to be decomposed *via* Pd(0)-assisted allylic cleavage. Intermolecular Heck-type product **6b** was not identified. We can assume that the electronic effect resulting from the alkyl substitution on the reactivity is very small, because the substituent is introduced at the meta position of the iodopalladium as shown in **2**. Therefore, it is reasonable to conclude that, in the case of **1b**, the favorable distribution of **1-syn** is the major factor to accomplish the intramoleular alkene insertions.



Scheme 1.

Recently, computer-assisted structural analysis has been widely applied to explain the experimental observations as well as to predict its results. To support the hypothesis asserted above, the compounds **1a** and **1b** were compared using conformational search method. Rotation of two bonds adjacent to the phenolic oxygen with 15° interval, followed by the minimization of each conformation provided stable conformers which are allowed energetically as well as sterically. By analysis of the each stereoisomer whose conformational energy is less than 10 kcal, we obtained 4 allowed conformers for **1a** and 53 ones for **1b**. To compare conformational distributions of each compound, we examined the rotamers in terms of the distance between C2 and iodine atom (Figure 1). This examination revealed that the conformers in **1b** are distributed in a way that C2-I distance lies relatively closer; for example, 40% of **1b** conformers has C2 -Idistance within 4.5 Å, in contrast to that there is no conformation within the range in **1a**. This calculation clearly shows that the equilibrium was shifted to the rotamer **1-syn** by the introduction of allyl side chain in **1b**.

In conclusion, we have shown the significance of the conformational effect in the Pd(0)-catalyzed cyclization process. This is particularly important when inter- and intramolecular Heck-type addition is competing such as tandem C-C bond



Scheme 2.

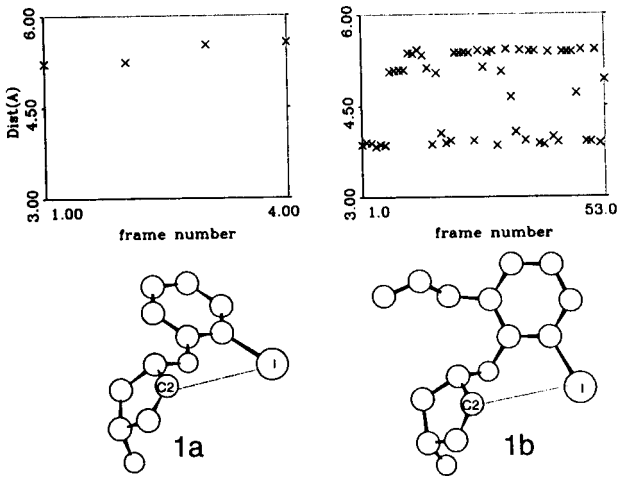


Figure 1. Distribution of C2-I distances in allowed conformers from conformational search. The ball-and-stick models represent C2-I distance in a conformer of each compound.

formation process. In addition, computer-assisted conformational analysis provides a useful tool to predict the synthetic result.

Experimental Section

General. All chemicals were used directly as obtained commercially unless otherwise noted. Iodophenol and n-Bu_4NCl were purchased from Lancaster. Tetrahydrofuran was distilled over sodium benzophenone ketyl and used immediately. DMF was distilled over sodium hydride and stored over 4 Å molecular sieves. NMR spectra were recorded on a Nicolet NT-300 spectrometer (^{1}H NMR, 300 MHz; ^{13}C NMR, 75 MHz), and chemical shifts are reported in ppm relative to TMS (δ 0.00) as an internal standard. IR spectra were obtained on an IBM IR 98. High-resolution mass spectra were recorded on a Kratos MS-50 Spectrometer. Conformational analysis was done with Silicon Graphics Indigo workstation, and default setting of INSIGHT II was used.

Synthesis of *cis*-4-(2-iodophenoxy)-2-cyclopenten-1-ol (1a). A solution of cyclopentadiene monoepoxide (820 mg, 10.0 mmol) in THF (3 mL) was added dropwise over 20 min to an ice-cooled solution of $Pd(PPh_3)_4$ (116 mg, 0.1 mmol) and 2-iodophenol (Lancaster, 2.2 g, 10.0 mmol) in THF (7 mL). The reaction mixture was warmed to room temperature and stirred for 15 h. The reaction was quenched by passing the mixture through silica gel pad. After the mixture was concentrated under reduced pressure, the residue was purified by flash chromatography to give the product **1a**: 1.88 g, 62% yield; ^{1}H NMR ($CDCl_3$) δ 7.78 (dd, J=7.8, 1.5 Hz, 1H), 7.29 (dt, J=1.5, 7.8 Hz, 1H), 6.88 (dd, J=7.8, 1.2 Hz, 1H), 6.72 (dt, J=1.2, 7,1 Hz, 1H), 6.21 (dd, J=5.7, 1.5 Hz, 1H), 6.17 (dd, J=5.7, 1.2 Hz, 1H), 5.14 (m, 1H), 4.75 (m, 1H), 2.83 (dt, J=14.4, 6.9 Hz, 1H), 1.89 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 156.1, 139.1, 138.3, 131.3, 129.0, 122.1, 113.0, 86.9, 81.1, 73.7, 40.9.

Synthesis of *cis*-4-(2-allyl-6-iodophenoxy)-2-cyclopenten-1-ol (1b). A solution of cyclopentadiene monoepoxide (1.4 g, 17.1 mmol) in 20 mL of THF was added dropwise over 10 min to an ice-cooled solution of $Pd(PPh_3)_4$ (173 mg, 0.15 mmol) and 2-allyl-6-iodophenol (3.0 g, 11.5 mmol) in 20 mL of THF. After stirring for 30 min at 0 ℃, the reaction was allowed to warm to room temperature, and the stirring was continued for 24 h. After being filtered through a silica gel pad, the reaction mixture was concentrated in vacuo and flash chromatographed to give product **1b**: 2.5 g, 64% yield; ^{1}H NMR ($CDCl_3$) δ 7.67 (dd, J=1.2, 7.8 Hz, 1H), 7.18 (dd, J=1.2, 7.8 Hz, 1H), 6.80 (t, J=7.8 Hz, 1H), 6.11 (m, 2H), 5.92 (ddt, J=16.8, 10.2, 6.6 Hz, 1H), 5.11 (m, 2H), 5.00 (m, 1H), 4.69 (m, 1H), 3.48 (t, J=6.0 Hz, 2H), 2.84 (dt, J=14.4, 7.2 Hz, 1H), 2.08 (dt, J=14.1, 4.2 Hz, 1H), 1.89 (m, 1H, OH); ^{13}C NMR ($CDCl_3$) δ 156.2, 138.0, 137.8, 136.4, 134.5, 134.0, 130.9, 125.8, 116.6, 92.8, 86.4, 74.8, 41.7, 35.1; IR (neat) 3464, 1433, 1360, 1250 cm^{-1}; HRMS m/z calcd for $C_{14}H_{15}O_2I$ 342.01168, found 342.01149.

General procedure for the tandem alkene insertion procedure. In a vial were placed compounds **1a** or **1b** (0.2 mmol), ethyl vinyl ketone (84 mg, 1.0 mmol), triethylamine (50 mg, 0.5 mmol), n-Bu_4NCl (61 mg, 0.22 mmol), Pd $(OAc)_2$ (2.2 mg, 0.01 mmol) and 0.4 mL of DMF. After the mixture was stirred for 6 h at 50 ℃, it was poured into 60 mL of diethyl ether and the overall solution was washed with saturated NH_4Cl (20 mL) and brine (20 mL). The solution was dried over $MgSO_4$ and concentrated *in vacuo*, and the residue was purified by flash chromatograhy.

Compound 5b: 44% yield; ^{1}H NMR ($CDCl_3$) δ 6.97 (d, J=7.5 Hz, 1H), 6.90 (d, J=7.5 Hz, 1H), 6.82 (dd, J=16.2, 9.6 Hz, 1H), 6.79 (t, J=7.5 Hz, 1H), 6.21 (d, J=16.2 Hz, 1H), 5.97 (m, 1H), 5.42 (dd, J=7.8, 5.7 Hz, 1H), 5.02 (m, 2H), 4.28 (m, 1H), 3.99 (t, J=8.4 Hz, 1H), 3.32 (d, J=6.3 Hz, 2H), 2.86 (dt, J=4.2, 9.6 Hz, 1H), 2.57 (dq, J=3.0, 7.5 Hz, 2H), 2.49 (d, J=15.3 Hz, 1H), 2.20 (dt, J=15.3, 5.4 Hz, 1H), 1.64 (d, J=7.5 Hz, 1H, OH), 1.08 (t, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 201.2, 157.2, 143.9, 136.2, 132.7, 129.2, 127.1, 123.9, 122.3, 120.5, 115.7, 89.0, 77.3, 52.6, 50.6, 42.9, 39.0, 32.3, 8.2; IR (neat) 3468 (OH), 1668 (C=O) cm^{-1}; HRMS m/z calcd for $C_{19}H_{22}O_3$ 298.15690, found 298.15741.

Compound 6a: 42% yield; ^{1}H NMR ($CDCl_3$) δ 7.87 (d, 16.5 Hz, 1H), 7.55 (dd, J=7.8 , 1.2 Hz, 1H), 7.28 (dt, J=1.2, 7.8 Hz, 1H), 6.90 (m, 2H), 6.71 (d, J=16.5 Hz, 1H), 6.02 (m, 2H), 5.09 (t, J=6.0 Hz, 1H), 4.75 (m, 1H), 2.82 (dt, J=13.8, 6.9 Hz, 1H), 2.60 (q, J=7.2 Hz, 2H), 2.00 (dt, J=13.8, 5.4 Hz, 1H), 1.05 (t, J=7.2 Hz, 3H).

Conformational Search. Initial 3D models were obtained from 2D drawing using 3D convert module in InsightII software developed by MSI. These models were minimized, then conformational search is applied. Two bonds adjacent to the phenolic oxygen were rotated with 15° interval. After each rotation, the molecule was minimized to obtain the stable conformer. The conformers which are sterically allowed and whose energy are within 10 kcal from the minimum value were collected and analyzed. Minimization and conformational search were performed using MSI software.

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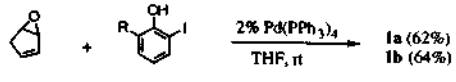
6. Synthesis of the compounds **1a** and **1b** was accomplished stereoselectively using the Pd(0) catalyzed reaction of cyclopentadiene monoepoxide. Deardoff%s procedure where phenol has been employed for the Pd(0)-mediated substitution reaction was utilized; for the reference see, Deardorff, D. R.; Myles, D. C.; Macferrin, K. D. *Tetrahedron Lett.* **1984**, *26*, 5615. The detailed procedure for the preparation of **1a** and **1b** is described in the experimental section.



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Investigation of Desolvation Process in Argon Inductively Coupled Plasma

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Atomic spectrometry has long provided excellent qualitative and quantitative trace element analysis. Recent developments, involving "non-flame" techniques such as furnace Atomic Absorption (AA), Inductively Coupled Plasma (ICP)-Atomic Emission Spectrometry (ICP-AES) as well as Mass Spectrometry (ICP-MS), have improved detection to the sub-ppb level. Despite the success of flame and plasma atomic spectrometry, elemental analysis is still limited in understanding the fundamental processes in an atomic source.[1]

Typically, a droplet is generated in a nebulizer and enters into an atomic source. And it goes through evaporation, melting, vaporization, excitation as well as ionization following molecular reactions such as molecular formation and dissociation. Various types of reactions and interferences can be involved in each step that has a very pronounced effect upon measuring the observed signal intensity, which is converted to the number of atoms or ions and finally to concentration. Any side reactions or interferences could happen during the processes and give erroneous results. Characterization and optimization is only possible when each step is studied separately. The nature of the source can be understood better and experimental parameters intelligently optimized only when each step is well characterized. To alleviate the interferences and more importantly to improve the analytical ability of atomic source, it is essential to understand the processes occuring in an atomic source.

Though there are a lot of experimental researches, relatively little investigations have been performed in the mechanistic study of the atomization processes. At the most, in atomic spectroscopy, studies have been limited to flames. Clampitt[2] showed that desolvation in an air-acetylene is due to the heat transfer process. Thermal conductivity plays the key role in desolvation of several aqueous and organic solvents. Bastiaans[3] has extended the desolvation of solvent model to vaporization of solute particles in an air-acetylene flame successfully. Hieftje[4] has proposed two models, heat and mass transfer, for the calculation of particle vaporization rate in a flame. Chen and Pfender[5~7] investigated that the Knudsen effect plays a significant role in heat transfer process for a particle vaporization in a thermal plasma. However, the studies have been focused on the vaporization process and the desolvation process in ICP has not been studied yet.

In this report, desolvation process is investigated for Ar Inductively Coupled Plasma. Earlier theoretical models used in the flame and plasma to describe a vaporization process have been successfully applied to describe the desolvation process in ICP. Calculated desolvation rate constant (k_d) has been compared with experimental one to determine which model describes the desolvation process the best. The desolvation rate of solvent has been determined by observing the first appearance of sodium emission (Na bullet). The distance between two bullets (those of the dried and wet aerosol) has been converted to the time taken for desolvation. Comparison of experimental and calculated results show that a simple heat transfer or mass transfer desolvation alone can not explain the desolvation process in ICP.

With a simple experiment, valuable information on the desolvation process in ICP could be obtained. For the matter of simplicity, modeling is restricted to water. This report is a preliminary study and a detailed investigation is further needed to understand the process completely.

Theory

Intuitively, one can consider that the rate of evaporation of the solute might be governed either by the rate at which energy (heat) can be transported to the solute surface or, alternatively, by the rate at which solute material can leave that surface. These cases are termed heat-transfer or mass transfer-limiting, respectively.

Heat-Transferred Evaporation. When thermal equilibrium is assumed between a droplet and the surrounding gases, *i.e.* when the temperature of the surface of a volatilizing droplet is constant during the evaporation process and the droplet is immersed in an infinite, stagnant medium, the rate of heat conducted through the medium to the surface is

$$dQ/dt = 4\pi r^2 h_c (T_g - T_s) \tag{1}$$

where h_c is the heat-transfer coefficient, r is the radius of the droplet, T_g is the plasma gas temperature, and T_s is the temperature of the droplet surface. The heat transfer coefficient is defined as

$$hc = \frac{\lambda N_s}{2r}\left[\frac{\ln(1+\Delta H_{av}/\Delta H_v)}{\Delta H_{av}/\Delta H_v}\right] = \frac{\lambda N_s}{2r}\Lambda \tag{2}$$

where Λ is the mass counter-flow coefficient, Ns is the Nusselt number, and λ is the thermal conductivity of the vapor or plasma gas, whichever is lower. The bracketed term is included to account for resistance to heat flow to the droplet