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Mechanism of Addition of Allylmetal to Vinylmetal. Dichotomy between Metallo−Ene Reaction and Metalla−Claisen Rearrangement

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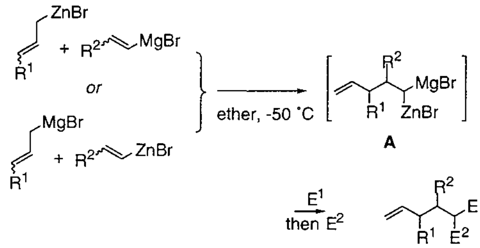
Abstract: The addition of an allylzinc compound to a vinylmetal compound takes place rapidly and in high yield to produce a 1,1-dimetallic organometallic species. This reaction has apparent kinetic and thermodynamic problems, and in addition, the nature of the true final product has not been known. Density functional (B3LYP) studies on this reaction for a combination of various metals including lithium, magnesium, zinc, and tin provided the first information on these unresolved issues. The key stage of the reaction was found to be an endothermic Lewis acid-assisted metalla−Claisen rearrangement that also shows some character of metallo−ene reaction of the vinylmagnesium species. The kinetic barrier of the C−C bond-forming step is quite low and the thermodynamic driving force of the reaction is provided by oligomerization of the initial product that occurs after the C−C bond formation. The high level of diastereoselectivity observed experimentally has been ascribed to the short length of the forming C−C bond in the transition structure, which is due to the late nature of the transition state of the endothermic metalla−Claisen rearrangement reaction.

Among numerous examples of addition reactions of an organometallic species to an olefin, the addition of an allylic zinc reagent to a vinylmagnesium halide is particularly striking and uniquely synthetically useful (Scheme 1). The reaction represents an addition of an allylic anion to a vinyl anion and seems to be an impossible reaction. However, it takes place smoothly when magnesium(II) and zinc(II) atoms are used as countercations. This reaction was initially discovered by Gaudemar nearly 30 years ago[1] and has recently been shown by Normant to be a versatile synthetic reaction,[2] serving as a valuable route to novel 1,1-dimetallic nucleophiles (referred to here as Gaudemar/Normant (G/N) coupling).[3] Recent discovery of the second case of such a reaction by Nakamura (Scheme 2),[4] wherein a zincated hydrazone reacts rapidly with vinylmagnesium bromide, provided evidence that the generality of such counterintuitive reactions is much wider than our intuition may suggest. There have been suggested two mechanistic rationales, a carbometalation pathway (i.e., metallo−ene reaction, Scheme 3a) and metalla−Claisen rearrangement (Scheme 3b).

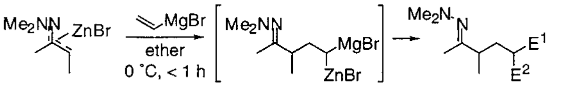
There are several fundamental issues in the G/N reaction that stand against chemists' common sense of kinetics, thermodynamics, and stereochemistry. First, the reaction is remarkably fast. For instance, the addition of an allylic magnesium reagent to a alkenyllithium reagent is complete in several hours even at −50 °C in the presence of zinc bromide (cf. Scheme 5). Note that the addition of the same allylic zinc reagent to ethylene requires an elevated temperature.[5] Similarly, the zincated hydrazone adds to a vinyl Grignard reagent within 1 h at 0 °C (Scheme 2),[4] while its addition to ethylene takes several days to complete.[6a] Thus, the vinyl Grignard reagent is far more reactive than a neutral olefin in these reactions.

Thermodynamics is another issue. The anion−anion coupling between an allylic anion and a vinyl anion may take place in two ways to give 1,1-dianion and 1,2-dianion, and both reactions should be highly unfavorable. Calculations (B3LYP/6-31+G*)

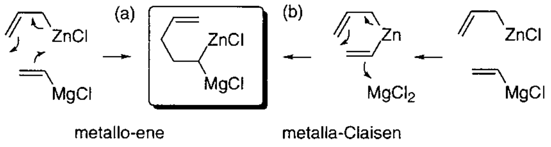
Scheme 1



Scheme 2



Scheme 3



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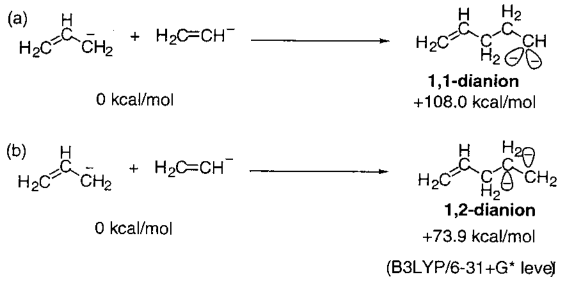
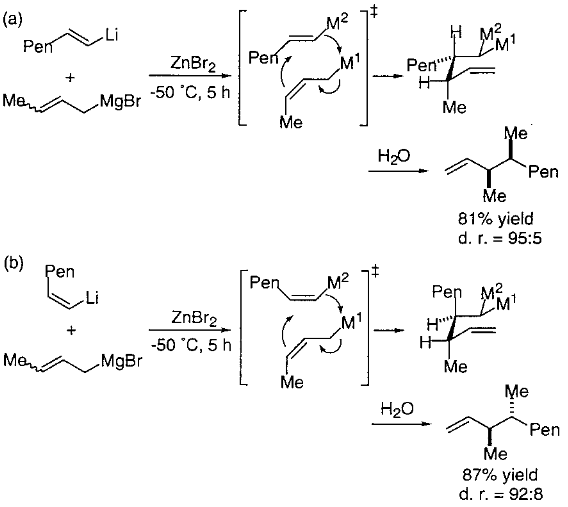
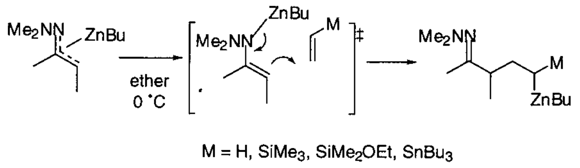
Scheme 4



Scheme 5



Scheme 6



support our intuition, demonstrating that the reaction between an allyl anion and vinyl anion affording the 1,1-dianion product is 108.0 kcal/mol endothermic (Scheme 4a). The alternative 1,2-dianion pathway (b) is 73.9 kcal/mol endothermic. This thermodynamic problem cannot be resolved even if metal atoms are included in the calculation, since the 1-magnesio-1-zincio product **A** in Scheme 1 is no more stable than the starting materials (vide infra).

The composition and structure of the dianionic product of the G/N reaction are unclear. The formation of the 1-magnesio-1-zincio product **A** is a mere speculation, largely based on experimental observations that this dianionic species reacts in a stepwise manner as if a Grignard reagent and an organozinc reagent are combined in one molecule.[7] However, recent studies on 1,1-dizincio species indicated that such a symmetrically metalated species reacts with electrophiles in a stepwise manner.[8]

The origin of diastereoselectivity (mutual face selectivity) of the reaction has also been a puzzle, since an *E/Z* equilibrium mixture of a crotylzinc reagent gives a single diastereomer. Interestingly, the observed stereochemistry requires us to consider that the reaction has taken place through the less stable (*Z*)-crotyl isomer (Scheme 5).[9]

Finally, an allylic zinc reagent or a zincated hydrazone adds smoothly to, ethylene, vinylsilane, and vinylstannane (Scheme 6).[6] This reaction has some formal similarity to the G/N-type reaction, though it is clearly a metallo−ene reaction (cf. Scheme 3a) rather than a metalla−Claisen reaction (Scheme 3b). The borderline between this reaction and the G/N-type reaction therefore needs to be clarified.

We report here the full details of the mechanistic studies on the addition of an allylic metal species to a vinylmetallic species, in particular, the G/N reaction, with the aid of quantum mechanic calculations. The theoretical studies indicated the synergetic action of the two different metals to circumvent the above-mentioned kinetic,[10] thermodynamic, and stereochemical problems expected in the G/N coupling.[11]

Computational Method

Calculations were performed with a GAUSSIAN 94 program package.[12] All calculations except those noted individually were performed with the B3LYP method[13,14] using the split valence basis set with polarization and diffuse functions for heavy atoms. Ahlrichs' SVP[15] all-electron basis set was used for the zinc atom and the 6-31+G* basis set[16] for other atoms (denoted here as B3LYP/631+A). LANL2DZ effective core potential was used for tin atom.[17] The intrinsic reaction coordinate (IRC) analysis of some reactions was performed at the B3LYP/631+A level.[18] Some calculations were performed with the Hartree−Fock method using Ahlrichs' SVP basis set for the zinc atom and 3-21G basis set for other atoms (HF/321A). When the HF method was used, the energies were recalculated at the B3LYP/631+A level for the HF/321A geometry. The HF/321A geometries (but not energetics) were in good accord with the B3LYP/631+A geometries and may be used as a less expensive substitute of the latter.[10]

Structures were optimized without any geometrical assumption unless otherwise noted. Zero imaginary frequency for equilibrium structures was confirmed by normal coordinate analysis. The energetics refers to potential energy, while zero point energy, enthalpy, and entropy were considered in the oligomerization studies as well as in some selected test reactions (which showed that potential energy is a good enough measure of the reaction profile).

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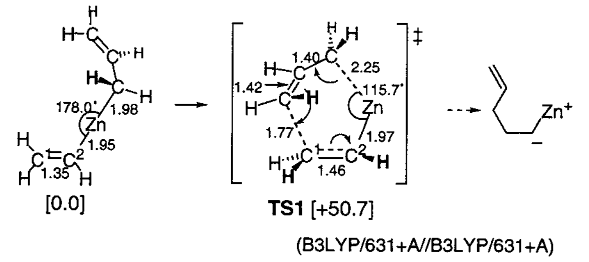


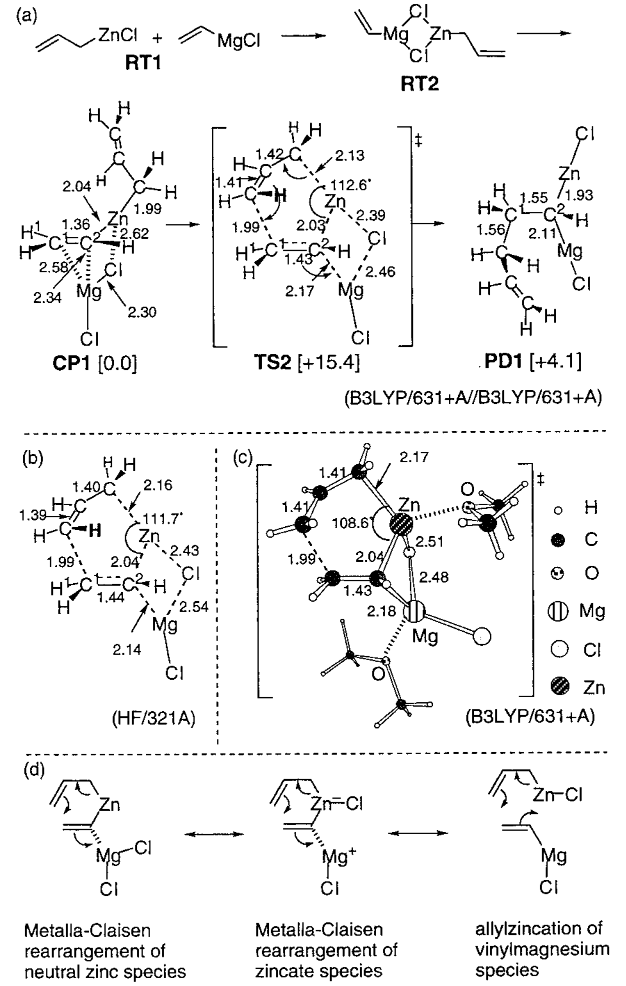
Figure 1. Metalla−Claisen rearrangement of of allylvinylzinc. Curved arrows in the TS show electron flow. Energies relative to allylvinylzinc (in brackets) are given in kcal/mol and bond lengths in angstroms.

Results and Discussion

Coupling between Allylzinc and Vinylmagnesium Bromide: A Prototype G/N Reaction. Without any concrete picture of the reaction pathway of the G/N coupling, we started our investigation from two directions, one considering the reaction as an extension of metallo−ene reaction, i.e., allylzincation of olefin (Scheme 3a) and another as that of metalla−Claisen rearrangement (Scheme 3b). We took the TS geometry of allylzincation of ethylene that we reported earlier[19] and modified some structural parameters to reach the TS geometry identical to the one obtained by starting from the metalla−Claisen rearrangement.

The prototype metalla−Claisen rearrangement was taken as the first model (Figure 1). The starting allylvinylzinc intermediate forms via transmetalation between a vinyl Grignard reagent and an allylic zinc reagent and undergoes [3,3] sigmatropic rearrangement. The molecule and the transition structure (TS), **TS1**, was found as a six-centered transition state of [3,3] sigmatropic rearrangement. The angle C−Zn−C in **TS1** is 115.7°. The linear shape of the allylvinylzinc species was in accord with the structure of diorganozinc compounds obtained experimentally.[20] **TS1** was found to be much higher in energy (50.7 kcal/mol) than the starting allylvinylzinc. In addition to this unrealistically high energy, this reaction is also chemically unlikely, since it will generate a zinc alkylidene complex $CH_2{=}CH(CH_2)_2CH{=}Zn$.

When we placed a molecule of $MgCl_2$ nearby C^2 in **TS1** to form **TS2**, the activation energy dropped dramatically because the Mg(II) atom stabilizes the developing negative charge on C^2 (Figure 2 and Figure 3). **PD1** is 4.0 kcal/mol less stable than **CP1**. (The issue of **PD** oligomer formation will be discussed later.)



Metalla-Claisen rearrangement of neutral zinc species

Metalla-Claisen rearrangement of zincate species

allylzincation of vinylmagnesium species

Figure 2. Reaction pathway of the coupling between allylzinc chloride and vinylmagnesium chloride. (a) Unsolvated model. (b) **TS2** calculated at the HF/321A level. (c) TS solvated with two molecules of Me_2O on the metal atoms. (d) Limiting structures of the G/N reaction. Curved arrows in TSs show electron flow. Energies relative to **CP1** (in brackets) are given in kcal/mol and bond lengths in angstroms.

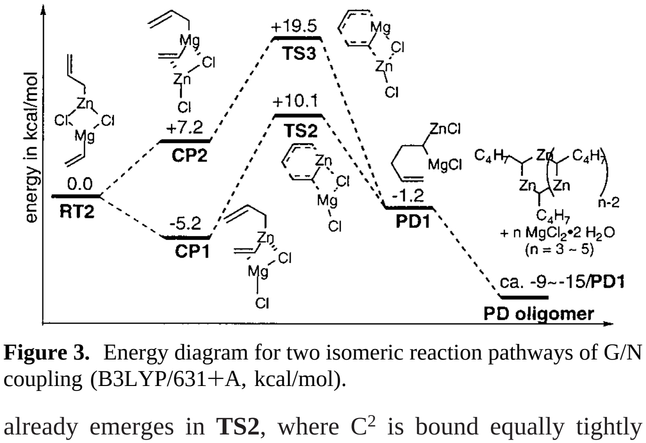


Figure 3. Energy diagram for two isomeric reaction pathways of G/N coupling (B3LYP/631+A, kcal/mol).

An overview of the "$MgCl_2$-assisted metalla−Claisen rearrangement" is shown in Figure 2a. A mixed μ-chloro-bridged cluster (**RT2**) may be formed first from the monomeric starting organometallics (**RT1**) and then go to a reactive complex **CP1** through transmetalation. The geometrical parameters of **CP1** indicate that the vinyl group is σ-bonded to Zn and π-coordinated to Mg (C^2−Zn = 2.04 Å, C^2−Mg = 2.34 Å; dihedral angle <H^{1}C^{1}C^{2}Zn = 14.8°, <H^{1}C^{1}C^{2}Mg = 69.8°), and hence, the intermediate can be considered as a complex of allylvinylzinc and $MgCl_2$.[21] **TS2** lies only 15.4 kcal/mol above **CP1** and goes smoothly downhill to the 1,1-dimetallic product (**PD**) as followed along the IRC. The 1,1-dimetallic character of **PD** already emerges in **TS2**, where C^2 is bound equally tightly to Zn and Mg (C^2−Zn = 2.03 Å, C^2−Mg = 2.17 Å; <H^{1}C^{1}C^2-Zn = 69.2°, <H^{1}C^{1}C^{2}Mg = 26.6°). In light of the geometrical similarity between **TS1** and **TS2** (as well as the molecular orbital discussions described later), the G/N coupling can be considered as a “Lewis acid-assisted metalla−Claisen rearrangement”. On the other hand, **TS2** has geometrical similarity to the TS of allylzincation of an olefin.[19,22] The slower reaction rate observed

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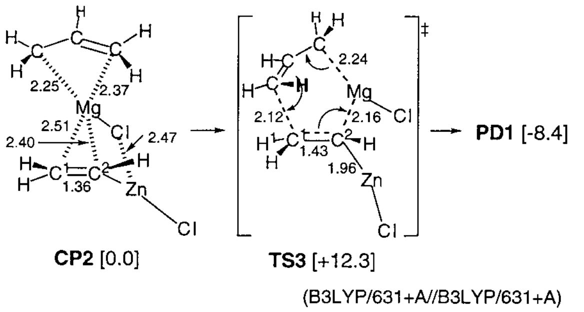

Figure 4. Reaction pathway of the coupling between allylmagnesium chloride and vinylzinc chloride. Curved arrows in **TS3** show electron flow. Energies relative to **CP2** (in brackets) are given in kcal/mol and bond lengths in angstroms.

in a strongly Lewis basic solvent (e.g., THF) also suggests the importance of the Lewis acidic role of $MgCl_2$ in the C—C bond-forming stage. The character of the G/N coupling can be described by the three limiting structures shown Figure 2d with the largest contribution of the far left structure.

To compare the performance of the less expensive HF calculations with that of the B3LYP calculations, we also calculated the structure of **TS2** at the HF/321A level (Figure 2b). The geometry is very similar to that of **TS2** obtained by the B3LYP method, but the activation energy was very high (24.0 kcal/mol). We also calculated a single-point energy of **TS2** at the MP2 level of theory (MP2/631+A//B3LYP/631+A),[23] and the activation energy was 15.6 kcal/mol, which is very close to the B3LYP value (15.4 kcal/mol).

Since diethyl ether is used as solvent, we examined the TS coordinated with two molecules of Me_2O. As shown in Figure 2c, solvent coordination did not significantly change the core six-centered structure.

An alternative pathway **CP2-TS3-PD1** to reach **PD1** involves a reverse combination of metals (Figure 3 and Figure 4). This reaction pathway is much higher in energy, which is due to instability of the C—Mg bond in **CP2** relative to the C—Zn bond in **CP1**. This energetics agrees with the fact that an alkyl Grignard reagent is a good alkyl donor to a zinc halide.[24] **CP2** is a π-complex between a π-allylmagnesium and a vinylzinc chloride, but the TS of C—C bond formation (**TS3**) is quite similar to **TS2**.

Coupling between Various Allyl- and Vinylmetals. Beside the best (and most practical) combination of zinc and magnesium, various combinations of allyl- and vinylmetals have been extensively studied in the Normant laboratory. Moderately effective to ineffective combinations of metals were studied to examine the energetic factors that affect the success of the G/N coupling.

(1) Coupling between Allylzinc Chloride and Vinylzinc Chloride. This is a moderately successful reaction that takes place in ether but not in THF.[25] In this reaction, each zinc atom is covalently attached to the allyl and the vinyl groups in the complex **CP3** (Figure 5), which is a metal—olefin complex similar to **CP2**. This intermediate proceeds to **TS4**, as found by following the IRC back from **TS4**. The energetics shown in Figure 6 is typical for allylzincation of an olefin, and the reaction gains some energy upon formation of the product **PD2**. The energetics stands in contrast to that in the reaction of zinc/magnesium combination (vide supra), where there is a large energy gain upon formation of **CP1** owing to the formation an additional C—Zn bond and an energy loss due to the loss of one C—Zn bond upon formation of **PD1**.

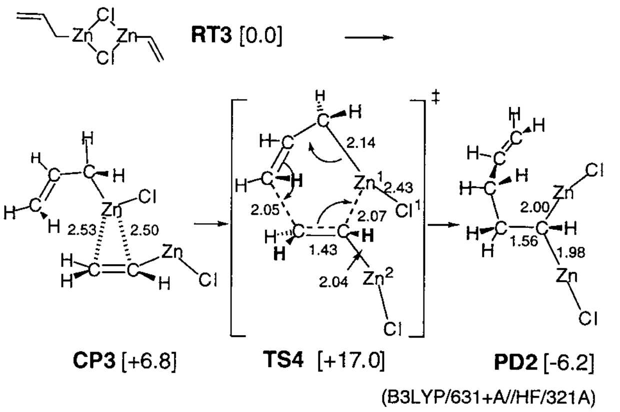

Figure 5. Reaction pathway of the coupling between allylzinc chloride and vinylzinc chloride at the B3LYP631+A//HF321A level. Curved arrows in TS show electron flow. Energy changes in brackets are given in kcal/mol and bond lengths in angstroms.

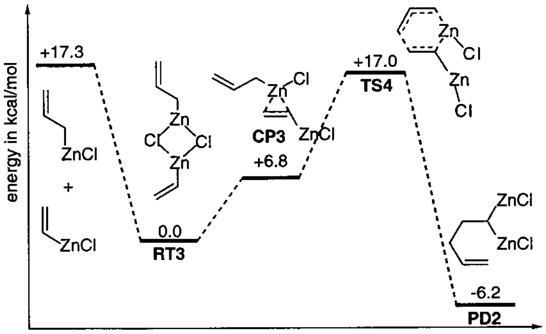

Figure 6. Energy diagram for the coupling of allylzinc chloride and vinylzinc chloride (B3LYP/631+A//HF/321A, kcal/mol).

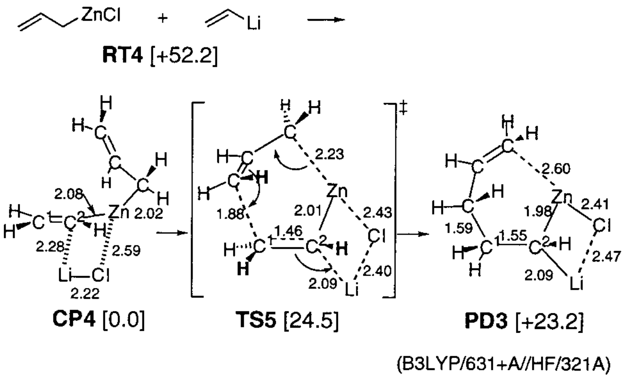

Figure 7. Reaction pathway of the coupling between allylzinc chloride and vinyllithium at the B3LYP631+A//HF321A level. Curved arrows in TS show electron flow. Energies relative to **CP4** (in brackets) are given in kcal/mol and bond lengths in angstroms.

(2) Coupling between Allylzinc Chloride and Vinyllithium. This is an experimentally viable combination.[2a] Because of very facile lithium-to-zinc transmetalation, **RT4** was converted to **CP4** with very large exothermicity (Figure 7), which has a structure similar to **CP1**. The transition structure, **TS5**, is also similar to **TS2**. The activation energy is high (24.5 kcal/mol) and the whole system loses 23.2 kcal/mol energy upon formation of the product **PD3** owing to the formation of a C—Li bond at the expense of loosing one C—Zn bond. Nonetheless, the actual reaction takes place at 0 °C in THF, clearly indicating that **PD3** is not the final reaction product (vide infra).

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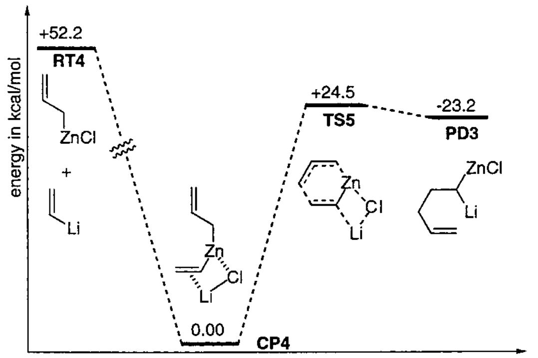

Figure 8. Energy diagram for the coupling of allylzinc chloride and vinyllithium (B3LYP/631+A//HF/321A, kcal/mol).

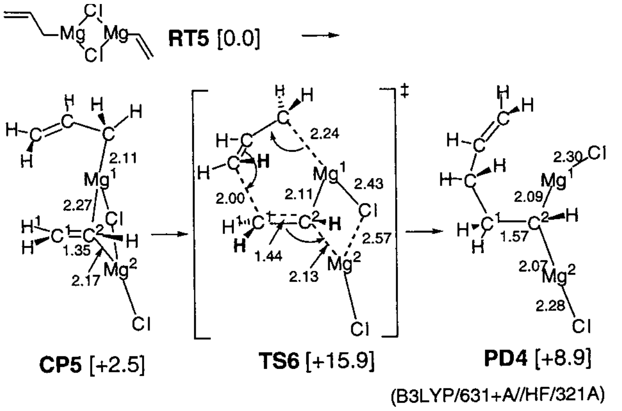

Figure 9. Reaction pathway of the coupling between allylmagnesium chloride and vinylmagnesium chloride at the B3LYP631+A//HF321A level. Curved arrows in TS show electron flow. Energies relative to **RT5** (in brackets) are given in kcal/mol and bond lengths in angstroms.

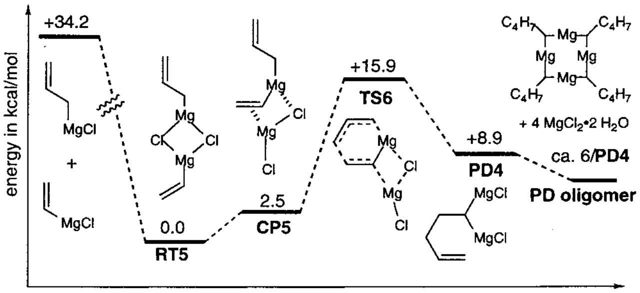

Figure 10. Energy diagram for the coupling of allylmagnesium chloride and vinylmagnesium chloride (B3LYP/631+A//HF/321A, kcal/mol).

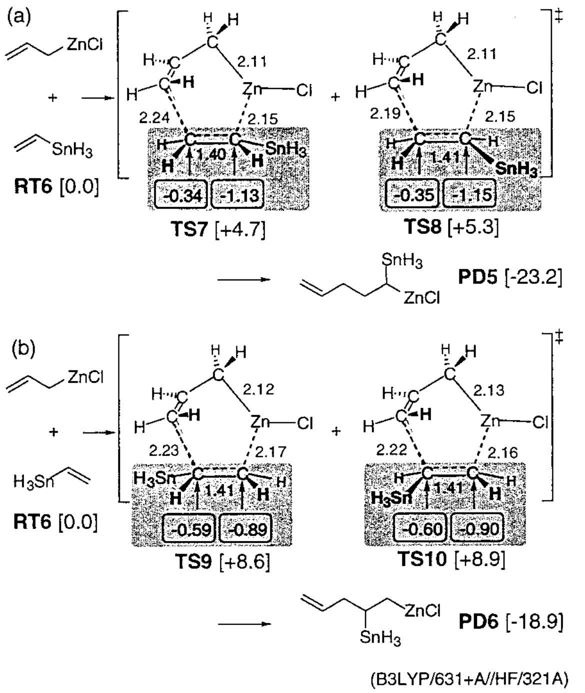

Figure 11. Regioselective allylzincation reactions of allylzinc chloride and vinylstannane: (a) the 1,1-dimetallic TSs and (b) the 1,2-dimetallic TSs. Energies relative to **RT6** (in brackets) are given in kcal/mol. Values in boxes show a natural population charge of carbons of vinylstannane in shadowed boxes.

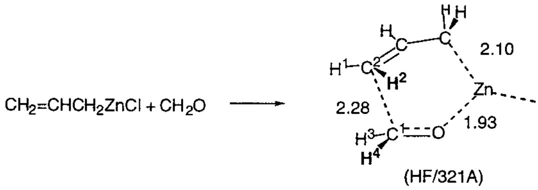

Figure 12. TS of allylzinc chloride addition to formaldehyde.

(3) Coupling between Allylmagnesium Chloride and Vinylmagnesium Chloride. Both the structures of the stationary points in this reaction (Figure 9, **CP5**, **TS6**, **PD4**) and the energetics (Figure 10) are similar to those of the Zn/Mg combination (vide supra). Nonetheless, this reaction does not take place experimentally. (The issue of the **PD** oligomer formation will be discussed later.)

(4) Addition of Allylzinc Chloride to Vinylstannane. For the sake of comparison with highly reactive vinylmetallic species studied above, we also studied vinylstannane (Figure 11). Tributylvinylstannane has proven to be a good acceptor of the zincated hydrazone with the relative reactivity order of vinylmagnesium bromide ≫ vinylstannane > vinylsilane > ethylene.[6] For the allylzincation of the vinylstannane, two diastereomeric pairs of two regioisomeric TSs (**TS7/TS8**, **TS9/TS10**) were obtained and compared for their energies. The energetic effect of the stereoisomerism for **TS7** and **TS8** is rather small (0.6 kcal/mol). **TS7** and **TS8** give the 1,1-dimetallic species **PD5** and are several kilocalories per mole lower in energy than the regioisomeric TSs, **TS9** and **TS10**. The electrostatic origin of such regioselection has previously been discussed for carbometalation of substituted acetylenes,[26] and the selectivity is controlled by the charge distribution of the substituted olefin fragment in the TS (as shown in the shadowed box in Figure 11). Recent experiments indeed showed that the addition of allylzinc species to vinylstannane occurs with the above predicted regioselectivity.[27]

The core six-centered structures of **TS7** and **TS8** are similar to but much less advanced than those found in the endothermic G/N coupling (e.g., **TS2**). Thus, the forming C−C bond length of 1.99 Å in **TS2** of the Zn/Mg G/N coupling is much shorter than the 2.24-Å length in **TS7** and the 2.28-Å length in the allylzinc addition to formaldehyde (Figure 12). The very short forming C−C bond length in the G/N TS (**TS2**) may explain the high diastereoselectivity of the G/N reaction (vide infra).

Diastereoselectivity of the G/N Reaction. The diastereoselectivity (mutual face selectivity) of the reaction provided an intriguing issue in the G/N reaction since an equilibrium mixture of (*E/Z*)-crotylzinc reagents (Scheme 5) gives a single diastereomer through the minor *(Z)*-crotyl isomer.[9] We examined this issue through comparison of the TS of addition of *(E)*- and (*Z*)-

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[26] Nakamura, E.; Miyachi, Y.; Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1992**, *114*, 6686−6692.

[27] Nakamura, M.; Inoue, T.; Sato, A.; Nakamura, E. *Org. Lett.* **2000**, *2* 2193-2196

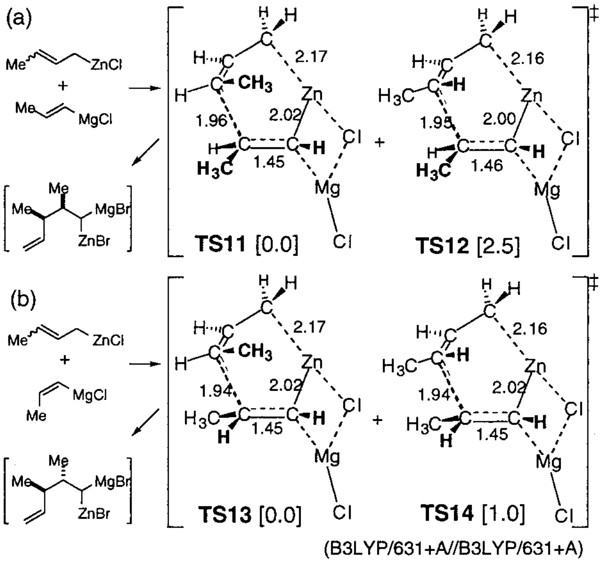
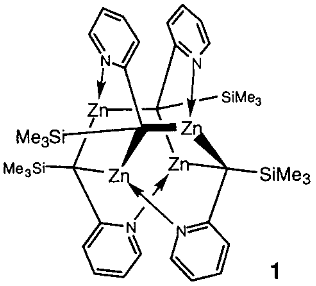


Figure 13. Diastereoselective coupling reactions of (*E*)- and (*Z*)-crotylzinc chlorides and 2-propenylmagnesium chloride: (a) with (1*E*)-propenylmagnesium chloride and (b) with (1*Z*)-propenylmagnesium chloride.

crotylzinc chlorides to *E* and *Z* isomers of 1-propenylmagnesium bromide ($R^1 = R^2 =$ Me, Scheme 1). We only needed to compare the relative energies of the diastereomeric TSs, since the *(E)*- and (*Z*)-crotylzinc reagents in solution are in equilibrium that is fast enough to satisfy the Curtin–Hammett boundary conditions. As shown in Figure 13a for (1*E*)-propenylmagnesium chlorides, the pathway through *(Z)*-crotylzinc (**TS11**) is favored over that through *E* reagent (**TS12**) by 2.5 kcal/mol (translates to 99.6:0.4 at −50 °C). The data account for the experimental selectivity (Scheme 5, 95:5 for $R^1 =$ Me, $R^2 =$ pentyl). Likewise, for the (*Z*)-propenylmagnesium chloride in Figure 13b, the *(Z)*-crotyl path (**TS13**) is favored over the *E* path (**TS14**) by 1.0 kcal/mol (90:10 at −50 °C; experimental data, 92:8 at −50 °C, $R^1 =$ Me, $R^2 =$ pentyl). The high diastereoselectivity must be due to the very short length of the forming C–C bond (~2.0 Å), which enhances steric interactions in the TS. For instance, the two methyl groups in **TS12** come very close to each other (H–H distance of 1.96 Å) than in **TS11** (2.37 Å). This hindrance must overwhelm the relatively small steric effect inherent to the *(Z)*-olefinic structure of the *(Z)*-crotylzinc reagent (*(Z)*-crotylzinc chloride is 0.9 kcal/mol more stable than *(Z)*-crotylzinc chloride, B3LYP/631+A).

Product Stabilization via Oligomerization. In the above paragraphs, we have described the reactions for the Zn/Mg, Mg/Zn, Zn/Zn, Zn/Li, Mg/Mg, and Zn/Sn combinations. Both carbometalation and Lewis acid-assisted metalla–Claisen pathways have been identified in these reactions. The calculated kinetics and thermodynamics of the reactions are quite diverse and clearly do not have direct correlation to the experimental success or failure of the G/N coupling. Kinetic barriers of all reactions are reasonably low for the reaction taking place at or below room temperature, but the thermodynamics is generally unfavorable. Therefore, we must consider yet another factor that provides the key to the success or failure of the reaction.

In light of the very facile transmetalation from magnesium (or lithium) to zinc (which is the first step of the G/N coupling), it is natural to consider that the bimetallic products such as **PD1** and **PD3** undergo self-transmetalation to oligomers of 1,1-dizincio species (e.g., Figure 3).[28] In fact, there are experimental data that 1,1-dizincio species is oligomeric $[(-Zn-CH_2-)_n]$[29] and there is a recent X-ray crystal structure of a tetrameric, cyclic 1,1-dizincio species **1** (Figure 14).[30]



1

Figure 14. Structure of 1,1-organodizinc complex **1**.

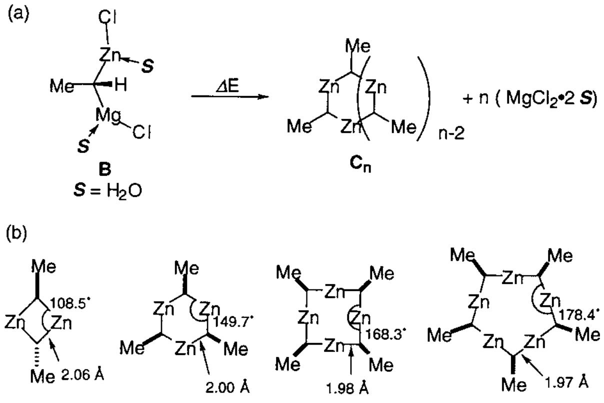


Figure 15. Formation of the dialkylzinc cyclic oligomer. (a) Reaction pathway and (b) structures of the oligomers (B3LYP/631+A level).

Table 1. Stabilization Energy by Formation of Oligmers $\mathbf{C}_n$ ($n = 2-5$, B3LYP/631+A Level)

	energy change (kcal/mol•monomer)			
energy	C_2	C_3	C_4	C_5
Δ*E* (with solvent)	+12.6	−9.0	−14.0	−14.8
Δ*E* (without solvent)	−4.8	−26.3	−31.3	−32.1
Δ*G* (with solvent)	+27.9	−5.2	−8.7	−8.9

We therefore studied the possibility of the formation of oligomeric 1,1-dizincio species as a final G/N coupling product (Figure 15). We examined a model species **B** (a solvated model of **PD1**) and determined the energetics of its conversion to a mixture of a series of cyclic oligomers ($\mathbf{C}_n$; $n =$ the degree of oligomerization, 2–5) and $n(MgCl_2{\bullet}2H_2O)$. The structures are shown in Figure 15 and the energies in the first row in Table 1.[31] The dimer $\mathbf{C}_2$ was calculated under the assumption of C_{2h} symmetry, and the other oligomers ($\mathbf{C}_3$–$\mathbf{C}_5$) under the assumption of C_{nv} symmetry. The calculated C–Zn bond lengths in cyclic oligomers $\mathbf{C}_n$ are good agreement with those in 1,1-organodizinc complex **1** (2.02~2.04 Å).

The four-membered ring dimer $\mathbf{C}_2$[28] is less stable than the monomer by 12.6 kcal/mol•monomer owing to the bending of the C–Zn–C bond that prefers to be linear. On the other hand, trimer $\mathbf{C}_3$, tetramer $\mathbf{C}_4$, and pentamer $\mathbf{C}_5$ are favored by 9.0, 14.0 and 14.8 kcal/mol•monomer, respectively. Taking this result together into the energy diagram in Figure 3, we find that the

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[28] Marek, I.; Lefrançois, J.-M.; Normant, J. F. *J. Org. Chem.* **1994**, *59*, 4154–4161.

[29] Matsubara, S.; Arioka, D.; Utimoto, K. *Synlett* **1999**, 1471–1473.

[30] Andrews, P. C.; Raston, C. L.; Skelton, B. W.; White, A. H. *Organometallics* **1998**, *17*, 779–782.

[31] Models without solvation of the magnesium atoms (the second row of Table 1) indicated overestimation of the stabilization energies due to too large stabilization of the $MgCl_2$ dimer.

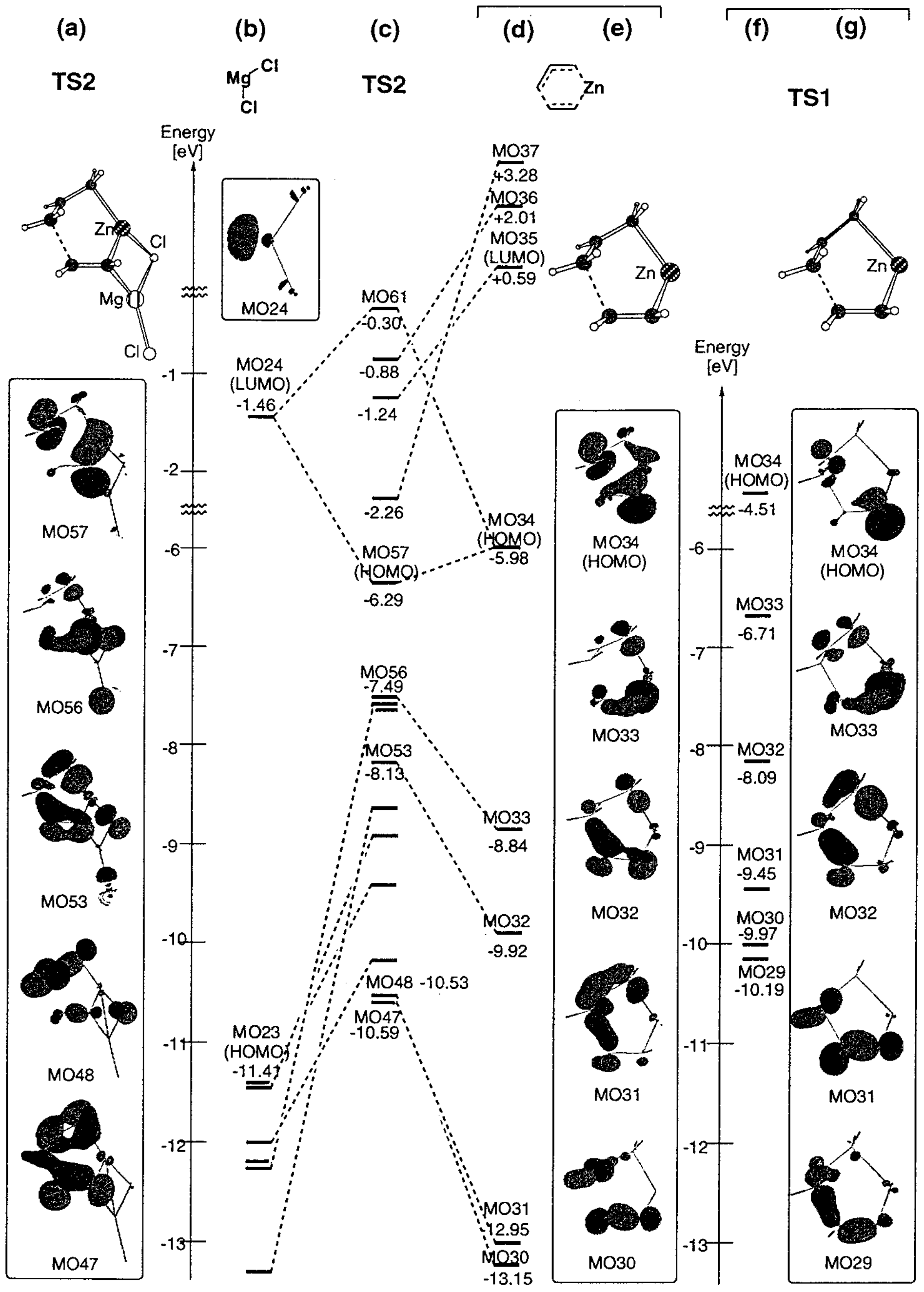
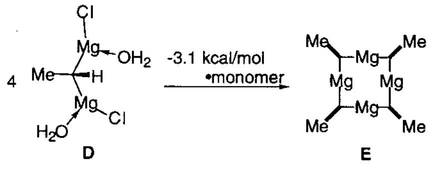


Figure 16. (a) 3D representation of molecular orbitals of **TS2**. (b) 3D representation of LIMO and MO energy levels of $MgCl_2$ fragment. (c)MO energy levels of **TS2**. (d) MO energy levels of allylvinylzinc fragment. (e) 3D representation of molecular orbitals of allylvinylzinc fragment of **TS2**. (f) MO energy levels of **TS1**. (g) 3D representation of molecular orbitals of **TS1**.

tetramerization of the initial product **PD1** will make the reaction exothermic by ~10 kcal/mol•monomer. The same conclusion was obtained when the energy comparison was made on the Gibbs free energy basis (taking into account entropy and zero point energy at 25 °C, 1 atm; the third row of Table 1). Thus, the oligomerization results in 5−9 kcal/mol energy gain for the overall transformation, which will be sufficient to drive the reaction to completion.

Similar oligomerization may take place with the Mg/Mg combination. Thus, the monomer **D** forms the tetramer **E** (under C_{4v} symmetry, eq 1). The structure of **E** (C−Mg bond; 2.12 Å, angle <C−Mg−C; 163.3°) is very similar to that of $\mathbf{C_4}$, but **E** is more stable than **D** only by 3.1 kcal/mol•monomer. Taking this result together into the energy diagram in Figure 10, we find that the tetramer is still several kcal/mol•monomer less stable. Hence, the Mg/Mg combination of the G/N coupling is not an energetically feasible reaction.



(1)

Analysis of Molecular Orbitals. The studies described in the foregoing paragraphs have demonstrated that the prototype G/N coupling is a unique class of reaction, a Lewis acid-assisted metalla−Claisen rearrangement. To obtain support to this interpretation, we analyzed the TS of the reaction (**TS2**) from the molecular orbital point of view. **TS2** (Figure 16a and c) was divided into a $MgCl_2$ fragment (Figure 16b) and an allylvinylzinc fragment (d and e). The molecular orbitals of the $MgCl_2$ fragment (b) consist of a magnesium vacant orbital MO24 and a series of low-lying chlorine lone pairs. The vacant MO24 (LUMO) interacts with MO34 (HOMO) of the allylvinylzinc fragment (d and e) to generate MO57 (HOMO) of **TS2** (a and c). Comparison among the molecular orbitals of **TS2** (a), the allylvinylzinc fragment (e), and **TS1** (g) indicates that the orbitals responsible for the bond alternation in the core metalla−Claisen reaction are essentially the same for all three cases.

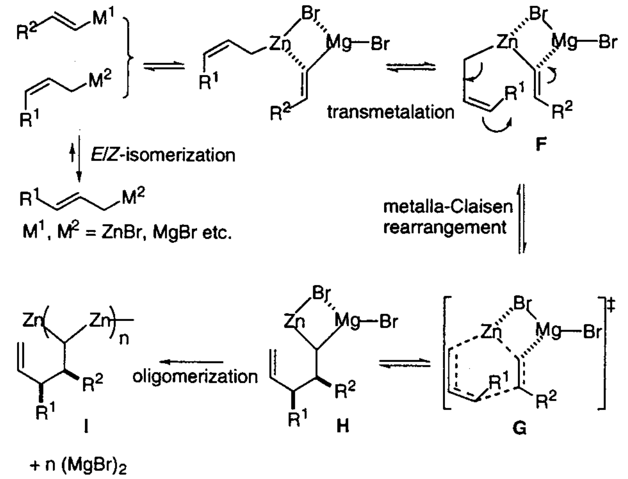
The molecular orbitals of the allylvinylzinc fragment (Figure 16d and e) were next compared with the parent metalla−Claisen **TS1** (Figure 16f and g). The molecular orbitals of the allylvinylzinc fragment (e) are very similar to those of **TS1** (g) (except that the levels of MO31 and MO29 have exchanged). With such similarity of molecular orbitals as well as the geometrical similarity (Figures 1 and 2), we can conclude that the allylvinylzinc fragment in **TS2** has much of the character of a metalla−Claisen rearrangement, and **TS2** can be regarded as the TS of the metalla−Claisen reaction stabilized by interaction with $MgCl_2$ (cf. correlation of MOs 57 and 61 in **TS2** (c) with MO24 of $MgCl_2$ (b) and MO34 in (e).

Conclusion

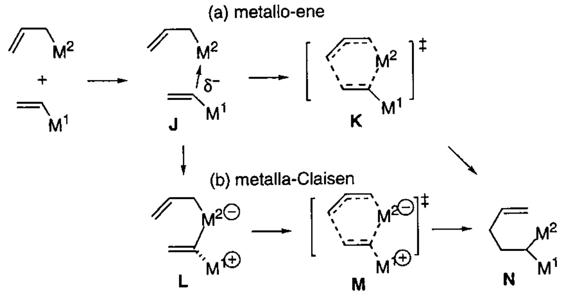
In the present work, we have determined the reaction pathways of the coupling of an allylmetal reagent with a vinylmetal reagent for various combinations of metal atoms (Zn/Mg, Mg/Zn, Zn/Zn, Zn/Li, Mg/Mg, Zn/Sn). The reaction mechanism provides an illustrative example of the importance of polymetallic clusters in synthetically important reactions.[32] The energy barrier and the thermodynamic stability of intermediates along the IRC as well as the stereochemical and molecular orbital analyses provided important mechanistic information as to the reasons for the success of the G/N coupling. The information obtained here will be valuable for further experimental studies, in particular, for designing enantioselective G/N coupling reactions, since it provided the first data set on the kinetics and thermodynamics of the G/N coupling.

Although we are as yet poorly informed of the detailed structures of the polymetallic intermediates of the reaction, we can draw a pathway for the archetypal G/N reaction between a crotylzinc bromide and a vinylmagnesium bromide (Scheme 7). Owing to the initial rapid transmetalation process, it does not matter if one starts from the allylic zinc/vinylic magnesium combination or from the allylic magnesium/vinylic zinc combination. The allyl vinyl zinc intermediate **F** is the crucial intermediate that goes through the TS (**G**) of $MgBr_2$-assisted metalla−Claisen rearrangement to give the 1,1-dimetallic initial product **H**. The **F**-to-**H** conversion being endothermic, the overall thermodynamic driving force of the G/N reaction is provided by the oligomerization of **H** into **I**. The degree of oligomerization (*n*) is currently uncertain and is likely dependent on the product structure and the solvent. Because of the endothermicity of the conversion of **F** to **H**, the TS **G** is quite advanced and the forming C−C bond is very short (~2.0 Å). Therefore, the stereoselectivity of the C−C bond formation (Scheme 5) is subject more to the nearby steric environment than the allylzincation of an aldehyde (Figure 12) or an olefin (Figure 11).

Scheme 7



Scheme 8



Although the **F**-to-**H** conversion is best described as a $MgBr_2$-assisted metalla−Claisen rearrangement, it has some character of metallo−ene of the vinylmetallic species, and this dichotomy depends on the nature of the metal atoms. We can thereofere rationalize, in two ways, the formation of the 1,1-dianionic product in preference to the 1,2-dianionic one (Scheme 4): (a) The regiochemistry is the direct consequence of the metalla−Claisen rearrangement. (b) The selectivity conforms to the general principle of carbometalation of heteroatom-substituted acetylene (and olefin) that we previously proposed.[26,27]

Extending the summary scheme in Figure 2d, we can generalize the metallo−ene/metalla−Claisen dichotomy as in Scheme 8. The extreme facility of the G/N coupling can be rationalized first in the context of the metallo−ene mechanism (Scheme 8a), since the rate of the addition will increase as the negative charge on the carbon-connected M^1 increases (i.e., as the $C-M^1$ bond becomes more ionic).[26] In an event that the M^1-C bond becomes as ionic as $M^1 = Mg(II)$, transmetalation to M^2 takes place and the reaction follows the metalla−Claisen pathway (Scheme 8b). Although the two pathways are clearly different from each other at stages **J** and **L**, they may become indistinguishable at the TS stage (**K** and **M**), and both pathways eventually give the same product **N**.

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(32) For theoretical studies on polymetallic effects and references, see: Nakamura, M.; Nakamura, E.; Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1993**, *115*, 11016−11017. Mori, S.; Kim, B. H.; Nakamura, M.; Nakamura, E. *Chem. Lett.* **1997**, 1079−1080. Nakamura, E.; Mori, S.; Nakamura, M.; Morokuma, K. *J. Am. Chem. Soc.* **1997**, *119*, 4887−489. Nakamura, E.; Mori, S.; Morokuma, K. *J. Am. Chem. Soc.* **1997**, *119*, 4900−4910. Nakamura, E.; Hirai, A.; Nakamura, M. *J. Am. Chem. Soc.* **1998**, *120*, 5844−5845. Mori, S.; Nakamura, E. *Chem. Eur. J.* **1999**, *5*, 1534−1543.