

Synergetic Dimetallic Effects in Gaudemar/Normant Coupling between Allylzinc and Vinyl Grignard Reagents

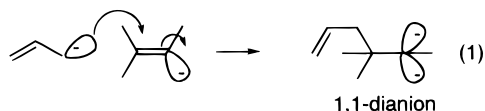
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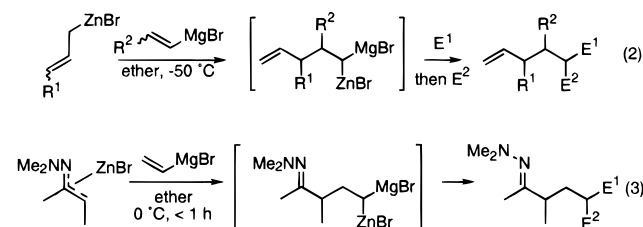
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An anion–anion coupling reaction between an allylic anion and a vinyl anion looks like an entirely impossible organic reaction (eq 1).¹ Most remarkably, however, the reaction becomes not only



experimentally feasible but highly efficient, when magnesium(II) and zinc(II) atoms are used as counterions as in eq 2. Thus, the addition of an allylic zinc reagent to a vinylmagnesium halide was discovered by Gaudemar nearly 30 years ago.² It has been proven recently by Normant to be a versatile synthetic reaction (eq 2),³ serving as a valuable route to novel 1,1-dimetallic nucleophiles.⁴ Recent discovery of the second case of such a reaction by Nakamura,⁵ wherein a zincated hydrazone reacts rapidly with vinylmagnesium bromide (notably, far slower with ethylene) (eq 3), provided evidence that the generality of such



counter-intuitive reactions is much wider than one might expect. Despite recent advance in understanding polymetallic organometallic systems, the mechanism of these reactions remained entirely unclear. We report here the first mechanistic studies on the reaction shown in eq 2 that indicated the synergetic action of the two different metals to circumvent the intrinsic kinetic and the thermodynamic problems expected from eq 1.⁶

It was suggested some time ago that an allylvinylyl zinc intermediate initially forms, and undergoes metalla–Claisen rearrangement in the presence of a magnesium salt.^{3a} The transition

(1) In consonance with the intuition, model B3LYP/6-31+G* calculations indicated that 1,1-dianion formation is 108 kcal/mol endothermic and the adduct would tend to decompose back to the two anions.

(2) Gaudemar, M. C. *R. Acad. Sci. Paris, Ser. C* **1971**, 273, 1669–1672.

(3) (a) Knochel, P.; Normant, J.-F. *Tetrahedron Lett.* **1986**, 27, 1039–1043. (b) Review: Normant, J.-F.; Marek, I.; Lefrançois, J.-M. *Pure Appl. Chem.* **1992**, 64, 1857–1864. (c) Suzuki, K.; Imai, T.; Yamanoi, S.; Chino, M.; Matsumoto, T. *Angew. Chem., Int. Ed. Engl.* **1997**, 36, 2469–2471.

(4) Marek, I.; Normant, J.-F. *Chem. Rev.* **1996**, 96, 3241–3267.

(5) Nakamura, E.; Kubota, K.; Sakata, G. *J. Am. Chem. Soc.* **1997**, 119, 5457–5458.

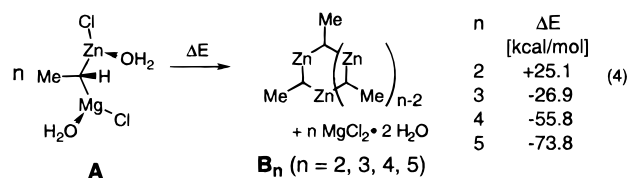
(6) The GAUSSIAN 94 program was used. Ahlrichs's SVP (Schäfer, A.; Horn, H.; Ahlrichs, R. *J. Chem. Phys.* **1992**, 97, 2571–2577) all-electron basis set was used for the zinc atom and the 6-31+G* basis set for other atoms (denoted here as B3LYP/6-31A). For the computational method, see: Nakamura, E.; Hirai, A.; Nakamura, M. *J. Am. Chem. Soc.* **1998**, 120, 5844–5845. As was the case with this report, HF/321A geometries (but not energetics) were in good accord with the B3LYP/631A geometries, and may be used as a much cheaper substitute of the latter.

structure (TS) of the prototype metalla–Claisen rearrangement of allylvinylyl zinc (TS1, Figure 1a) was found to be much higher in energy (50.7 kcal/mol) than the starting material, and hence the process does not look reasonable. This reaction is also chemically unlikely, since it will generate a zinc alkylidene complex $\text{CH}_2=\text{CH}(\text{CH}_2)_2\text{CH}=\text{Zn}$.

When we placed a molecule of MgCl_2 nearby C^2 in TS1 to form TS2, the activation energy dropped dramatically to 15.4 kcal/mol (15.6 kcal/mol, MP2/631A//B3LYP/631A) because the Mg(II) atom stabilizes the developing negative charge on C^2 (Figures 1b and 2). Thus, we have constructed a mixed μ -chloro-bridged cluster (RT2) from monomers (RT1), and also a complex between allylvinylyl zinc and MgCl_2 (CP1).⁷ Geometry of CP1 indicates that the vinyl group is σ -bonded to Zn and π -coordinated to Mg ($\text{C}^2\text{–Zn} = 2.04 \text{ \AA}$, $\text{C}^2\text{–Mg} = 2.34 \text{ \AA}$; dihedral angle $\angle \text{H}^1\text{C}^1\text{C}^2\text{Zn} = 14.8^\circ$, $\angle \text{H}^1\text{C}^1\text{C}^2\text{Mg} = 69.8^\circ$). TS2 goes smoothly downhill to the 1,1-dimetallic product (PD) as followed along the intrinsic reaction coordinate. The 1,1-dimetallic character of PD already emerges in TS2, where sp^3 -hybridized C^2 is bound equally tightly to Zn and Mg ($\text{C}^2\text{–Zn} = 2.03 \text{ \AA}$, $\text{C}^2\text{–Mg} = 2.14 \text{ \AA}$; dihedral angle $\angle \text{H}^1\text{C}^1\text{C}^2\text{Zn} = 69.2^\circ$, $\angle \text{H}^1\text{C}^1\text{C}^2\text{Mg} = 26.6^\circ$). In light of the geometrical similarity between TS1 and TS2, the reaction can be considered as “Lewis acid assisted metalla–Claisen rearrangement”. On the other hand, TS2 also can be viewed as “allylzincation of vinylmagnesium chloride” because of its geometrical similarity to the TS of allylzincation of an olefin.^{8–10} The Lewis acidic role of MgCl_2 is consistent with the slower reaction rate in a basic medium.

An alternative pathway $\text{CP2} \rightarrow \text{TS3} \rightarrow \text{PD}$ to reach PD involves a reverse combination of metals (Figure 2). This path 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. In consonance with this energetics, an alkyl Grignard reagent is a good alkyl donor to a zinc halide in experiments.¹¹

In light of the smoothness of the reactions in eq 2, the nearly thermoneutral thermodynamics from RT2 to PD (Figure 2) seems rather unreasonable, which put into question the identity of PD as the final product. It has been suggested from experiment¹² that the final product may be a 1,1-dizincio four-membered dimeric species (e.g., B₂, eq 4). To probe this possibility (eq 4), we



calculated the energetics of conversion of A (a solvated model of PD) into a series of a mixture of $n(\text{MgCl}_2 \cdot \text{H}_2\text{O})$ and a cyclic oligomer (B_n; n = the degree of oligomerization, 2–5). Except for the strained four-membered dimer B₂, all higher oligomers enjoy stabilization of 9–15 kcal/(mol·A) due to formation of

(7) Prototypes of the heterodimer CP1 (e.g., homo μ -chloro-bridged dimers of halomagnesium and halozinc species) are well-known. See: Al-Juaid, S. S.; Eaborn, C.; Habtemariam, A.; Hitchcock, P. B.; Smith, J. D.; Tavakkoli, K.; Webb, A. D. *J. Organomet. Chem.* **1993**, 462, 45–55.

(8) We also examined LiCl and ZnCl₂ in place of MgCl₂ in the CP1/TS2 pathway to find that the activation energy indeed decreases in the order of LiCl, MgCl₂, and ZnCl₂. The details will be discussed in a full paper.

(9) Nakamura, M.; Nakamura, E.; Koga, N.; Morokuma, K. *J. Chem. Soc., Faraday Trans.* **1994**, 29, 1789–1798. Kubota, K.; Mori, S.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* **1998**, 120, 13334–13341.

(10) HOMO of TS2 is located mainly on the olefinic C² atom as well as on the C–C double bond of the allyl group. This picture suggests that the reaction has the character of nucleophilic allylation of olefin.

(11) Laloë, E.; Srebnik, M. *Tetrahedron Lett.* **1994**, 35, 5587–5591.

(12) Marek, I.; Lefrançois, J.-M.; Normant, J.-F. *J. Org. Chem.* **1994**, 59, 4154–4161.

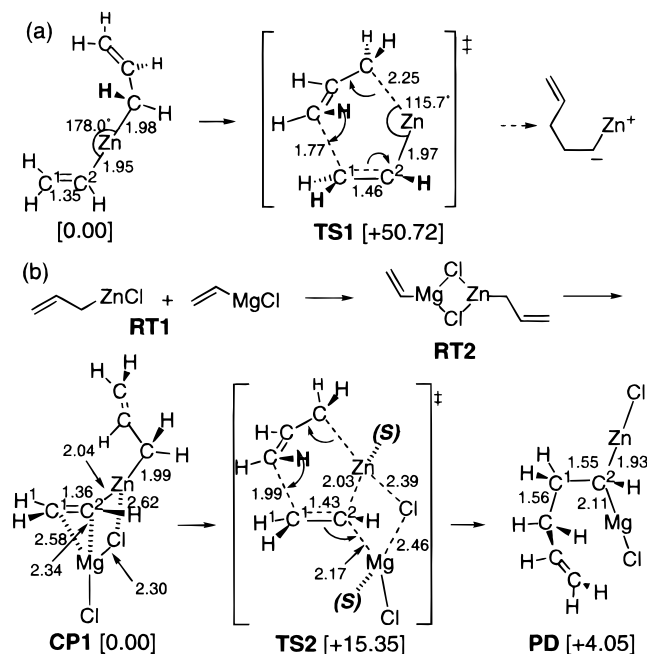


Figure 1. (a) Metalla-Claisen rearrangement of allylvinylyl zinc. (b) The pathway of the reaction between allylzinc chloride and vinylmagnesium chloride. Curly arrows in TSs show electron flow. Energies relative to CP1 (in bracket) are in kcal/mol, and bond lengths are in angstroms. Note: Solvation of the two metal atoms in TS2 with Me₂O (shown as S) did not much change the core six-centered structure (<0.05 Å changes), only to elongate the Zn–Cl bond by 0.11 Å.

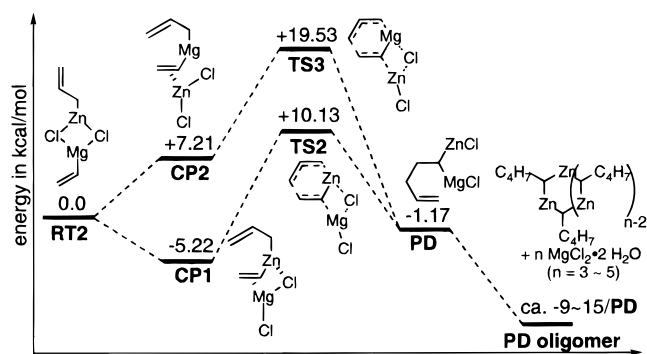


Figure 2. Energy diagram for two isomeric pathways of Gaudemar/Normant coupling (B3LYP/631A, kcal/mol).

stable C–Zn bonds. Recent crystallographic structure of an analogue of B₄¹³ confirmed the existence of such oligomers. We thus suggest that the initial product (PD) will rapidly generate 1,1-dizincio oligomers (either cyclic or linear) to gain the overall driving force of the reaction. In view of the enthalpic and entropic terms, trimer and tetramer products are most likely.

Diastereoselectivity (mutual face selectivity) of the reaction has been a puzzle in that a *cis/trans* equilibrium mixture of a crotylzinc reagent (R¹ = Me, eq 2) gives a single diastereomer through the minor *cis*-crotyl isomer (cf. Figure 3).¹⁴ We examined this issue through comparison of *cis*- and *trans*-crotylzinc chlorides (R¹ = R² = Me).¹⁵ As shown in Figure 3a for *trans*-propenylmagnesium chlorides, the pathway through *cis*-crotylzinc

(13) Andrews, P. C.; Raston, C. L.; Skelton, B. W.; White, A. H. *Organometallics* **1998**, *17*, 779–782.

(14) Marek, I.; Lefrançois, J.-M.; Normant, J.-F. *Synlett* **1992**, 633–634.

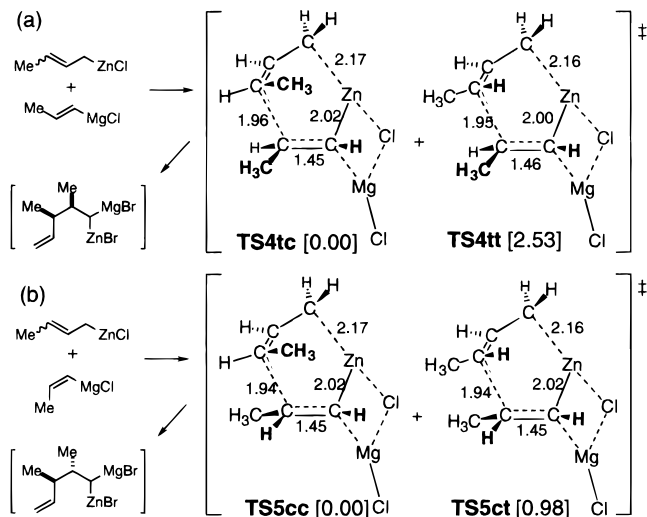


Figure 3. Diastereoselective coupling reactions of *cis*- and *trans*-crotylzinc chloride and 2-propenylmagnesium chloride: (a) with *trans*-2-propenylmagnesium chloride and (b) with *cis*-2-propenylmagnesium chloride.

(TS4tc) is favored over that through *trans* reagent (TS4tt) by 2.5 kcal/mol (translates to 99.6:0.4 at –50 °C). The data account for the experimental selectivity (eq 1, 95:5 for R¹ = Me, R² = pentyl). Likewise, for the *cis*-propenylmagnesium chloride in Figure 3b, the *cis*-crotyl path (TS5cc) is favored over the *trans* path (TS5ct) by 0.98 kcal/mol (90:10 at –50 °C; experimental data, 92:8 at –50 °C, R¹ = Me, R² = pentyl). The selectivity stems from the unique properties of the six-centered TS fused to the four-centered μ -chloro bridge. Thus, for instance, the rigid bicyclic system forces the two methyl groups in TS4tt to come closer to each other (H–H distance of 1.96 Å) than in TS4tc (2.37 Å). This hindrance must overwhelm the steric effect inherent to the *cis*-olefinic structure of the *cis*-crotylzinc reagent.

The present studies revealed, for the first time, that the success of the Gaudemar/Normant coupling depends on the intricate synergy of the polymetallic system to achieve low activation energy and favorable thermodynamics.¹⁶ The transition state of the reaction possesses a novel, mixed feature of two reactions, metalla-Claisen rearrangement and carbometalation of olefin. The 1,1-dimetallc regioselectivity conforms to the general principle that we reported previously¹⁷ for olefin carbometalation.¹⁸ The present results will have a bearing to the hydrazone reaction (eq 3), and will serve for development of enantio-controlled reactions.¹⁹

Supporting Information Available: Structures of RT2, CP1, TS1, TS2, TS4tc, TS4tt, TS5cc, TS5ct, PD, and B₄ (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(15) *cis*- and *trans*-crotylzinc reagents in solution are in rapid equilibrium with each other and hence we need only to compare the energies of isomeric TSs.

(16) 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. Mori, S.; Nakamura, E. *Chem. Eur. J.* **1999**, *5*, 1534–1543. Nakamura, E.; Hirai, A.; Nakamura, M. *J. Am. Chem. Soc.* **1998**, *120*, 5844–5845.

(17) Nakamura, E.; Miyachi, Y.; Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1992**, *114*, 6686–6692.

(18) Marek, I.; Normant, J.-F. In *Metal catalyzed cross coupling reactions*; Diederich, F., Stang, P., Eds.; Wiley VCH: New York, 1998; pp 271–337.

(19) 3D pictures and Cartesian coordinates are located at <http://www.chem.s.u-tokyo.ac.jp/~common/Theo/GN1/title.html>.