Mechanism and Regioselectivity of Reductive Elimination of π-Allylcopper (III) Intermediates

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Abstract: Reductive elimination of a π-allylcopper(III) compound leading to the formation of a C—C bond on an allylic terminal has been considered to occur via the corresponding σ-allylcopper(III) species. The present B3LYP density functional study has shown however that the C—C bond formation occurs directly from the π-allyl complex via an enyl[σ+π]-type transition state, which has structural features different from a simple σ-allylcopper(III) intermediate. In the case of unsymmetrically substituted π-allylcopper(III) compound that has a partial σ-allylcopper(III) structure, the reductive elimination occurs preferentially at the σ-bonded allylic terminal since, in this way, the copper atom can recover most effectively its d-electrons shared with the allyl system. The regioselectivity of the reductive elimination of a substituted π-allylcopper(III) intermediate is mainly controlled by the electronic effect, and correlated well to the Hammett σ_p^+ constant. The analyses revealed mechanistic kinship between the allylic substitution and the conjugate addition reaction of organocopper reagents.

Substitution reaction of an organocopper reagent with an allylation reagent provides an invaluable tool in organic synthesis (Scheme 1).[1] The mechanism of the reaction has attracted considerable attention per se, and in relation to the effort to control the regio- and stereoselectivity of the reaction, since the selectivity has been known to be more or less case-dependent. Generally speaking, the C—C bond formation can take place either at the position α or γ to the position of the leaving group, or on the face anti or syn to the side of the leaving group. For instance, the reaction of a lithium dialkylcuprate reagent with an allylic acetate takes place in such a manner that the C—C bond forms stereospecifically anti to the leaving group, but tends to give a mixture of α and γ-products[2] as an E/Z stereomixture.[3e,f,g] Recent studies by Bäckvall on the copper-catalyzed cross coupling between an allyl Grignard reagent and

Scheme 1. Conventional Mechanism of Allylation Reaction of Lithium Diorganocuprate
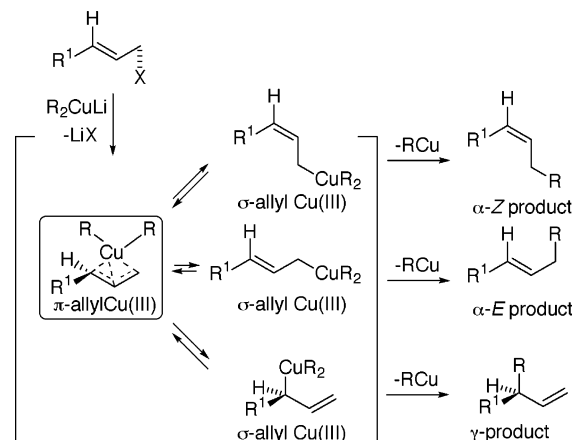

an allyl ester concluded the presence of a π-allylcopper(III) intermediate in the allylation reaction.[4]

The allylation reaction of a lithium dialkylcuprate is presently considered to involve three steps (Scheme 1).[3] The initial loss of the leaving group generates a π-allylcopper(III) intermediate, in which the memory of the position of the leaving group is lost. This intermediate equilibrates with a σ-allylcopper(III) intermediates, from which a mixture of α- and γ-allylation products form. The formation of E- and Z-products has been taken as evidence of the presence of the σ-allylcopper(III) intermediate,[3e,f,g] and the regioselectivity has been considered to depend on the reactivity of these intermediates from which the allylation products form.[3i]

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(1) (a) Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135−631. (b) Krause, N.; Gerold, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 186−204 (c) Nakamura, E.; Mori, S. *Angew. Chem., Int. Engl.* **2000**, *39*, 3751−3771. (d) *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: 2002.

(2) Anderson, R. J.; Hendrick, C. A.; Siddall, J. B. *J. Am. Chem. Soc.* **1969**, *91*, 735−737.

(3) (a) Goering, H. L.; Singleton, V. D., Jr. *J. Org. Chem.* **1976**, *41*, 7854−7855. (b) Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1981**, *46*, 2144−2148. (c) Goering, H. L.; Seitz, E. P.; Tseng, C. C. *J. Org. Chem.* **1981**, *46*, 5304−5308. (d) Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1983**, *48*, 721−724. (e) Goering, H. L.; Singleton, V. D., Jr. *J. Org. Chem.* **1983**, *48*, 1531−1533. (f) Goering, H. L.; Tseng, C. C. *J. Org. Chem.* **1983**, *48*, 3986−3990. (g) Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1984**, *49*, 422−426. (h) Goering, H. L.; Tseng, C. C. *J. Org. Chem.* **1985**, *50*, 1597−1599. (i) Goering, H. L.; Kantner, S. S.; Seitz, E. P., Jr. *J. Org. Chem.* **1985**, *50*, 5495−5499. (j) Nakamura, E.; Sekiya, K.; Arai, M.; Aoki, S. *J. Am. Chem. Soc.* **1989**, *111*, 3091−3093. (k) Bäeckvall, Jan-E.; Sellén, M.; Grant, B. *J. Am. Chem. Soc.* **1990**, *112*, 6615−6621. (l) Persson, E. S. M.; van Klaveren, M.; Grove, D. M.; Bäeckvall, Jan-E.; van Koten, G. *Chem. Eur. J.* **1995**, *1*, 351−359.

(4) Karlstrom, A.; Sofia E.; Bäeckvall, J.-E. *Chem. Eur. J.* **2001**, *7*, 1981−1989.

Scheme 2. π-Allylcopper(III) Chemistry in Conjugate Addition

conjugate addition

Scheme 3. Two Pathways for Reductive Elimination of **CPa**
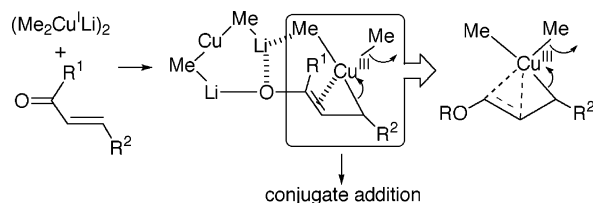
The π-allylcopper(III) species is also an important intermediate in the conjugate addition chemistry. Namely, the rate- and stereochemistry-determining step of the reaction has been shown to be the reductive elimination of the β-cuprio(III) enolate intermediate[5] (Scheme 2). This can be viewed as an unsymmetrical π-allylcopper(III) compound, from which a C−C bond forms on the side distant from the strongly electron-donating oxygen anion.

Despite wide acceptance of the π-allylcopper(III) intermediates, they have been identified neither by spectroscopy nor by crystallography (except the case in Scheme 2, where the β-cuprio enolate can be detected at low temperature).[6] There has been reported no theoretical analysis on such intermediates. To obtain pertinent structural, energetic and theoretical information on these elusive intermediates, we performed density functional studies on their reductive elimination reaction focusing on two issues: (1) The intermediacy of the σ-allylcopper(III) compound along the pathway to the allylation product, and (2) the reactivity of π-allylcopper(III) intermediates bearing one or two substituents on the terminal methylene groups. As the result, we made several important observations which will be detailed this article: (1) Both the σ- and the π-allylcopper(III) intermediates exist as minima, but the latter is more stable both in the gas phase and in the presence of Me_2O as a ligand on the metal. (2) The σ- and the π-allylcopper(III) intermediates are in rapid equilibrium with each other, and the reductive elimination of the π-allylcopper(III) intermediate takes place much faster than that of the σ-allylcopper(III) intermediate. (3) The transition state of the reductive elimination of the π-allylcopper(III) intermediate resembles an enyl[σ+π] complex.[7,8] (4) For a 1-substituted π-allylcopper(III) intermediate, reductive elimination always takes place at the C^3 position, and the rate of reductive elimination increases as the C^1-substituent become more electron-donating. (4) The substituent effect on the regioselectivity of the reductive elimination is largely controlled by the resonance effect of the substituent (Hammett, σ_p^+). (5) An electron-donating substituent deforms the π-allylcopper(III) intermediate into an unsymmetrical enyl[σ+π] complex, in which the Cu−C^3 bond now bears the character of a σ-bond. The Cu(III) center can recover electrons through this σ-bond, which is mainly composed of the copper $3d_{xz}$ electrons. As the result, the electron-donating group not only accelerates the
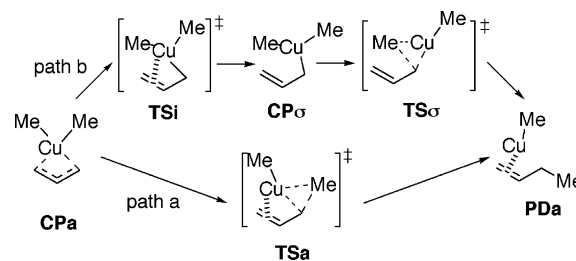
reductive elimination, but also directs the C−C bond formation to take place selectively at the C^3 position.

Computational Methods

All calculations were performed with a Gaussian98 package[9] without symmetry assumption unless noted otherwise, by using the B3LYP hybrid functional, which is a combination of Becke's three-parameter hybrid functional[10] with correlation functional of Lee−Yang−Parr.[11] All electron SVP basis set by Horn and Ahlrichs[12] was used for copper and 6-31G*[13] for other atoms. For some cases, we also examined the Stuttgart quasirelativistic pseudo potential (SDD)[14] to find very similar results.[15] All stationary points were adequately characterized by normal coordinate analysis, and were confirmed to lie on the intrinsic reaction coordinate of the reported reaction pathways. Energies are shown in kcal/mol and bond lengths in Å. The natural charges were calculated by the natural population analysis at the same level as the one used for geometry optimization.[16]

Results and Discussion

1. Reductive Elemination of Unsubstituted π-Allylcopper-(III) Intermediate. 1.1. Solvent-Free Model. Both the π-(**CPa**) and the σ-allylcopper(III) intermediates (**CPσ**) were examined for their reductive elimination (Scheme 3). In the π-allyl pathway (path a), the symmetrical π-allyl intermediate **CPa** becomes symmetric to arrive, with 14.2-kcal/mol activation energy, at the enyl[σ+π] transition state (**TSa**), where one terminal methylene carbon is σ-bonded to the metal and the remaining two carbon atoms are π-coordinated to the metal. After **TSa**, the product **PDa** forms.

In the σ-allyl pathway (path b), **CPa** first isomerizes to the σ-allyl complex **CPσ** via **TSi** with a high activation energy (19.1 kcal/mol). The σ-allyl complex **CPσ** reductively eliminates with a 0.8-kcal/mol activation energy via **TSσ** to the product **PDa**.

(5) Nakamura, E.; Mori, S.; Morokuma, K. *J. Am. Chem. Soc.* **1997**, *119*, 4900−4910.

(6) (a) Hallnemo, G.; Olsson, T.; Ullenius, C. *J. Organomet. Chem.* **1984**, *265*, C22−C24. (b) Hallnemo, G.; Olsson, T.; Ullenius, C. *J. Organomet. Chem.* **1985**, *282*, 133−144. (c) Christenson, B.; Hallnemo, G.; Ullenius, C. *Chemia Scripta* **1987**, *27*, 511−512. (d) Ullenius, C.; Christenson, *Pure Appl. Chem.* **1988**, *60*, 57−64. (e) Bertz, S. H.; Smith, R. A. J. *J. Am. Chem. Soc.* **1989**, *111*, 8276−8277.

(7) An enyl complex is by difinition a complex which contains discreet σ- and π-metal−carbon interactions toward a single ligand. (a) Sharp, P. R. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: New York, 1995; Chapter 2, p 272.

(8) Evans, P. A.; Nelson, J. D. *J. Am. Chem. Soc.* **1998**, *120*, 5581−5582.

(9) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.6; Gaussian Inc.: Pittsuburgh PA, 1998

(10) Becke, A. S. *J. Chem. Phys.* **1993**, *98*, 5648−5652.

(11) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785−789.

(12) The basis set character was given according to EMSL Gaussian Basis Set Order Form (http://www.emsl.pnl.gov/forms/basisform.html) (a) Schafer, A.; Horn, H.; Ahlrichs, R. *J. Chem. Phys.* **1992**, *97*, 2571−2577.

(13) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; John Wiley: New York, 1986. References cited therein.

(14) Dolg, M.; Wedig, U.; Stoll, H.; Preuss, H. *J. Chem. Phys.* **1987**, *86*, 866−872.

(15) Yamanaka, M.; Inagaki, A.; Nakamura, E. *J. Comput. Chem.* **2003**, *24*, 1401−1409.

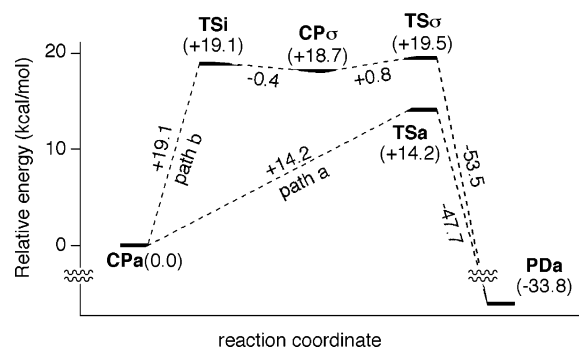(16) Reed, A. E.; Weinstock, R. B.; Weinhold, F. *J. Chem. Pys.* **1985**, *83*, 735−746.

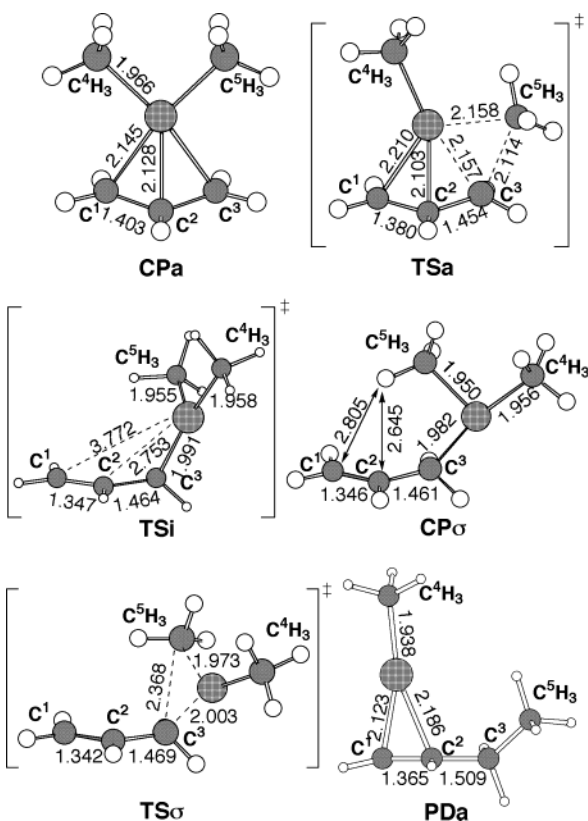**Figure 1.** Energy diagram of solvent-free models of reductive elimination.

Figure 2. 3D Structures of complexes and transition states of solvent-free models.
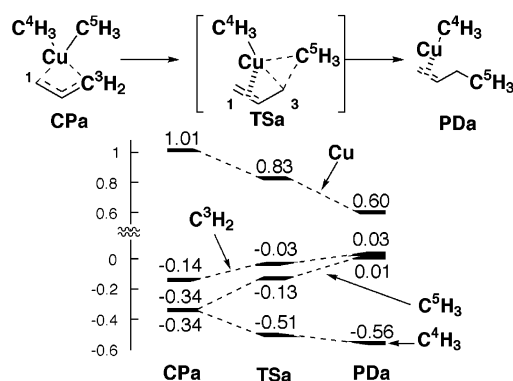

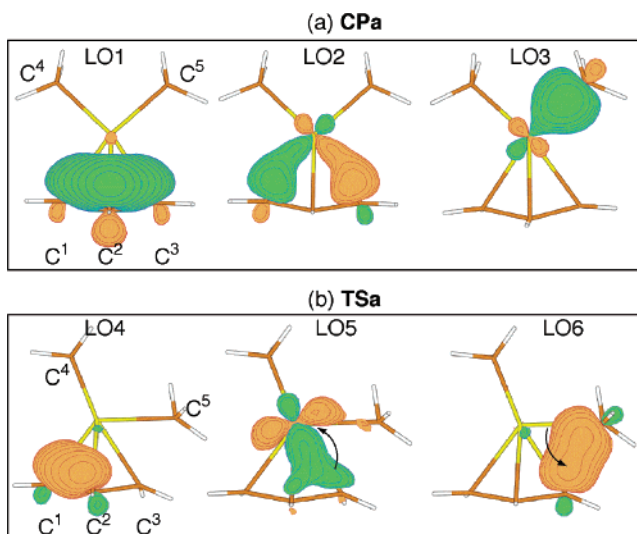**Figure 3.** Charge distribution along path a.

Figure 4. Localized Kohn–Sham Orbitals (occupied) of **CPa** (a) and **TSa** (b). Arrows in **TSa** indicate electron flow toward product formation.

The energy diagram indicates that path a is overwhelmingly favored over path b.

Figure 2 shows representative 3D structures. The π-allylcopper(III) complex (**CPa**), which is a local minimum, is a d^8-square planar complex bearing the two methyl ligands and the two terminal methylene carbon atoms in the coordination plane. In **TSa**, the Cu–C^3 and the Cu–C^5 bonds are elongated, and the C^3–C^5 is shortened with considerable decrease of the positive charge on the copper atom (Figure 3). It is also notable that the C^1–C^2 bond is shortened as it eventually becomes a double bond.

In path b, the CuMe$_2$ moiety rotates around the C^2–C^3 bond and arrives at the TS of π-to-σ isomerization (**TSi**). Here, the bonds between Cu and C^1/C^2 is entirely broken, while Cu and C^3 are σ-bonded (Figure 2). Further rotation leads to the σ-complex **CPσ**, where the copper is T-shaped and coordinatively unsaturated.[17] **CPσ** is less stable than **CPa** by 18.7 kcal/mol. The copper atom in the TS of reductive elimination (**TSσ**) is

still coordinatively unsaturated, which accounts for the high energy barrier of reductive elimination through the σ-allyl intermediate.

Figure 3 shows the charge distribution in the reductive elimination of the π-allyl complex. The charge of copper in **CPa** (+1.01) decreases at **TSa** to +0.83, and finally to +0.60 in the final product (**PDa**).[18] It is worth remembering that the negative charge of C^4H_3 increases monotonically from −0.34 in **CPa** to −0.56 in **PDa**, while that of C^5H_3 decreases to near zero as it becomes σ-bonded to C^3.

Boys localized orbitals[19] of **CPa** and **TSa** indicated the presence of the standard donative (LO1; allyl π- and copper 4s orbitals) and back-donative (LO2; π-allyl and $3d_{xz}$ orbitals) interactions between the metal and the π-allyl moiety (Figure 4a). LO3 corresponds to the Cu–C σ-bond formation.

As the symmetry in **CPa** is broken to go to **TSa**, LO1 is transformed into LO4, and LO2 to LO5. Thus, the desymmetrization causes the desymmetrization of donative and back-donative interactions so that the C^1 terminal donates electron to the copper atom and the copper atom back-donates to the C^3 terminal. LO6 is the forming C–C σ-bond. As it goes further

(17) Nakamura, E.; Yamanaka, M.; Mori, S. *J. Am. Chem. Soc.* **2000**, *122*, 1826–1827.
(18) The copper charge in **CPa** (+1.01) much smaller than the one expected from the Cu(III) formalism is commonplace for transition metal organometallics. Kaupp, M.; von Schnering, H. G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 986.
(19) Boys, S. F. Quantum Theory of Atoms, Molecules, and the Solid State; Lowdin, P. O., Ed.; Academic Press: New York, 1968; p 253.
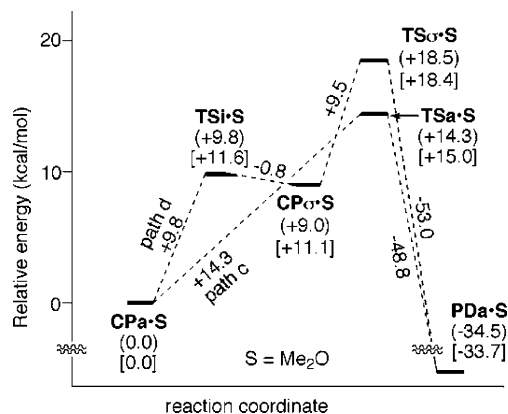
Figure 5. Energy diagram of solvent-coordinated model of reductive elimination. Potential energy (kcal/mol) is given in parentheses, and Gibbs free energy at 195.5 K (−78 °C), 1 atm in brackets.

Scheme 4. Solvent-Coordinated Model of Reductive Elimination of Allylcopper(III) Intermediate via [σ+π]- and σ-Pathways. Note that the Hatched Line Indicates Both Strong Coordination and Extremely Weak Coordination (see Figure 6 for the exact distances between the copper atom and the solvent molecule)
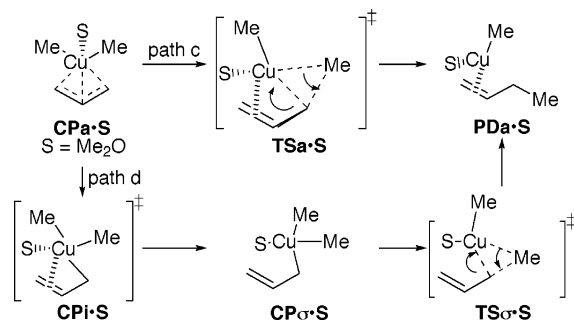
to the product, the electron density of the C^3−C^5 bond increases and that of the Cu−C^3 bond decreases. In this process, the copper(III) center is reduced to Cu(I) by "recovering" electrons (LO5) that were once given to the allyl moiety through back-donative interaction in **CPa**.

1.2. Solvent-Coordinated Model. Being coordinatively unsaturated, the σ-allylcopper(III) complexes **CPσ** and **TSσ** are thermodynamically much less stable than the π-allyl complex **CPa**. With these energetics, the π-allyl complex **CPa** will directly form **PDa** without intervention of the σ-isomer. When an ether molecule is allowed to coordinate on the copper atom (Scheme 4), this energetics changed so that the π-complex undergoes equilibrium with the σ-isomer before going to **PDa** (Figure 5).

The energy profile of the π-allyl route (path c) is similar to the solvent-free path discussed above. On the other hand, the σ-pathway is stabilized by ca. 10 kcal/mol up to the stage of the σ-allylcopper(III) complex **CPσ·S**, which is due to solvent coordination to the copper(III) atom. In the TS of reductive elimination (**TSσ·S**) where the copper(III) atom already acquires significant electrons (cf. Figure 3), the solvent molecule is released from the metal. Hence the overall activation energy from **CPa·S** to **TSσ·S** remains similar to that from **CPa** to **TSσ** in the solvent-free path b (Figure 1). The Gibbs free energy profile at −78 °C (brackets in Figure 5) is essentially the same as that of the potential energy profile. Thus, we expect that the π- and σ-allyl complexes can equilibrate with each other before C−C bond formation, thereby allowing geometrical isomerization of the π-allylic intermediate (i.e., when it is substituted on C^1 and C^3).
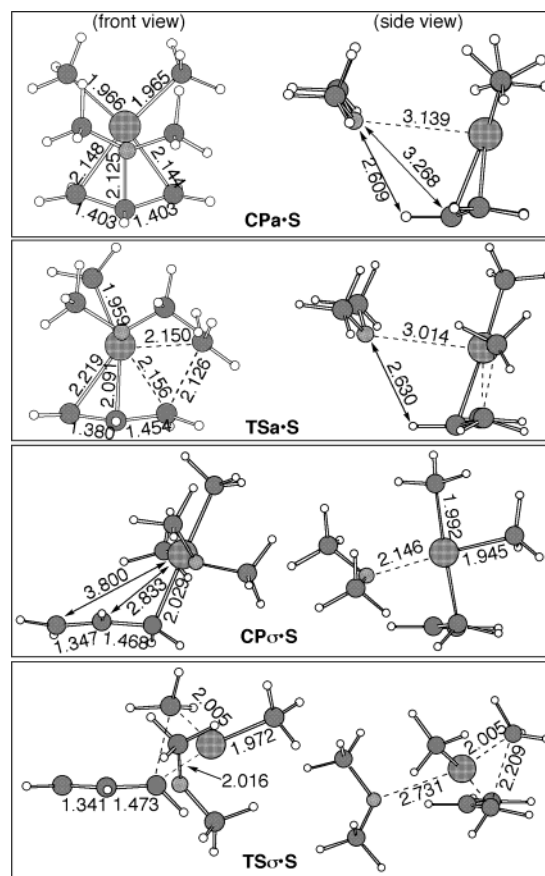
Figure 6. 3D Structure of complexes and transition structures in solvent-coordinated model.
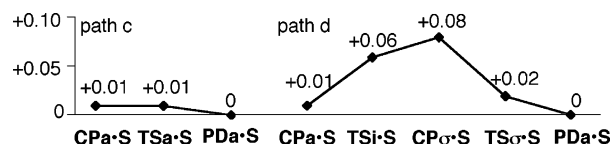

Figure 7. Natural population analysis of Me₂O along reaction pathway (paths c and d).

Figure 6 shows representative 3D structures. The π-allylcopper(III) complex **CPa·S** is coordinatively saturated with the four carbon ligands and therefore the Me₂O molecule is located far away from to the metal center. The same is true for **TSa·S**. On the other hand, **TSi·S** (not shown) and **CPσ·S** complex form stable tetracoordinated square planar complexes. The Me₂O molecule does *not* coordinate to the copper atom (Cu−O = 2.731 Å) in **TSσ·S** since the copper atom is halfway reduced to Cu(I) (Figure 3).

The nature of the Me₂O coordination at various stages of the reaction is reflected in the charge distribution (Figure 7). Thus, the natural charges on Me₂O do not change much in path c, while, in path d, it reaches the maximum positive value of +0.08 at **CPσ·S**. The positve charge at **TSσ·S** is very small, indicating that Me₂O strongly coordinates to copper atom in **CPσ·S** but not in **TSσ·S**.

2. Regioselectivity of Reductive Elimination of Monosubstituted π-Allylcopper(III) Intermediate. The results in the previous section indicated that the reductive elimination occurs predominantly from π-allylcopper(III) intermediate rather than from the σ-allyl intermediate. We next studied the regioselectivity of decomposition of 1-substituted π-allylcopper(III)
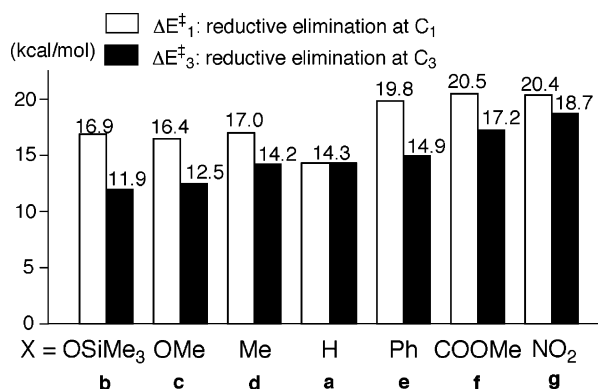
Figure 8. Substituent effect on the activation energy of reductive elimination. Substituents are ordered according to their electron-donating and withdrawing abilities.

Scheme 5. Two Isomeric Pathways of Reductive Elimination of Substituted Allylcopper(III) Intermediates. Reductive Elimination at C1 Position Is Denoted as Series 1 and that at C3 as Series 3
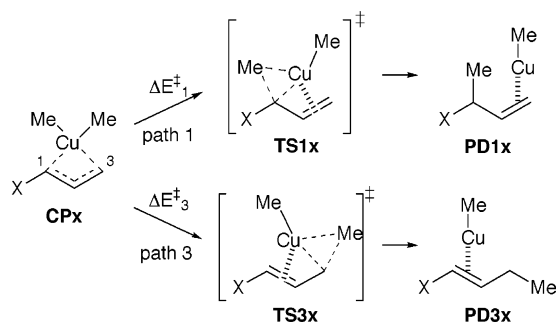
a : X = H, b : X = OSiMe$_3$, c : X = OMe, d : X = Me, e : X = Ph,
f : X = COOMe, g : X = NO$_2$

compound, for which we can a priori consider two pathways (Scheme 5). Path 1 refers to the C−C bond formation at C^1 and path 3 at C^3. To probe electronic and steric effects, we examined various substituted allyl systems (a−g).

Stationary points for various X groups at C^1 and C^3 positions were determined first (**CPx**, **TS1x**, **PD1x**, **TS3x**, **PD3x**). The activation energies as the function of substituent and position are shown in Figure 8. It is readily apparent that the activation energy of reductive elimination at C^3 ($\Delta E^{\ddagger}_3$) is always much lower than that at C^1 ($\Delta E^{\ddagger}_1$), and both increases roughly in the order of increasing electron-withdrawing ability of the X group. The 11.9-kcal/mol energy of activation for the OSiMe$_3$ group suggests very facile decomposition of the copper intermediate, whereas the 18.7-kcal energy for the NO$_2$ group suggests rather slow decomposition.

The results were analyzed in terms of the Hammett rule,[20] specifically the Swain-Lupton equation ($\sigma = fF + rR$).[21] The σ-parameter is generalized by the following equation, where f and r are specific to the reaction type and, changes according to the electronic requirement of the reaction in question. The parameters such as σ_m, σ^+, σ^- are defined with different values of f and r. The term f reflects the inductive effect, while R reflects the resonance effect and are group specific.

Among eight known σ parameters, we found that the $\Delta E^{\ddagger}_1/\sigma$ correlation is best for $f = 0$ and $r = 1$ (with correlation

(20) (a) Hammett, L. P. *J. Am. Chem. Soc.* **1937**, *59*, 96−103. (b) Hine, J. *Physical, Organic Chemistry*, 2nd ed.; McGraw-Hill Book Co., Inc.: New York, 1962; p 90.
(21) Swain, C. G.; Lupton, E. C., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4328−4337.
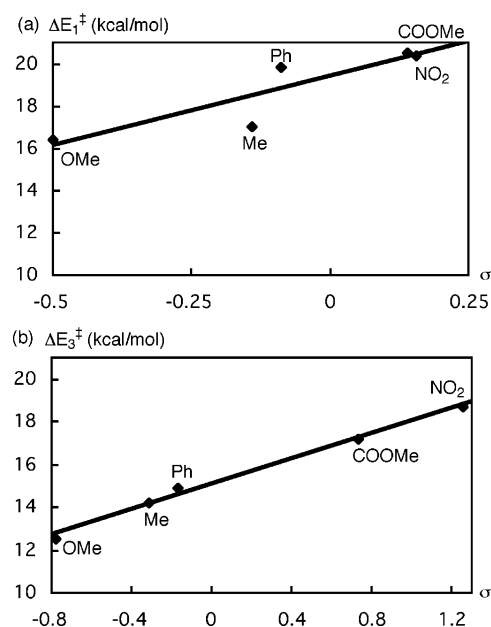

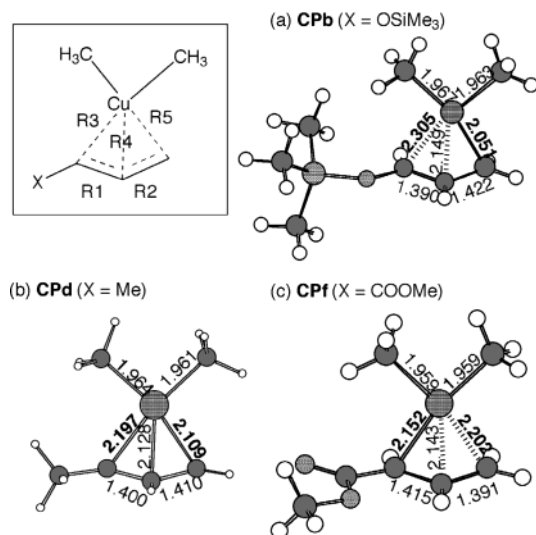**Figure 9.** Hammett plot of activation energies of reductive elimination (a) at C1 and (b) at C3.

Figure 10. 3D structure of **CP**, (a) X = OSiMe$_3$, (b) X =Me, (c) X = CO$_2$Me.

coefficient $R^2 = 0.889$) (Figure 9a), while the $\Delta E^{\ddagger}_3/\sigma$ correlation is the best for $f = 0.51$, $r = 1.58$, namely, for σ_p^+ ($R^2 = 0.996$) (Figure 9b). This analysis indicates that both pathways are controlled largely by resonance effect. The C−C bond formation at C^1 destroys conjugation between X and the π-allylic system in the complex, which agrees with the analysis. The bond formation at C^3 conforms to the σ_p^+ parameter that is known to fit well with the kinetics of the hydrolysis of substituted benzyl chloride. Therefore the electron-donation from the X group to the Cu(III) complex plays an important role in path 3. (In the following paragraphs, only the representative substituents H (a), OSiMe$_3$ (b), Me (d), CO$_2$Me (f) will be discussed since other groups show the same trend.)

The 3D structures of representative stationary points are shown in Figure 10. The parent complex **CPa** is C_s-symmetric: C^1−C^2 (R1) = C^2−C^3 (R2) = 1.403 Å, Cu−C^1 (R3) = Cu−C^3 (R5) = 2.153 Å. The siloxy complex **CPb** is unsymmetrical: R1 = 1.390 Å, R2 = 1.422 Å (C^1−C^2 becoming

Table 1. Subsitutent-Dependent Change of Structure of π-Allylcopper(III) Complex. ΔR: Difference between **CPa** (X = H) and Other Complexes (**a**–**g**)[a]

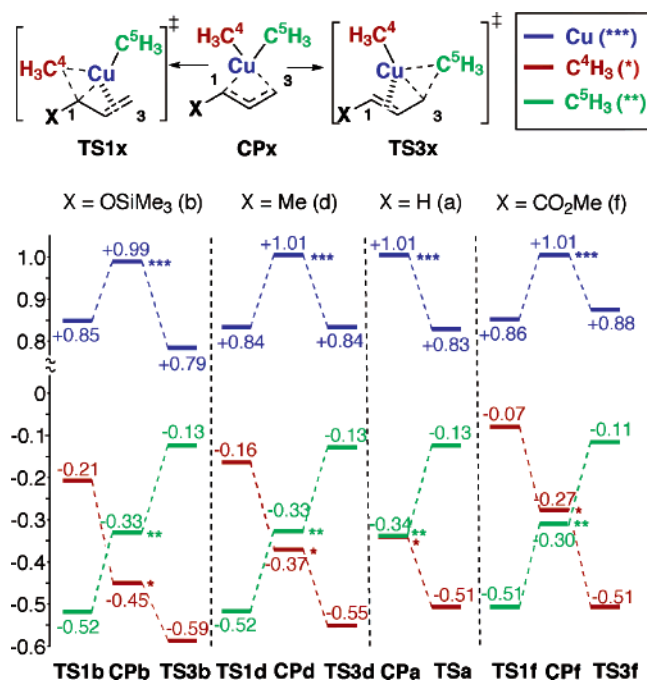| X		$\Delta R1$ (%)	$\Delta R2$ (%)	$\Delta R3$ (%)	$\Delta R4$ (%)	$\Delta R5$ (%)
OSiMe$_3$	**CP$_b$**	−0.016 Å (−1.2)	+0.016 Å (+1.1)	+0.152 Å (+**6.6**)	+0.018 Å (+0.8)	−0.012 Å (−**5.0**)
OMe	**CP$_c$**	−0.017 Å (−1.2)	+0.014 Å (+1.0)	+0.143 Å (+**6.2**)	+0.018 Å (+0.8)	−0.095 Å (−**4.6**)
Me	**CP$_d$**	−0.006 Å (−0.4)	+0.004 Å (+0.3)	+0.044 Å (+2.0)	−0.003 Å (−0.1)	−0.056 Å (−2.6)
Ph	**CP$_e$**	0 Å (0)	−0.001 Å (−0.1)	+0.076 Å (+3.4)	+0.011 Å (+0.5)	−0.033 Å (−1.6)
COOMe	**CP$_f$**	+0.009 Å (+0.6)	−0.015 Å (−1.)	−0.001 Å (0)	+0.012 Å (+0.6)	+0.049 Å (+2.2)
NO$_2$	**CP$_g$**	+0.011 Å (+0.8)	−0.022 Å (−1.6)	−0.025 Å (−1.2)	+0.027 Å (+1.3)	+0.096 Å (+4.3)

[a] Notably large changes are indicated in bold.

Figure 11. Charge distribution in reductive elimination at C1 and C3. For the use of asterics, see text.

double bond like, and C^2–C^3 single bond like). The structure assumes much of the character of an enyl[$\sigma+\pi$] complex: R3 = 2.305 Å, R4 = 2.149 Å, R5 = 2.051 Å. Smaller but similar trend was found for the methyl complex **CPd**. In the ester complex **CPf**, on the other hand, the trend slightly reverses: R1 = 1.415 Å, R2 = 1.391 Å.

The structural changes are summarized in Table 1. There is found strong correlation between X and the structural parameters (except for R4, which is for the weakly bonded Cu–C^2). For electron-donating X groups, R1 becomes shorter and R2 becomes longer. R3 becomes longer with electron-donating X group, but is insensitive to electron-withdrawing X group. R5 closely follow the electronic properties of X.

In summary, an electron-donating group deforms the π-complex into an enyl[$\sigma+\pi$]-like structure similar to the transition structure of reductive elimination: Therefore, the C–C bond formation at C^3 occurs readily. On the other hand, an electron-withdrawing group favors the π-allylic structure. As the result, the reductive elimination becomes more difficult, and prefers to occur at C^3 due to breaking conjugation between an electron-withdrawing group and π-allylic system.

Electronic effect of the X group both at C^1 and at C^3 is found in the charge distribution. Thus, the negative charge on the two methyl ligands is affected by X (Figure 11). Focusing on the C^{4}H$_3$ charge in **CPx** (marked with an asterisk), one notes that it becomes more negative as X becomes more electron-donating

Scheme 6. Regioselectivity of Reductive Elimination of 1,3-disubstituted π-allylcopper (III)Intermediate. Energy Changes Are Shown in kcal/mol
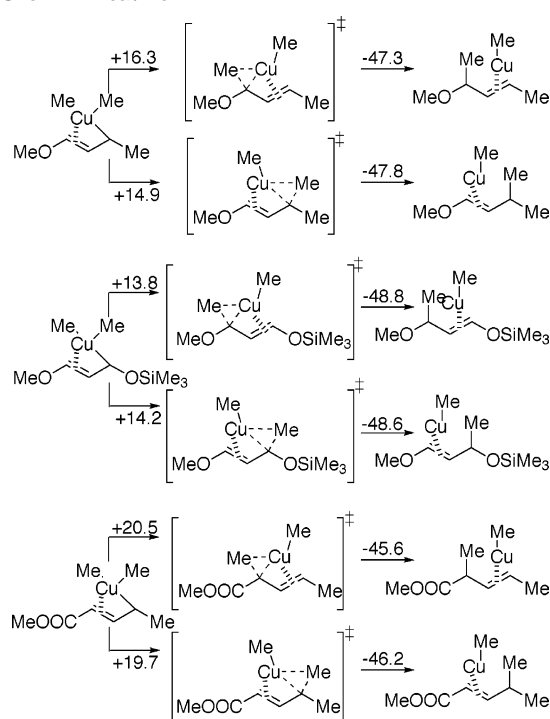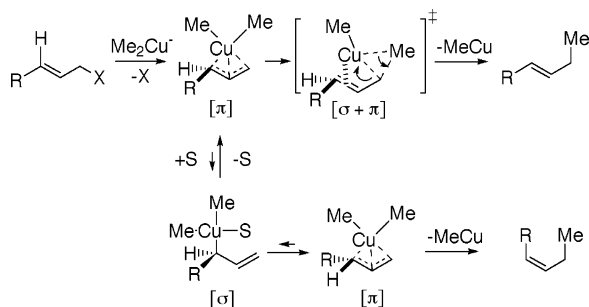

($f < a < d < b$). This trend generally holds also for **TS1x** and **TS3x**. We consider that X-dependent increase of the charge on the C^{4}H$_3$ group is due to the trans influence of C^3, which is, in turn, subject to the electronic effect of the X group on the C^1 terminal of the allylic resonance system. In contract to C^{4}H$_3$, the electronic effect of the X group does not appear on C^5 (marked with **) and Cu (***). As the C^{4}H$_3$ group receives more negative charge from the X group along path 3, it becomes eventually a part of MeCu(I) in **PD3**.

3. Regioselectivity in 1,3-Disubsituted π-Allyl Complex. To be more realistic, we examined several 1,3-disubsituted complexes for various combinations of siloxy, methoxy, methyl, methoxycarbonyl groups. The results are shown in Scheme 6. Qualitative additivity rule holds for the energetics, which is supported also by analysis of Boys local molecular orbitals (not shown). Thus, a MeO group overrides a methyl group, while it is overridden by a siloxy group. A methoxycarbonyl group is a slightly more powerful directing group than a methyl group.

Conclusion

Reductive elimination of a π-allylcopper(III) intermediate leading to the formation of a C–C bond on an allylic terminal has often been described to occur via the corresponding σ-allylcopper(III) species (Scheme 1). The present study has
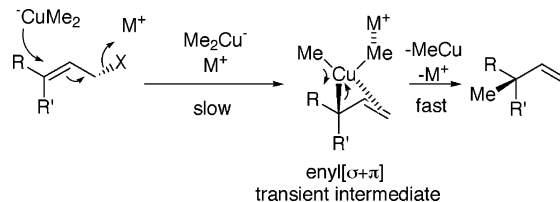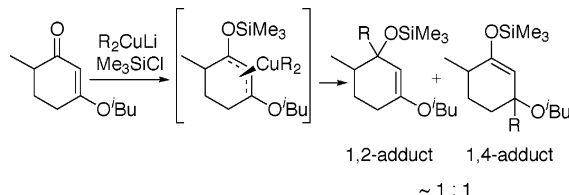
Scheme 7. Mechanism of Allylation Reaction Accompanied by Stereoisomerization

Scheme 8. Model Pathway of Allylic Substitution Reaction of a Lewis Acid (M$^+$) Complexed Diorganocuprate

Scheme 9. Me$_3$SiCl-Mediated Conjugate Addition to γ-Alkoxy-α,β-unsaturated Ketone

shown however that the C−C bond formation via the π-allyl complex is energetically favored for good reasons. The σ-allylcopper(III) intermediate however plays some roles, for instance, in structural isomerization. The conventional mechanism is therefore modified as shown in Scheme 7.

Orbital analysis (Figure 4) indicated that the decomposition of the π-allyl intermediate proceeds through an enyl[σ+π]-type transition state of C−C bond formation because of the structural desymmetrization upon going to the TS. The dissymmetry of the enyl[σ+π] complex induced by a substituent(s) is not a simple steric issue but an electronic issue. The σ-like bond in the enyl[σ+π] complex comprises predominantly of the Cu 3d$_{xz}$ orbital (i.e., due to back-donation), while the π-like bond comprises of the C 2p orbital (i.e., due to donation). *The reductive elimination of this complex therefore occurs preferentially at the σ-bonded allylic terminal since the metal atom can recover most effectively its d-electrons by this way rather than by the reductive elimination at the π-bonded terminal (cf. Figure 4).* We expect that this concept is generally applicable to the reductive elimination reactions of π-allylic transition metal complexes.[22]

It has been reported that that Lewis acid favors anti and γ-selective reaction.[23] When a carbamate is employed as a leaving group,[3d,24] syn and γ-selective allylation has been observed even in the reaction of a lithium cuprate. In light of a recent report by Evans on a Rh-catalyzed allylation reaction,[8] these reactions may occur directly via an enyl[σ+π]-complex without going through a π-allylcopper(III) complex (Scheme 8). Therefore, the first step of the reaction sequence in Scheme 7, which we did not consider this time, needs further investigation.

The regioselectivity of the reductive elimination of a substituted π-allylcopper(III) intermediate has been shown to be mainly controlled by the electronic effect. Steric effects play a minor role. Reductive elimination takes place selectively at the C^3 atom of 1-substituted π-allylcopper(III). Reduc-

tive elimination at C^1 is disfavored because it destroys the conjugation between the 1-substituent and the π-allylic system. The activation energy of the reductive elimination at C^3 follows the Hammett rule with σ_p^+ constant. Thus, the reaction becomes faster as the substituent becomes more electron-donating.

Structural analysis indicated that an electron-donating substituent causes deformation of the π-allyl complex into an enyl-[σ+π] complex, whose geometry and charge distribution are to close to those of the TS of reductive elimination. Reductive elimination of a 1,3-disubstituted π-allylcopper(III) follows the same rule, where there exists a qualitative additivity rule of the substituent effects. When the characters of the two substituents are close to each other, the regioselectivity disappears (Scheme 6). This analysis explains the anomalously low selectivity between 1,2- and 1,4-addition in the Me$_3$SiCl-mediated conjugate addition reaction (Scheme 9), where the presence of a silylated intermediate can be assumed.[25]

If two allylic substituents of very different nature such as an ester and an alkyl group compete with each other, the more electronically influential (ester) group wins.[26] Similarly, when an alkyl group and an oxygen anion compete with each other, the latter wins. This analysis supports the kinship between allylic substitution and conjugate addition reactions of organocopper reagents (cf. Scheme 2).

Supporting Information Available: Cartesian coordinates of the representative stationary points (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(22) Unfortunately, the conventional notation of bonding cannot deal with this important difference of bonding. A color coding such as the one shown below may be useful in this regard.

blue: mainly Cu 3d
red: mainly C 2p
green: mainly C 2p + Cu 3d
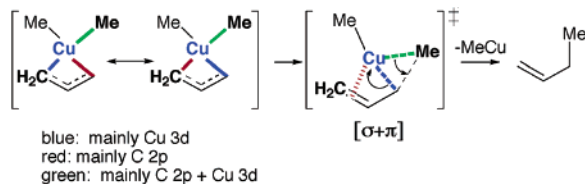
(23) (a) Nakamura, E.; Sekiya, K.; Arai, M.; Aoki, S. *J. Am. Chem. Soc.* **1989**, *111*, 3091−3093. (b) Arai, M.; Nakamura, E. *J. Org. Chem.* **1991**, *56*, 5489−5491. (c) Yamamoto, Y.; Yamamoto, S.; Yatagai, H.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 2318−2325.
(24) Gallina, C.; Ciattini, P. G. *J. Am. Chem. Soc.* **1979**, *101*, 1035−1036.

(25) (a) Matsuzawa, S.; Horiguchi, Y.; Nakamura, E.; Kuwajima, I. *Tetrahedoron* **1989**, *2*, 349−362. (b) Arai, M.; Nemoto, T.; Ohashi, Y.; Nakamura, E. *Synlett.* **1992**, 309−310.
(26) (a) Ibuka, T.; Taga, T.; Habashita, H.; Nakai, K.; Tamamura, K.; Fujii, N.; Chounan, Y.; Nemoto, H.; Yamamoto, Y. *J. Org. Chem.* **1993**, *58*, 1207−1214.