Theoretical Studies of the Role of Complexation in the Conjugate Addition of Dialkylcuprates to Electron-deficient C=C Bonds. Influence on the Stereochemistry of the Reaction

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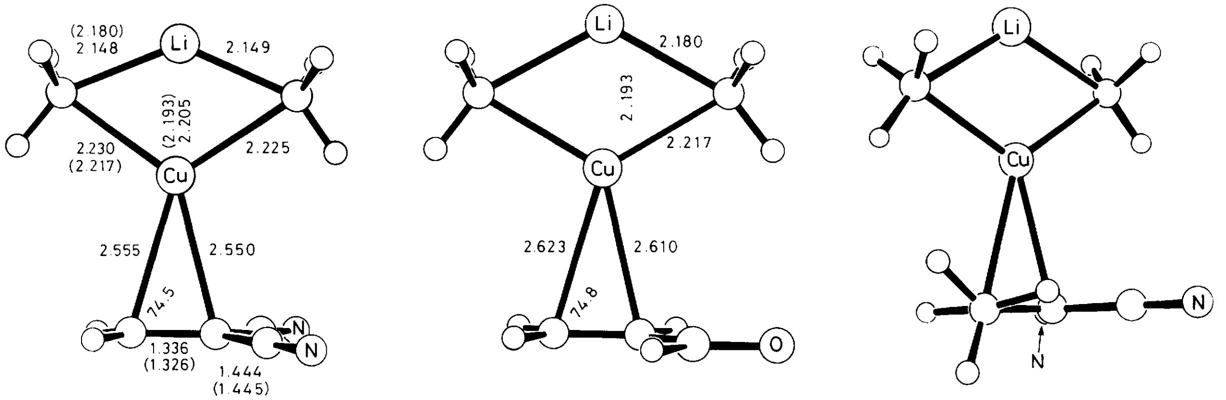
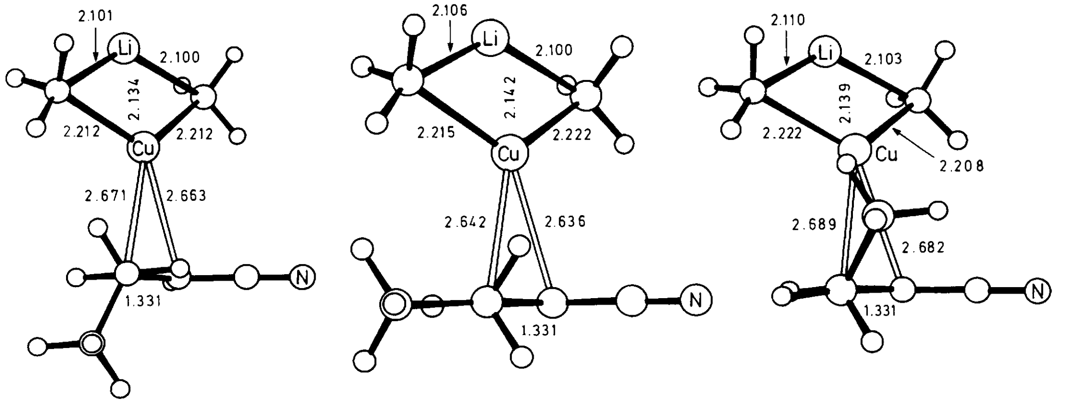
Ab initio molecular orbital calculations suggest that dialkylcuprates add to conjugated C=C bonds *via* a mechanism which involves pre-complexation of the copper centre with the double bond, implying an acute angle of attack onto the C=C bond; this may explain the opposite stereoselectivities observed in the reactions of dialkylcuprates on the one hand and of alkylcopper reagents (and other conventional nucleophiles) on the other.

The mechanism of conjugate addition of dialkylcuprates (R_2CuLi) to electron-deficient alkenes (R^1R^2–R^3Z) C=C is a continuing source of discussion. Electron transfer[1] and nucleophilic attack by the copper atom[2–4] have been proposed as viable mechanistic pathways. The nucleophilic mechanism provides a plausible rationale for the stereoselectivity observed in the reaction of both acyclic[5] and cyclic[2,6] substrates. Here we present theoretical studies of the addition of (i) a methyl radical to the acrolein radical anion, and (ii) lithium dimethylcuprate to acrolein and 1,1-dicyanoethylene. Reac-



(4) (5) (6)

Figure 1. (a) Optimized geometry (in Å and ° at the HF/3-21G level) of (**4**). The numbers in parentheses refer to the isolated reactants. (b) HF/3-21G optimized geometry (at fixed reactant geometries) of the π-complex (**5**) between Me_2CuLi and acrolein. (c) HF/3-21G conformational minimum (see text) of (**6**). The same geometry as in (**4**) was assumed, and an alkenic hydrogen was replaced with a methyl group (see text).

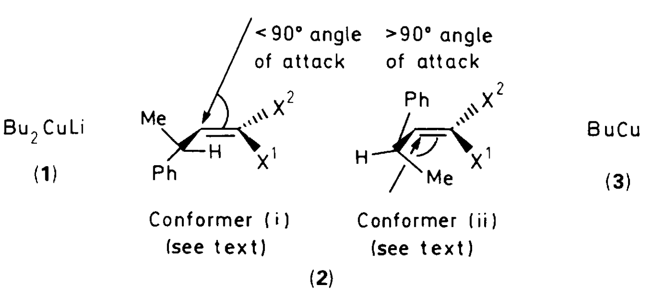


(7a) (7b) (7c)

$\angle_{Cu-C_\beta=C_\alpha}$ 75.2° $\phi_{C-C-C=C}$ = 114.8° $\angle_{Cu-C_\beta=C_\alpha}$ 75.1° $\phi_{C-C-C=C}$ = 178.1° $\angle_{Cu-C_\beta=C_\alpha}$ 75.4° $\phi_{C-C-C=C}$ = −64.7°

E = 0.0 E = 1.44 E = 2.32

Figure 2. Optimized geometries (in Å and ° at the HF/3-21G level) and relative energies (in kcal mol^{-1}) of conformers of (7). (a) *anti* conformer; (b) *outside* conformer, (c) *inside* conformer.



(2)

a; X^1 = CO_2Me, X^2 = CN
b; X^1 = X^2 = CO_2Me
c; X^1 = X^2 = CO_2Bu^t

tions of this type have been postulated[2,7] (*vide infra*) in electron transfer sequences and nucleophilic addition pathways, respectively.

The addition of $Bu^n{}_2CuLi$ (**1**) to the C=C bond of the chiral substrates (**2a—c**) proceeds with opposite stereochemical sense to that of butylcopper (**3**).[7] Yamamoto and co-workers[7] have postulated that (**1**) transfers an electron to (**2**), and that the intermediate $(\mathbf{2})^{\cdot -}$ is subsequently attacked by the butyl radical formed from $(\mathbf{1})^{\cdot +}$. They proposed that the angle of attack (∠C · · · C=C) should be smaller than 90° [see (**2a—c**), conformer (i)], by analogy with the mode of common electrophilic additions. This would account for the opposite stereoselection relative to the reaction of (**3**),[8] where the angle of attack is larger than 90° and the expected[7] conformational preference of the phenethyl group is different [conformer (ii)]. This hypothesis implies, however, that coupling between $(\mathbf{2})^{\cdot -}$ and the butyl radical should be rate-determining, which is unlikely.[9]

Moreover, frontier molecular orbital theory predicts an angle of attack larger than 90° for this reaction, because the SOMO of $(\mathbf{2})^{\cdot -}$ is antibonding between C_β and C_α. We have confirmed this prediction by *ab initio* molecular orbital calculations.[10,11]† The geometry of attack of a methyl radical

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† Unrestricted Hartree–Fock (UHF) theory was used for geometry optimization with the 3-21G basis set. UHF energies corrected for the removal of triplet and quintet spin contamination (termed APUHF[11] energies) were obtained using Yamaguchi's scheme.[11]

onto C_β of the acrolein radical anion was optimized (UHF/3-21G) at fixed values for the length of the forming $C \cdots C$ bond. The optimized value of $\angle C \cdots C{=}C$ was found to be close to 115° for all $r_{C \cdots C}$ values considered.[‡] This is essentially the same value as that calculated for the nucleophilic attack of methylcopper on C_β of enals.[12] Thus, the conformation of the phenethyl group at C_β should be the same [*i.e.*, (**2**), (ii)] in the reaction of cuprates and alkylcopper reagents; the same sense of stereoselection should therefore be expected,[13][§] contrary to experimental evidence.[7] Constraining $\angle C \cdots C{=}C$ to smaller values destabilizes the system substantially. Thus, for $r_{C \cdots C}$ = 2.2 Å and $\angle C \cdots C{=}C$ = 95 and 75°, the energy rises by 5.89 and 31.02 kcal mol^{-1}, respectively, at the APUHF[11]/3-21 + G level (1 cal = 4.184 J).

On the other hand, an 'acute' angle of attack at C_β is expected if it leads to a π-complex. We have optimized (HF/3-21G[¶]) the structure of such a complex (with C_s symmetry) for the reaction of lithium dimethylcuprate with dicyanoethylene [(**4**), Figure 1a].[‖] The complexation energy was found to be 4.63 kcal mol^{-1} at this level[¶] and 8.15 kcal mol^{-1} at the MP2/6-31G*d*//HF/3-21G level. The geometries of the cuprate and alkene fragments in (**4**) are very similar to the optimized geometries of the isolated reactants. This prompted us to optimize (HF/3-21G) the analogous π-complex with acrolein at fixed reactant geometries. In this structure [(**5**), Figure 1b], the forming $Cu \cdots C$ bond lengths and $Cu \cdots C{-}C$ angles are very similar to those in (**4**).

Replacement of a C_β-hydrogen in (**4**) with a methyl group (C–H bond lengths and H–C–C angles fixed at the values for ethane, HF/3-21G optimised structure[14]) and calculation (HF/3-21G) of the energy for various rotamers revealed that the conformational minimum corresponds to (**6**) (Figure 1c). This suggested that the *anti* position should be the least sterically hindered, followed by the *outside* and *inside* positions in this order. Support for this hypothesis came from geometry optimization (HF/3-21G) of the complex with (Z)-EtCH=CH–CN [(**7**), Figure 2]. The relative energies of the *anti* (**7a**), *outside* (**7b**), and *inside* (**7c**) conformers are 0.0, 1.44, and 2.32 kcal mol^{-1}. These results suggest that a phenethyl group should adopt the conformation having the phenyl group *anti*, the methyl *outside*, and the hydrogen in the hindered *inside* position. This is conformation (**2**) (i), which rationalizes Yamamoto's experimental results.[7]

In conclusion, these calculations indicate that *the stereoselectivity of the addition process can be rationalized from the analysis of the π-complex formation*,[15][**] though they do not rule out the possibility of *subsequent* electron transfer. A more detailed discussion of the effect of substitution at C_γ will be presented in a subsequent full paper.

Calculations were carried out at the Computer Center of the Institute for Molecular Science. A. E. D. is grateful to the Inoue Foundation for Science, Tokyo, for generous financial support during his stay in Okazaki.

Received, 15th May 1989; Com. 9/02024A

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[‡] Optimized $C \cdots C{=}C$ values: 115.2° ($r_{C \cdots C}$ 2.1 Å); 115.2° (2.2 Å); 115.0° (2.3 Å); 114.7° (2.4 Å).

[§] This is true if the conformational preference at C_β is determined primarily by steric factors. This is most probably the case for alkyl and unsubstituted aryl groups, as confirmed by force field calculations of 1,2-additions to carbonyl groups.[13]

[¶] Optimization with the 3-21G*d* basis set gave a similar geometry and a complexation energy of 2.09 kcal mol^{-1}. At the MP2/6-31G*d*//HF/3-21G*d* level, the complexation energy was 8.36 kcal mol^{-1} where *d* indicates additional d orbitals on the C=C atoms (exponent = 0.8).

[‖] Absolute calculated energies (hartrees): (**4**) −399.34296 (MP2/6-31G*d*//HF/3-21G); (**5**) −326.30465 (HF/3-21G); (**6**) −435.46234 (HF/3-21G); (**7a**) (*anti*) −383.06884; (**7b**) (*outside*) −383.06654; (**7c**) (*inside*) −383.06514. We chose dicyanoethylene for computational simplicity. For this molecule, the same diastereoisomer is obtained with dialkylcuprates and alkylcopper reagents; however, it is the behaviour of the latter which is exceptional.[7] Thus, dicyanoethylene is a viable model for the cuprate reactions.

[**] The exception is when complex formation is reversible. This can be true in sterically hindered cyclic systems;[2] even here, however, the reaction becomes irreversible if the π-complex is trapped.[2]