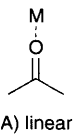
Importance of steric hindrance in linear coordination of Lewis acids with α-enones

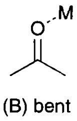
Shunichi Fukuzumi,*[a] Toshihiko Okamoto,[a] Morifumi Fujita[a] and Junzo Otera*[b]

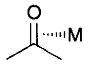
[a] *Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan*
[b] *Department of Applied Chemistry, Okayama University of Science, Ridai-cho, Okayama 700, Japan*

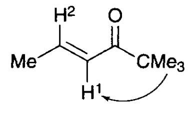
The complexation of α-enones [(E)-MeC(H)=C(H)COR] with $SnCl_4$ and $TiCl_4$ has been studied with NMR spectroscopy as well as semiempirical and *ab initio* SCF-MO methods, which indicate a preference for linear coordination of Lewis acids with α-enones due to the steric effect of R group (R = Bu^t, Ph, 2,4,6-$Me_3C_6H_2$, 4-$MeOC_6H_4$) in the *s-cis* conformation.

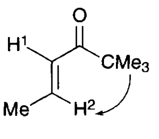
Complex formation between Lewis acid and carbonyl plays a pivotal role in various reactions of synthetic value.[1] Elucidation of coordination mode[2] is therefore very significant for understanding the stereochemical features of reaction. Three modes are plausible: linear (A) and bent (B) ones, both of which involve the in-plane coordination, and π-bonded out-of-plane version (C).[3] In general, cationic metal species give rise to the mode A in which electrostatic interactions essentially work as attractive forces.[4] Lanthanide shift reagents also coordinate linearly since the empty 5d orbitals of the metal have the appropriate symmetry and size for interacting with the p-orbital on sp-hybridized oxygen in a π fashion.[5] The coordination mode C is encountered in some complexes of transition metals.[6] From a synthetic point of view, main group and early transition metal Lewis acids are most important because they are employed most frequently for activation of carbonyls. It is usually accepted that the bent mode B is normal in their complexation for which an sp^2 lone pair of the carbonyl oxygen is responsible.[3,4,7,8] We have recently reported that complexation of these Lewis acids with α-enones involving a bulky acyl moiety may be effective for attaining high diastereoselectivity in the Michael addition of ketene silyl acetals.[9] The pronounced dependence of stereochemistry on the steric demand of Lewis acid complexes of α-enones emphasized the importance of disclosing the coordination mode as well as the stability of the Lewis acid complexes in solution. However, neither the coordination mode nor the formation constant has so far been known for Lewis acid complexes of α-enones. This study reports the formation constants (K) of Lewis acid complexes of α-enones, which are very sensitive to steric hindrance of a bulky acyl moiety. The comparison of the K values and the calculated values of enthalpy of the complex formation (ΔH) with the fully optimized geometries† suggests that enones involving a bulky acyl moiety exhibit unprecedented linear coordination (mode A) with $SnCl_4$ and $TiCl_4$.


(A) linear


(B) bent


(C) out of plane





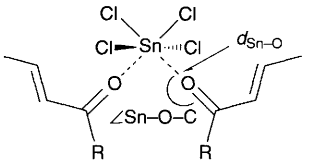
The ^{13}C NMR signals of α-enones exhibit large downfield shifts (*ca.* 10–20 ppm for carbonyl carbons and β-carbons) by the complex formation with $SnCl_4$ and $TiCl_4$ in $CDCl_3$ at 298 K. What is observed is a weighted average of the chemical shifts of free α-enones and the Lewis acid complexes depending on the Lewis acid concentration, indicating that the α-enone ligand exchanges rapidly with the Lewis acid on the NMR time scale. The observed chemical shifts referenced to free α-enones $\Delta\delta$ increase with an increase in the Lewis acid concentration to approach a constant value at the 2 : 1 ratio of α-enone and Lewis acid. Such dependence of $\Delta\delta$ on [Lewis acid] indicates clearly the formation of 2 : 1 complexes of α-enones and Lewis acid ($SnCl_4$ and $TiCl_4$). The formation constants K can be determined from eqn. (1), where $\Delta\delta_\infty$ is the chemical shift of the complex referenced to free α-enone. The best fit K values of various α-enones are listed in Table 1. The K value of *tert*-butyl enone with $TiCl_4$ is significantly larger than that with $SnCl_4$, in accordance with the stronger Lewis acidity of $TiCl_4$. It is particularly important to note that the K value of *tert*-butyl enone is much smaller than that of ethyl enone, demonstrating the significant steric effect of the bulky *tert*-butyl group on the complex formation with $SnCl_4$.

$$[SnCl_4]_0 = \frac{\Delta\delta\Delta\delta_\infty}{2K(\Delta\delta_\infty - \Delta\delta)^2[\alpha\text{-enone}]_0} + \frac{\Delta\delta[\alpha\text{-enone}]_0}{2\Delta\delta_\infty} \qquad (1)$$

The conformation of the α,β-enol unit (*s-cis vs. s-trans*) was examined by the use of difference NOE measurements. Irradiation of protons of *tert*-butyl group of *tert*-butyl enone resulted in a 7.9% NOE to H^1, but only 1.2% to H^2. Likewise irradiation of *tert*-butyl group of the 2 : 1 complex of *tert*-butyl enone and $SnCl_4$ resulted in a 19.5% NOE to H^1, but only 2.4% to H^2. Thus, *tert*-butyl enone and the $SnCl_4$ complex reside primarily in the *s-cis* conformation. Such preference of *s-cis* conformation of *tert*-butyl enone shows a sharp contrast with the predominant *s-trans* conformation of the corresponding aldehyde.[10]

In order to clarify the origin of the large variation in the K values of the 2 : 1 complexes of α-enones and $SnCl_4$ in Table 1 we have calculated the enthalpy of the complex formation (ΔH) by using the semiempirical PM3 SCF-MO method.[11] The final geometries and energetics were obtained by optimizing the total molecular energy with respect to all structural variables with no symmetry constraints. The calculations confirmed that the *s-cis* conformation for *tert*-butyl enone and the $SnCl_4$ complex is more stable than the *s-trans* conformation. The ΔH values are obtained as the difference between the heat of formation (ΔH_f) of complex and the sum of each component. The ΔH values thus obtained are also listed in Table 1, where the K value generally increases with an increase in strength of the complex as the ΔH value becomes more negative. In the optimized structure of the 2 : 1 complex, two α-enone molecules are nearly symmetrical with respect to the σ_d plane of $SnCl_4$ group as

Table 1 Formation constants (K), enthalpy of the complex formation (ΔH), bond length (d_{Sn-O}), and bond angle (∠Sn–O–C) of 2 : 1 complexes between α-enones [(E)-MeC(H)=C(H)COR] and $SnCl_4$



α-Enone	K^a/dm^6 mol^{-2}	ΔH^c/ kcal mol^{-1}	$d_{Sn-O}{}^{c,d}$/Å	∠Sn–O–C^{c,d,e}/°
R = H	—	−9.9	2.16	136 (138)
Et	3.8×10^2	−10.5	2.09	163 (164)
Bu^t	$4.3\ (6.5 \times 10^2)^b$	−7.6	2.11	170 (172)
Ph	5.0×10	−10.6	2.10	175 (172)
2,4,6-$Me_3C_6H_2$	2.2×10^2	−11.7	2.07	173 (171)
4-$MeOC_6H_4$	1.1×10^3	−11.9	2.09	174 (171)

[a] Determined from the dependence of chemical shifts referenced to free α-enones Δδ on the Lewis acid concentration in $CDCl_3$ at 298 K. The experimental errors are within ±10%. [b] The K value with $TiCl_4$ is given in parenthesis. [c] Calculated by the PM3 method. [d] Average of two values. [e] The values in parentheses show those for the 1 : 1 complexes.

shown on the top of Table 1. The bond lengths (d_{Sn-O}) and bond angles (∠Sn–O–C) of the complexes are also listed in Table 1 in which the change in the bond angle with R is particularly noteworthy. The ∠Sn–O–C value of the aldehyde (R = H) is 136°, in agreement with the reported bent coordination through an sp^2-type lone pair on oxygen (∠Sn–O–C = 127°) in the X-ray structure of the 2 : 1 complex between 4-Bu^tC_6H_4CHO and $SnCl_4$.[7] However, the ∠Sn–O–C value increases with an increase in the size of R to approach a linear coordination.

Such nearly linear coordination of $SnCl_4$ with α-enones, (E)-MeC(H)=C(H)COR having a bulky R group (R = Bu^t, Ph, 2,4,6-$Me_3C_6H_2$, 4-$MeOC_6H_4$) is also preferred in the 1 : 1 complex as indicated by the ∠Sn–O–C values in the parentheses in Table 1. The ΔH values of the 1 : 1 complexes are about 3–5 kcal mol^{-1} (1 cal = 4.184 J) less negative than those of the corresponding 2 : 1 complexes. The structure of the 1 : 1 complex of H_2C=C(H)COBu^t and $TiCl_4$ is also examined through fully optimized *ab initio* SCF-MO calculation using the 3-21 G basis set. The nearly linear coordination of $TiCl_4$ (∠Ti–O–C = 173°) is also attained, showing a sharp contrast with the normal bent coordination of $TiCl_4$ with H_2CO (∠Ti–O–C = 147°) in the same calculation using the 3-21 G set.[12] In the $TiCl_4$–H_2CO complex the balance between stabilizing interaction of the b_2 orbital of oxygen lone pairs, which is energetically more favourable than the other a_1 orbital, with the LUMO of $TiCl_4$ and repulsive interactions of the b_2 orbital with occupied Cl-centred orbitals of the $TiCl_4$ moiety determines the ∠Ti–O–C value.[12] In the case of the α-enone complexes with bulky R in the s-*cis* conformation, the additional repulsive interaction of both the vinyl and R groups with chlorine atoms of the $TiCl_4$ moiety reduces the stabilizing interaction of the b_2 orbital of oxygen lone pairs with the LUMO of the Lewis acid, resulting in the nearly linear coordination in which the maximum overlap between the a_1 oribtal of oxygen lone pairs with the LUMO of $TiCl_4$ may be attained. Thus, the steric interaction of two bulky substituents in α-enones is ascribed to the linear coordination of the Lewis acid with the carbonyl oxygen, resulting in a decrease in the formation constant.

This work was partially supported by a Grant-in-Aid from the Ministry of Education, Science, and Culture, Japan.

Footnote

† The PM3 and *ab initio* calculations were performed by using the MOPAC (Ver. 6.0) and GAUSSIAN 92 programs with the MOL-GRAPH program Ver. 2.8 by Daikin Industries, Ltd. The *ab initio* calculations were also carried out with the SPARTAN Ver. 2.0 (Wave Function Inc., Asahi Kasei Joho System Co., Ltd.).

References

1 C. H. Heathcock, *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, New York, 1984, vol. 3, part B, p. 111; M. T. Reetz, *Angew. Chem., Int. Ed. Engl.*, 1984, **24**, 556; S. Shambayati and S. L. Schreiber, *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 1, p. 283.

2 S. Shambayati, W. E. Crowe and S. L. Schreiber, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 256.

3 T. J. LePage and K. B. Wiberg, *J. Am. Chem. Soc.*, 1988, **110**, 6642.

4 R. J. Loncharich, T. R. Schwartz and K. N. Houk, *J. Am. Chem. Soc.*, 1987, **109**, 14; D. J. Nelson, *J. Org. Chem.*, 1986, **51**, 3185.

5 D. J. Raber, C. M. Janks, M. D. Johnston, Jr. and N. K. Raber, *J. Am. Chem. Soc.*, 1980, **102**, 6591.

6 W. D. Harman, D. P. Fairlie and H. Taube, *J. Am. Chem. Soc.*, 1986, **108**, 8223; R. C. Corcoran and J. Ma, *J. Am. Chem. Soc.*, 1991, **113**, 8973; R. C. Corcoran and J. Ma, *J. Am. Chem. Soc.*, 1992, **114**, 4536; D. P. Klein and J. A. Gladysz, *J. Am. Chem. Soc.*, 1992, **114**, 8710; N. Q. Méndez, J. W. Seyler, A. M. Arif and J. A. Gladysz, *J. Am. Chem. Soc.*, 1993, **115**, 2323.

7 S. E. Denmark, B. R. Henke and E. Weber, *J. Am. Chem. Soc.*, 1987, **109**, 2512.

8 M. T. Reetz, M. Hüllmann, W. Massa, S. Berger, P. Rademacher and P. Heymanns, *J. Am. Chem. Soc.*, 1986, **108**, 2405; O. F. Guner, R. M. Ottenbrite, D. D. Shillady and P. V. Alston, *J. Org. Chem.*, 1987, **52**, 391; P. Laszlo and M. Teston, *J. Am. Chem. Soc.*, 1990, **112**, 8750; J. M. Goodman, *Tetrahedron Lett.*, 1992, **33**, 7219.

9 J. Otera, Y. Fujita, T. Sato, H. Nozaki, S. Fukuzumi and M. Fujita, *J. Org. Chem.*, 1992, **57**, 5054; S. Fukuzumi, M. Fujita, J. Otera and Y. Fujita, *J. Am. Chem. Soc.*, 1992, **114**, 10271.

10 S. E. Denmark and N. G. Almstead, *J. Am. Chem. Soc.*, 1993, **115**, 3133.

11 J. J. P. Stewart, *J. Comput. Chem.*, 1989, **10**, 209, 221.

12 V. Branchadell and A. Oliva, *J. Am. Chem. Soc.*, 1992, **114**, 4357.

Received, 31st July 1995; Com. 5/05050B