the case, the source of stereoselection in olefin metathesis may result from factors other than those arising from the conformational effects due to puckering of the intermediate. In this titanium system, the symmetrical metallacyclobutane appears to rest at the minimum of a broad potential surface, such that distortion toward the required transition state for metathesis is facile.

Acknowledgment. We acknowledge financial support from the National Science Foundation (Grant CHE-801652) and the Department of Energy (Contract DE-AT03-79ER10491), the technical aid provided by the Southern California High Field NMR Facility supported by the NSF (NSF Grant No. 7916324A1), and the NSF for Predoctoral Fellowships to D.A.S. and G.J.G.

Supplementary Material Available: Atomic coordinates, thermal parameters, and structure factors for compounds IIc and IIe (19 pages). Ordering information is given on any current masthead page.

Reactivity of Distorted $C_5H_5Fe(CO)_2$(olefin) Cations toward Nucleophilic Attack

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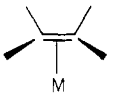
It has recently been suggested that endogenous activation of metal-complexed olefins for nucleophilic attack is derived from displacement of the metal fragment, in the course of reaction, toward one end of the olefin (**1** → **2**). Calculations show that



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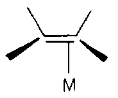
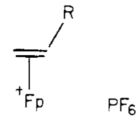


2

such a deformation leads to stabilization and increased localization of the fragment ligand LUMO (π^*–λb_2) through its interaction with the olefin π orbital.[1] The results of these changes is to greatly increase the overlap population associated with the interaction of the nucleophile orbital and the olefin-centered LUMO.

Complexes whose *ground-state* structures are distorted, as in **2**, might therefore be expected to exhibit enhanced reactivity, in the absence of compensating factors. The crystal structures of two such distorted complexes (**3b** and **3c**) together with a comparison of their reactivities and that of the undistorted parent complex **3a** with the comparatively soft nucleophile Fp (η^1-allyl)[2] (**4**) are now reported.



3a, R = H
b, R = OMe
c, R = NMe_2

Fp = $C_5H_5Fe(CO)_2$

The preparation of Fp(vinyl ether)PF_6 complexes has previously been described.[3] The vinylamine complex (**3c**) is readily obtained from **3b** by treatment with excess dimethylamine in ether (30 °C, 10 min, then 25 °C, 10 min). The product is filtered and recrystallized from Et_2O–CH_2Cl_2 to give **3c** as yellow crystals, dec 158 °C (94%).[4] Complex **3b** forms as monoclinic crystals, with $a = 13.494$ (4) Å, $b = 7.539$ (2) Å, $c = 16.501$ (5) Å, $\beta = 121.09$ (4)°, $Z = 4$, $\rho_{calcd} = 1.76$ g·cm^{-3}, $\rho_{obsd} = 1.78$ g·cm^{-3} (λ(Mo K$_\alpha$) = 0.71073 Å). The complex occupies a $2a$ site in space group $C2/m$, requiring disorder of the cation. Full-matrix least-squares refinement of positional and thermal parameters for all nonhydrogen atoms using 1620 data for which $|F_o| > 3.92\sigma(|F_o|)$ led to $R = \sum(||F_o| - |F_c||)/\sum|F_o| = 0.080$. Crystals of complex **3c** belong to the monoclinic system, space group $P2_1/n$ with $a = 7.447$ (2) Å, $b = 25.642$ (6) Å, $c = 8.293$ (2) Å, $\beta = 100.11$ (3)°, $Z = 4$, and $\rho_{calcd} = 1.67$ g·cm^{-3} (λ(Mo K$_\alpha$) = 0.71073 Å). Full-matrix least-squares refinement of positional and anisotropic thermal parameters for all nonhydrogen atoms using 1897 data for which $|F_o| > 3.92\sigma(|F_o|)$ gave $R = 0.048$.

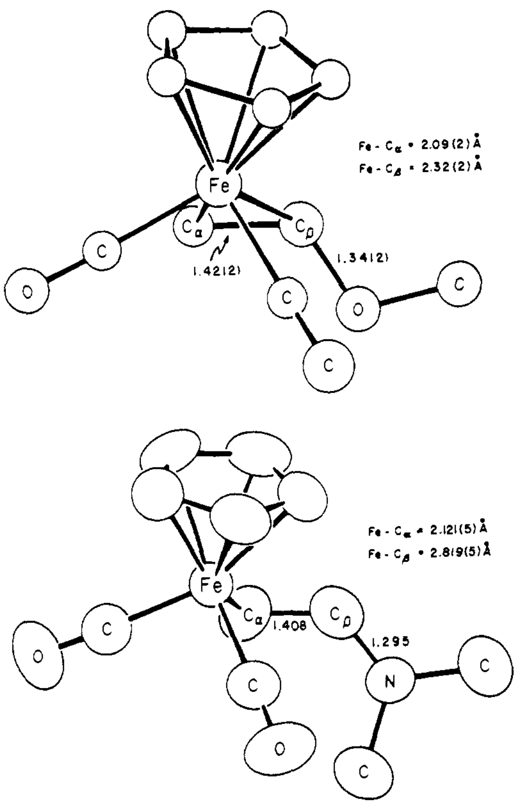


Figure 1. Molecular structures: (top) [(η^5-C_5H_5)Fe(CO)$_2$(CH$_2$CHOCH$_3$)] cation (**3b**); (bottom) [(η^5-C_5H_5)Fe(CO)$_2$(CH$_2$CHN(CH$_3$)$_2$)] cation (**3c**).

Inspection of Figure 1 indicates that the ligand in the vinyl ether complex **3b** is an unsymmetrically bound η^2-olefin, while the ligand in the vinylamine complex **3c** is more nearly σ bonded, its geometry closely approximating that expected for an iminum ion, with a C=N length of 1.295 (7) Å. Despite the long Fe–C$_\beta$ distance (2.819 (5) Å), it is likely that this complex retains some η^2-olefinic character.[5] This is clearly evidenced by the short C$_\alpha$-C$_\beta$ bond length (1.408 (8) Å)[6] and by the Fe–C–C–N torsion angle of 102.3°, which is indicative of interaction[7] between the Fe–C$_\alpha$ σ

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(1) Eisenstein, O.; Hoffmann, R. *J. Am. Chem. Soc.* **1980**, *102*, 6148.

(2) Lennon, P. J.; Rosan, A.; Rosenblum, M.; Tancrede, J.; Waterman, P. *J. Am. Chem. Soc.* **1980**, *102*, 7033.

(3) Cutler, A.; Raghu, S.; Rosenblum, M. *J. Organomet. Chem.* **1974**, *77*, 381.

(4) IR (KBr) 2020, 1975, 1645 cm^{-1}; NMR (CD$_3$NO$_2$) δ 8.0 (t, 1, CHNMe$_2$), 5.25 (s, 5, Cp), 3.5, 3.1 (2 s, 6, NMe$_2$), 2.05 (d, 2, $J = 9$ Hz, FpCH$_2$). The BF$_4^-$ salt has been analyzed. Anal. Calcd for C$_{11}$H$_{14}$BF$_4$FeO$_2$N: C, 39.40; H, 4.19; N, 4.18. Found: C, 39.26; H, 4.23; N, 4.12. Madhavarao, M. Ph.D. Thesis, Brandeis University, 1977.

(5) A similar interaction has been observed and discussed previously in [(η^5-C$_5$H$_5$)Fe(CO)$_2$(CH$_2$COOH)]$_2$, where the Fe···C$_\beta$ distance is 2.85 (2) Å: Ariyaratne, J. K. P.; Bierrum, A. M.; Green, M. L. H.; Ishaq, M.; Prout, C. K.; Swanwick, M. G. *J. Chem. Soc. A* **1969**, 1309.

(6) It would appear that the C$_\alpha$–C$_\beta$ and C–N bond lengths are indicative of 50% double-bond character in each of these bonds: (a) Ammon, H. L. *Acta Crystallogr., Sect. B* **1974**, *B30*, 1731. (b) Lubke, B.; Behrens, U. *J. Organomet. Chem.* **1978**, *149*, 327.

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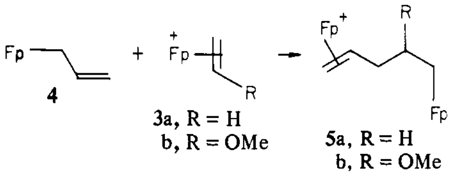
bond and the p oribital on C_β. Furthermore the C_α–C_β rotational barrier, determined from the coalescence temperature (–60 °C) of the AB set of vinyl proton resonances, is 10.5 kcal·mol^{-1}, well above the value expected for a relatively uncrowded σ-bonded complex.[8]

The vinyl ether complex is far less distorted. The complex cation is disordered about a crystallographic mirror plane which relates the α-carbon atom of the ligand to (approximately) a carbonyl carbon atom; the location of the β-carbon atom is largely unaffected by this disorder. The disorder is not completely resolved and thus has the effect of *lengthening* the Fe–CO distance and *shortening* the Fe–C_α distance. A realistic value for the latter distance is ~2.20 Å, based on structure determinations on Fp(tetramethylallene)[10] and Fp(propene).[11] Hence a lower limit for the value of the difference between the Fe–C_α and Fe–C_β distances is 0.12 Å. The greater olefinic character of the C_α–C_β bond is also evidenced by the NMR spectrum of the cation, which does not show line broadening of its AB set of proton resonances up to 80 °C. The C_α–C_β rotational barrier is estimated to be greater than 18 kcal·mol^{-1} in this cation.[12]

A measure of the chemical effect of these distortions is provided by a comparison of the reactivity of complexes **3a**,**3b**, and **3c** toward nucleophiles. In the absence of other electronic effects substitution of a vinyl hydrogen atom in **3a** by a group 5 or 6 heteroatom would be expected to result in decreased reactivity, since the interaction of the filled heteroatomic orbital with both vacant $(a_1-\lambda'\pi)$ and $(\pi^*-\lambda b_2)$[1] orbitals must raise their energies and increase their delocalization. Furthermore, such interactions should be more important for **3c** than for **3b**, since the energy levels of interacting orbitals are closer for the amine complex. The effects of molecular distortions such as those postulated by Eisenstein and Hoffmann[1] may be expected to countervail this reactivity sequence, although it is not clear that the theoretical treatment is applicable to the vinylamine complex since the iron atom is more nearly σ bonded to the ligand in this substance.[13]

Decreased reactivity of **3c** compared with **3b** is observed in reactions with water. The amine complex is inert to hydrolysis at room temperature and can be recovered from its aqueous solutions unchanged even after warming to 40 °C, while **3b** is instantaneously hydrolyzed at room temperature to give $FpCH_2CHO$. The reactivities of **3a**, **3b**, and **3c** with a relatively soft nucleophile such as **4** (eq 1), for which frontier orbital interactions would be expected to be more important, is of greater interest. Both **3a** and **3b** condense rapidly with **4** at room temperature to give dinuclear complexes **5a** and **5b**, but **3c** fails to react on prolonged standing or even on warming to 40 °C. Interactions of the heteroatom lone-pair orbital with the ligand LUMO appear to play a dominant role in the reactivity of the amine complex. Significantly, this does not appear to be so for **3b**. The half-life for the reaction of **3a** with **4** at 10 °C is 82 min, while that for **3b** for the same concentration of reactants, but at –3 °C, is 3 min. A comparison of rate constants, obtained for the reaction of **4** with **3a** from 10 to 30 °C and extrapolated to –3 °C, with that for **3b** at this temperature shows that the vinyl ether complex is 530 times more reactive than the ethylene complex.[14]



4

3a, R = H
b, R = OMe

5a, R = H
b, R = OMe

(1)

The results provide the first experimental evidence that molecular distortions in metal–olefin complexes, of the form defined by Eisenstein and Hoffmann,[1] may play a significant role in determining their reactivity with nucleophiles.

Acknowledgment. This research was supported by a grant from the National Science Foundation (CHE-7816863) which is gratefully acknowledged.

Supplementary Material Available: Tables of atomic coordinates for complexes **3b** and **3c** (2 pages). Ordering information is given on any current masthead page.

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(7) Where there are favorable steric effects,[5] the Fe–C–C–X torsion angle is quite close to 90°, while when no possible interaction exists, e.g., in similar complexes with saturated ligands, the torsion angle is 180°: Pope, L.; Sommerville, P.; Laing, M.; Hindson, K. J.; Moss, J. R. *J. Organomet. Chem.* **1976**, *112*, 309.

(8) Coalescence temperatures were determined at 90 MHz in CD_2Cl_2 solution over a temperature range of –103 to +10 °C. The rotational barrier was calculated by using the approximate equation $k_c = \pi\Delta\nu/2^{1/2}$, which has been shown to give reliable values of free energies of activation for coalescence of uncoupled pairs of doublets.[9] We are indebted to Dr. W. Priester for carrying out the measurement.

(9) Kost, D.; Carlson, E. H.; Raban, M. *J. Chem. Soc., Chem. Commun.* **1971**, 656.

(10) Foxman, B. M. *J. Chem. Soc., Chem. Commun.* **1975**, 221.

(11) Foxman, B. M.; Goverman, J. M., unpublished observations.

(12) The C_α–C_β rotational barrier in Fp(isopropenyl methyl ether)BF_4 is estimated from NMR coalescence experiments to be 14.8 kcal·mol^{-1}.

(13) For example, the M–C_α–C_β bond angle in **3c** (104.2°) is close to that expected for a σ complex, while the theoretical treatment of Eisentstein and Hoffmann retains a maximum angle of 90° for the most distorted model system.

(14) Reactions were carried out on BF_4^- salts and were monitored by NMR spectrometry, employing a Bruker W-90 spectrometer. All reactions were carried out in CD_3NO_2 solutions and followed over 2–3 half-lives. Rate plots exhibited good second-order behavior throughout. The activation energy calculated from these measurements for the reaction of **3a** with **4** is 19.4 kcal·mol^{-1} (log A = 11.8).

Identification of Three Alkylated Nucleotide Adducts from the Reaction of Guanosine 5′-Monophosphate with Phosphoramide Mustard

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The chemical basis of the induction of the cytotoxic, mutagenic, and carcinogenic effects of alkylating agents is generally believed to be the covalent reaction with cellular DNA. Thus elucidation of molecular modification involved in the interactions of these agents with nucleic acids is of primary importance. The advent of a new ionization technique, fast atom bombardment (FAB) mass spectrometry,[1] has permitted us to identify successfully a series of alkylated nucleotide adducts from the reaction of guanosine 5′-monophosphate with phosphoramide mustard.

The bifunctional alkylating agent phosphoramide mustard was first synthesized in 1959 and has been shown to be active against a wide variety of animal tumors.[2] It was later isolated as an in vitro[3] and an in vivo[4] metabolite of the anticancer drug cyclophosphamide. It is now believed that the interaction of phosphoramide mustard with nucleic acids is responsible for the cytotoxic effect of the parent drug, cyclophosphamide. While cross-linking of DNA by phosphoramide mustard has been re-

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(1) Barber, J.; Bordooli, R. S.; Sedgwick, R.; Tyler, A. N. *J. Chem. Soc., Chem. Commun.* **1981**, 325.

(2) Maddock, S. L.; Hangler, A. H.; Friedman, O. M.; Foley, G. E.; Farber, S. *Cancer* Chemother. *Rep.* **1966**, *50*, 629.

(3) Colvin, M.; Padgett, C. A.; Fenselau, C. *Cancer Res.* **1973**, *33*, 915.

(4) Fenselau, C.; Kan, M.-N. N.; Billets, S.; Colvin, M. *Cancer Res.* **1975**, *35*, 1453.

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