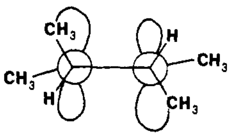

Figure 1. Pyramidalization of 1,2,3,4-tetramethylcyclobutene.

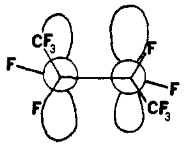

Figure 2. Pyramidalization of perfluoro-3,4-dimethylcyclobutene.

deviations from planarity calculated to be from 20° to 40°, for the conrotatory ring opening of cyclobutenes.[7] It is not apparent that the steric factors in such a transition state should be so significant as to give rise to the specificity observed for the **2** → **4** conversion. It appears moreover that there have been *no* theoretical examinations of such competitive conrotatory processes.

Freedman, in an interesting study of 1,2,3,4-tetraphenylcyclobutenes,[8] attempted to correlate ground-state conformational geometry with rates of electrocyclic ring closure. While there is little doubt that the ground-state geometry of *Z,Z*-diene **9** is skewed (the UV λ_{max}'s for **9**, **8**, and **10** are 207, 214, and 219 nm, respectively), and perhaps closer to the required transition-state geometry than the *E,E*-isomer **10**, there is no reason to believe that a significant energy would be required for **10** to reach a similar reactive conformation[9] or that ground-state energy differences could thus give rise to the observed dramatic kinetic results.

One should consider the possibility that the specificity of cyclobutene **2** ring opening to diene **4** is only fortuitously in accord with steric prejudices and that the driving force for that stereospecific electrocyclic process, as well as for the contrary observations in the case of cyclobutene **7**, is a nonsteric substituent effect on the cyclobutenes. Houk has predicted the effect of allylic substituents on the tendency for double bonds to pyramidalize wherein pyramidalization is maximized for electron-deficient, eclipsing allylic σ-bonded substituents.[11] It was hypothesized, moreover, that such pyramidalization "reflects interactions in the ground state of molecules which are related to much larger energetic effects in transition states".[12]

Consistent, then, with Houk's generalizations is our hypothesis that the differences observed in the hydrocarbon cyclobutene (**2**) and the perfluorocyclobutene (**7**) systems may be due to a difference in their directions of pyramidalization as shown in Figures 1 and 2.

Theoretical and experimental probes of this hypothesis are under way.

Acknowledgment. We gratefully acknowledge the National Science Foundation (W.R.D., D.J.B) and the Air Force Office of Scientific Research (D.J.B.) for their generous support of this research.

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Stereocontrolled Lactone Synthesis Using Diene-Molybdenum Chemistry

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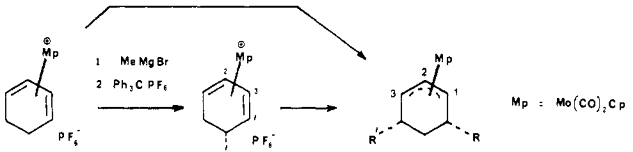
We recently showed that the $Fe(CO)_2L$ moiety (L = CO, PPh_3, $P(OPh)_3$) bound to a cyclic dienyl cation may be used to direct stereochemistry during the attachment of two substitutents, giving 1,2-stereocontrol in the six-membered ring[1] and 1,3-stereocontrol in the seven-membered ring.[2] Other transition metals can be expected to show analogous and complementary stereocontrol. Arene-manganese complexes have been used to establish 1,2-stereocontrol in the six-membered ring.[3] Faller et al.[4] showed that the molybdenum complex **1** is converted to **2** in very high yield and that **2** is stereospecifically methylated (MeMgBr) to give **3**. This offers a useful complementarity to the cyclohexadienyl-$Fe(CO)_3$ cations,[1] but currently available methods for demetalation of π-allyl complexes such as **3** use harsh conditions ((i) $NOPF_6$; (ii) $NaBH_4$; (iii) O_2), less useful when sensitive functional groups are present. We have investigated potentially milder methods for decomplexation, recognizing that **2** might be useful for generating the relative stereochemistry at C(5), C(6), and C(8) in compounds such as tylosin (**4**) and magnamycin B



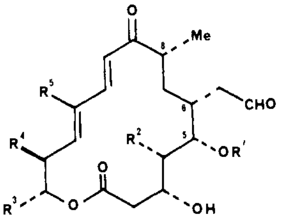
1

2

3, R = R′ = Me

6a-l

6a, R = H; R′ = $CH(CO_2Me)_2$
b, R = H, R′ = $CH(SO_2Ph)CO_2Me$
c, R = H; R′ = $CH(COMe)CO_2Me$
d, R = Me; R′ = $CH(CO_2Me)_2$
e, R = Me; R′ = $CH(SO_2Ph)CO_2Me$
f, R = Me; R′ = $CH(COMe)CO_2Me$
g, R = H; R′ = $CH(CO_2Me)CO_2H$
h, R = Me; R′ = $CH(CO_2Me)CO_2H$
i, R = H; R′ = CH_2CO_2Me
j, R = Me; R′ = CH_2CO_2Me
k, R = H; R′ = CH_2CO_2H
l, R = Me; R′ = CH_2CO_2H



4, R^1 = sugar residue;
R^2 = Me; R^3 = Et;
R^4 = CH_2Omycinase;
R^5 = Me
5, R^1 = sugar; R^2 = OMe;
R^3 = Me; R^4 = R^5 = H

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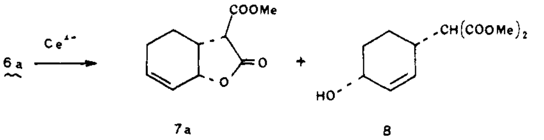
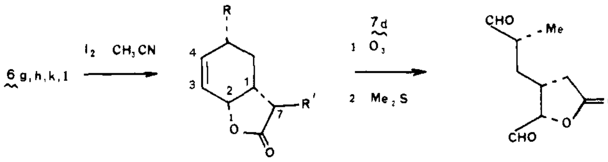
(**5**), both important macrolide antibiotics.[5] Our preliminary results are reported in this communication.

The diene complexes **1** and **2** reacted with $NaCH(CO_2Me)_2$, $NaCH(SO_2Ph)CO_2Me$, and $NaCH(COMe)CO_2Me$ in THF at 20 °C to give π-allyl complexes **6a–f** in high yield (75–95% isolated, pure compounds).[6] Attempted direct demetalation of diester **6a** ($Ce(NO_3)_6(NH_3)_2$, wet acetone, NaOAc)[7] gave a mixture of lactone **7a** (36% isolated) and hydroxy diester **8** (24% isolated). This method is therefore unsuitable for an approach to macrolide subunits. We envisioned a solution to the decomplexation problem by recognizing a possible analogy between the π-allyl–$Mo(CO)_2Cp$ unit and uncomplexed olefins. Thus, both types of molecule might show similar behavior toward electrophilic reagents, and on this basis we anticipated that iodolactonization of appropriate π-allyl–$Mo(CO)_2Cp$ derivatives might be accomplished. Accordingly, the diester complexes **6a** and **6d** were converted to the half acids **6g** and **6h** (KOH, MeOH, H_2O, THF, 20 °C, 10 h, 98% yield), and the phenylsulfonyl ester complexes **6b** and **6e** were converted to monoesters **6i** and **6j** (6% Na, Hg amalgam, Na_2HPO_4, MeOH, THF)[8] and thence to monoacids **6k** and **6l** (KOH, MeOH, THF, 20 °C, 5 h, 68% overall yield). Treatment of **6g** with *excess* iodine (4 equiv of I_2, CH_3CN, 20 °C) led to a rapid change in its IR spectrum: the $Mo(CO)_2$ bands at 1805 and 1927 cm^{-1} due to **6g** were replaced by two new bands at 2050 and 2082 cm^{-1}, their higher frequency suggesting the formation of a cationic π-allyl–$Mo(CO)_2ICp$ series. These new peaks slowly disappeared, with concomitant appearance of a γ-lactone absorption at 1780 cm^{-1}. On completion of the reaction, as judged from IR spectroscopy (ca. 30 min), aqueous workup and ether extraction afforded the lactone **7a**, pure according to TLC (90–95% yield). Simiarly, the acids **6h**, **6k** and **6l** were converted to lactones **7b–d** in very high yield. Ozonoloysis of **7d** (O_3, CH_2Cl_2, MeOH, −78 °C; Me_2S workup) afforded the dialdehyde **9**, which now has stereochemistry corresponding to C(5), C(6), and C(8) of tylosin and magnamycin B.



7a 8



7a, R = H; R′ = α-CO_2Me
b, R = Me; R′ = β-CO_2Me
c, R = R′ = H
d, R = Me; R′ = H

9

Thus, cyclohexadiene–$Mo(CO)_2Cp$ cations may be used for controlled functionalization of the six-membered ring, and the metal can be removed efficiently by using a novel iodolactonization/demetalation procedure to give potentially useful organic intermediates. Further aspects of this chemistry are currently under investigation in our laboratory.[9]

Acknowledgment. We are grateful to the National Institutes of Health for their financial support (GM-30757 and RR-07113-16) and the National Science Foundation for a grant toward the purchase of the Varian XL200 NMR spectrometer used in this research (CHE 80-24633).

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(6) All compounds were obtained as racemic mixtures and were fully characterized by IR and 200-MHz ^1H NMR spectroscopy, high resolution mass spectrometry, and/or combustion analysis, exemplified by the following data for **6j**. Further details will be published in a full paper describing this work, as will the details of X-ray structure determination showing that addition of enolate nucleophiles occurs trans to the $Mo(CO)_2Cp$ group. **6j**: IR ν_{max} (CCl_4) 1945, 1870, 1740 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.29 (5 H, s, C_5H_5), 4.17 (1 H, t, $J = 7.0$ Hz, 2-H), 3.69 (3 H, s, CO_2Me), 3.75–3.5 (2 H, m, obscured, 1-H, 3-H), 2.55 (2 H, d, $J = 6.8$ Hz, CH_2CO_2Me), 2.3 (1 H, m, 4-H), 1.9 (1 H, m, 6-H), 1.22 (3 H, d, $J = 7.2$ Hz, Me), 0.85 (1 H, dm, $J_{gem} = 14.5$ Hz, *endo* 5-H), 0.65 (1 H, d, $J_{gem} = 14.5$ Hz, exo 5-H). The pattern observed for endo 5-H and exo 5-H is consistent with structure and stereochemistry **6j**. The absence of large coupling constants between exo 5-H and 4-H or 6-H is particularly diagnostic of the cis relationship between R and R′ by comparison with the spectral data given by Faller[4] for complex **3**.

(7) We have previously used this method successfully with dienyl–$Mn(CO)_3$ complexes. Details are given in: Pearson, A. J.; Richards, I. C.; Bruhn, P. R. *Tetrahedron Lett.* **1984**, *25*, 387.

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(9) This mild decomplexation method appears to be general. Similar treatment of ester complexes related to **6a** leads to the formation of substituted iodocyclohexenes, and these aspects will be discussed in a full paper.

Observation of Cis and Trans Oxaphosphetanes in the Wittig Reaction by High-Field ^{31}P NMR Spectroscopy

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Vedejs and co-workers, in pioneering work on the Wittig olefination reaction, established oxaphosphetanes (e.g., **1** and **2**; see Scheme I) as key intermediates by low-temperature ^{31}P NMR spectroscopy (at 40.5 MHz), observing them as narrow multiplets (partial proton decoupling) between −55 and −75 ppm.[1] However, resolved ^{31}P NMR resonances for cis and trans oxaphosphetanes have generally not been observed,[1,2] thereby precluding direct quantitation and application of such data to mechanistic analyses.[3]

In connection with our research on Wittig reactions of carboxy and oxido ylides,[4] we initiated ^{31}P NMR studies to probe the effect of anionic groups on stereochemistry. Since experiments conducted with such ylides on a Bruker AM-360 instrument at 145.8 MHz (broad-band proton decoupling) revealed pairs of singlets between −55 and −65 ppm, attributable to diastereomeric oxaphosphetanes, we reexamined Wittig reactions involving simple alkylidene ylides. Salient features of our work include (1) the first observation of cis and trans oxaphosphetanes in the reaction of nonstabilized phosphorus ylides with aldehydes, (2) direct quantitation of the diastereomeric pairs by electronic integration, (3) assignment of the peaks via chemical arguments, and (4) demonstration of noncorrespondence between the ratios of cis/trans oxaphosphetanes

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(3) Many mechanistic discussions of the Wittig reaction have been presented: (a) Schlosser, M. *Top. Stereochem.* **1970**, *5*, 1. (b) Schlosser, M.; Christman, K. F. *Justus Liebigs Ann. Chem.* **1967**, *708*, 1. (c) Gosney, I.; Rowley, A. G. In "Organophosphorus Reagents in Organic Synthesis"; Cadogan, J. I. G, Ed.; Academic Press: New York, 1979; pp 17–153. (d) Schlosser, M.; Schaub, B. *J. Am. Chem. Soc.* **1982**, *104*, 5821. (e) McEwen, W. E.; Cooney, J. V. *J. Org. Chem.* **1983**, *48*, 983. (f) References 1 and 2 b. (g) Bestmann, H. J. *Pure Appl. Chem.* **1980**, *52*, 771. Although much effort has been devoted to relating reaction stereochemistry with mechanism, through alkene *Z*/*E* ratios, the stereochemistry of reaction intermediates has generally been ignored.

(4) Maryanoff, B. E.; Reitz, A. B.; Duhl-Emswiler, B. A. *Tetrahedron Lett.* **1983**, *24*, 2477. Maryanoff, B. E.; Duhl-Emswiler, B. A. *Ibid.* **1981**, *22*, 4185.

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