3-hydroxyl group. Synthetic **17** was identical with a sample of naturally derived maytansinol 9-*O*-methyl ether (**17**).[18] 4,5-Epoxidation of **16** with *m*-chloroperbenzoic acid forms **17** with complete stereoselectivity, although the yield is diminished by side reactions involving the other double bonds. That the oxidation of the 4,5-double bond of **16** would be highly stereoselective was predicted in advance from a knowledge of the conformation of maytansinoids,[1a] and the directing effect of the 3α-hydroxyl function.[20] Hydrolysis of **17** affords maytansinol (**18**) in >90% yield.

The conversion of maytansinol to maytansine has already been described by the Takeda group.[21] The conversion of maytansinol 9-*O*-methyl ether to maytansine 9-*O*-methyl ether has also been carried out in the present study by using the imidazolide of *N*-acetyl-*N*-methyl-L-alanine in DMF–DME in the presence of imidazole at 45–47 °C for 75 h. Finally, hydrolysis of maytansine 9-*O*-methyl ether by using a 1% solution of pyridinium chloride in 1:1 THF–water at 25 °C for 14 h provides maytansine in 95% yield to complete our synthetic sequence.

The realization of the total synthesis of maytansine depended on the successful solution of a large number of critical problems including (1) control of stereochemistry, (2) introduction, protection, utilization, and manipulation of a formidable collection of functional groups, (3) carbon chain elaboration, and (4) macrocyclization. A number of new strategies and synthetic methods were crucial as were the availability of micro-scale physical measurements (notably ^{1}H NMR and mass spectral) and separations (high-performance LC). To our knowledge, no other stereocontrolled routes to maytansinoids or routes to chiral maytansinoids have been accomplished to date.[22]

(20) Interestingly, reduction of the 3-keto function of maytansin-3-one can be easily controlled to afford the 3β-alcohol stereospecifically, but does not seem to lead to the 3α-alcohol as the major product with the gamut of applicable reagents (unpublished work in these laboratories). This fact played a major role in dictating the successful stereochemical strategy outlined herein.

(21) Hashimoto, N.; Matsumura, K.; Motohashi, M.; Ootsu, K.; Kozai, Y.; Kishi, T. 177th National Meeting of the American Chemical Society, Honolulu, HI, 1979; Abstr. Medicinal Section No. 26.

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An Equilibrium between Carbene and a Metal–Carbene Complex. Homogeneous Catalysis by Mercury(II)

Sir:

Metal–carbene complexes have usually been prepared by modification of noncarbene carbon ligands.[1,2] Preparation by direct reaction of the metal with a neutral carbene has seldom been observed.[1,3] We report herein that mercury(II) reacts directly with dibromocarbene to form a metal–carbene complex.

(1) For a complete compilation of methods, see: Cardin, D. J.; Çetinkaya, B.; Lappert, M. F. *Chem. Rev.* **1972**, *72*, 545–574.

(2) For other reviews, see: Kochi, J. K. "Organometallic Mechanisms and Catalysts", Academic Press: New York, 1978; pp 285f. Katz, T. J. *Adv. Organomet. Chem.* **1977**, *16*, 283–317. Farona, M. F. *CHEMTECH.* **1978**, *8*, 40–42.

(3) Some difficulties are described for an Ir complex by Cooke, J.; Cullen, W. R.; Green, M.; Stone, F. G. A. *J. Chem. Soc. A* **1969**, 1872–1874.

Scheme I

The free and the complexed carbenes lead to separate products whose ratio demonstrates the presence of the two distinct intermediates.

Reaction of *trans*-dichloroethene (A) with phenyl(tribromomethyl)mercury (M) gives two products in comparable amounts, the stereospecifically formed cyclopropane (C) and the rearranged propene (P) (eq 1).[4] A similar reaction is observed with the *cis*-

and *trans*-dibromoethenes, and the cyclopropane in each case is formed stereospecifically. This stereochemical result has traditionally been accepted as prima facie evidence for a singlet carbene.[5] The propene P is reasonably derived from a diradical of the structure ·CHCl–CHCl–CBr$_2$· (D), via a 1,2 shift of the chlorine atom. Chlorine has a high migratory aptitude toward a radical site.[6]

It is very unlikely that this open diradical, if produced by reaction of the singlet dibromocarbene (S) with dichloroethene, could be a common precursor of both C and P, because of the stereospecific formation of the cyclopropane product. Moreover, a stepwise reaction of the singlet carbene would contradict the Skell hypothesis.[5] Consequently, we sought to prove separate pathways for production of the propene and the cyclopropane.

Proof that the two products derive from distinct intermediates can come from the dependence of their ratio on the concentration of the alkene.[7] If the singlet carbene reacted directly with the alkene to produce both C and P via a common pathway, then their ratio would be independent of alkene concentration. If, however, the carbene either gives C directly by a concerted reaction with alkene or is competitively converted to a second intermediate that in turn reacts with alkene to give P via D, then the ratio [P]/[C] will show the following dependence

$$\frac{[P]}{[C]} = \frac{k_2}{k_3}\frac{1}{[A]}$$

in which k_2 is the rate of interconversion of the carbene to the second intermediate and k_3 is the rate of direct reaction of carbene with alkene.[8] *We observed a very clean, linear dependence of this ratio on* $1/[A]$. Consequently, we can conclude that there are two intermediates. Furthermore, the $1/[A]$ dependence requires that C come from the first-formed intermediate (free singlet carbene) and that P come from the second-formed intermediate

(4) Lambert, J. B.; Kobayashi, K.; Mueller, P. H. *Tetrahedron Lett.* **1978**, 4253–4256.

(5) Skell, P. S.; Valenty, S. J.; Humer, P. W. *J. Am. Chem. Soc.* **1973**, *95*, 5041–5042.

(6) Friedlina, R. K. *Adv. Free-Radical Chem.* **1965**, *1*, 231f.

(7) McConaghy, J. S., Jr.; Lwowski, W. *J. Am. Chem. Soc.* **1967**, *89*, 2357–2364. A kinetically equivalent study has been carried out on a noncarbene system: Corwin, L. R.; McDaniel, D. M.; Bushby, E. J.; Berson, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 276–287. It should be noted that their product ratio plot, Figure 7, uses the ratio of the second product to the first product, analogous to our [C]/[P].

(8) The steady-state approximation in the second intermediate gives a ratio (second intermediate to first intermediate) of $k_2/(k_4[A] + k_{-2})$. Substitution into the expression for the ratio of products gives [P]/[C] = $(k_4/k_3)(k_2/(k_4[A] + k_{-2}))$. The right-hand side of this equation reduces to $(k_2/k_3)(1/[A])$ if $k_4[A] \gg k_{-2}$. In our kinetic runs, we kept [A] extremely high in order that its concentration remain essentially constant throughout the reaction. This experimental requirement may have assisted the maintenance of the inequality. The validity of the inequality, however, is confirmed by the fact that the plots both of [P]/[C] vs. $1/[A]$ and of [C]/[P] vs. [A] are linear.

(whose structure is as yet unspecified). If C came from the second intermediate and P from the first, then [P]/[C] would have been directly proportional to [A], contrary to the observation.

We originally thought that the second intermediate was the triplet carbene.[4] In related work on the reaction of diphenyl-carbene with dichloroethene, we concluded that the singlet and triplet forms are almost certainly the respective product-forming intermediates leading to the structures analogous to C and P.[9] In the present case, however, there is a marked dependence of the product ratio [P]/[C] on the concentration of the starting mercury compound, PhHgCBr$_3$ (M). Since the initial decomposition of M to form the carbene precedes the branching point to the two intermediates, the ratio should have been independent of [M]. Even if M went directly to the two intermediates, there should be no dependence.[7] The single ⇌ triplet interconversion should be fast and independent of [M]. *A detailed study of the kinetics revealed a first-order dependence of [P]/[C] on [M].* Such a kinetic result requires the intervention of an additional molecule of M during the conversion of the singlet carbene to the second intermediate. The ratio [P]/[C] did not depend on the concentration of PhHgBr, which is poorly soluble in benzene. The combined dependence of [P]/[C] on [M] and 1/[A] (eq 2) is

$$\frac{[P]}{[C]} = \frac{k_2 [M]}{k_3 [A]} \qquad (2)$$

consistent with the mechanism in Scheme I.

Although the kinetics demand the existence of both free and complexed carbene, the events after the formation of the second intermediate are not well-defined. A possible structure of the metal–carbene complex is (Ph)(CBr$_3$)Hg$^+$—C̈Br$_2$ ↔ (Ph)-(CBr$_3$)Hg = CBr$_2$.[1,10] Reaction with the alkene could give a metallacyclobutane or its open-chain analogue, (Ph)(CBr$_3$)-Hg$^+$CBr$_2$CHClČHCl.[11] Loss of the molecule of PhHgCBr$_3$ then produces the dipolar intermediate $^+$CBr^{2}CHClČHCl, of which the diradical D is a resonance structure. Because the second molecule of M is regenerated, it has served in a homogeneous catalytic role in the production of P.[12] These suggestions at present are hypothetical.

The low reactivity of dichloroethene is the key to the entire mechanistic scenario. Its poor reactivity with the electrophilic singlet carbene in the metal-free system[9] permits intersystem crossing to the triplet and formation of the rearranged propene. More reactive alkenes such as the 2-butenes would have led solely to the stereospecific cyclopropane via the singlet as the only intermediate.[13,14] In the presence of the metal (M), the carbene forms a more nucleophilic intermediate by complexation rather than by intersystem crossing. This complex then reacts more readily with the weak substrate, dichloroethene. This pathway leads to chlorine migration and to the product P.

In summary, we have observed kinetic evidence that requires an interconversion between dibromocarbene and its complex with PhHgCBr$_3$.[15] The free carbene reacts with the alkene to form

the cyclopropane C. The complexed carbene leads to the rearranged propene P. The primary function of the complexing PhHgCBr$_3$ is to heighten the reactivity of the carbene with the relatively unreactive dichloroethene. These results suggest numerous experiments with other carbenes, other alkenes, and other metallic complexing agents, which we currently are prosecuting.

(15) These studies confirm Seyferth's original mechanism of cyclopropane formation from a free carbene: Seyferth, D.; Mui, J. Y.-P.; Burlitch, J. M. *J. Am. Chem. Soc.* **1967**, *89*, 4953–4959. Our additional conclusions all derive from the rearranged propene product that was previously not of interest.

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Cobalt–Nitro Complexes as Oxygen Transfer Agents: Oxidation of Olefins

Sir:

Recently, the need has been emphasized for developing non-radical systems for specific oxidation of organic substrates by molecular oxygen.[1] Previously, we have offered a novel appraoch consisting of oxygen transfer from the nitro ligand of metal–nitro complexes to organic substrates accompanied by the formation of the corresponding nitrosyl complexes. The catalytic cycle is then completed by reoxidation of the nitrosyl ligand by molecular oxygen.[2] Using py·Co(saloph)·NO$_2$ (I) (saloph = *N,N'*-bis(al-icylidene-*o*-phenylene)diamino), we have demonstrated oxidation of phosphines to phosphine oxides and oxomolybdenum(IV) complexes to dioxomolybdenum(VI) species.[2] Interaction of the nitro ligand in I and in py·Co(TPP)·NO$_2$ (II) (TPP = tetra-phenylporphyrin) with Lewis acids [e.g., BF$_3$, Li$^+$] enhances its electrophilicity and thus its oxidation power. This combination of cobalt–nitro complexes with Lewis acids extended this oxidation chemistry to organic sulfides, alcohols, and 1,3-cyclohexadiene,[3] but not to monoolefins. We now report a system which represents an important modification of the above concept. It enables us to employ cobalt–nitro complexes as stoichiometric oxidants and as catalysts for the oxidation of monoolefins.

Cobalt–Nitro Complexes as Oxygen Transfer Agents. The nitro ligand in I and II can formally be regarded as a nitrogen-bound monoanionic ligand (Co$^+$–NO$_2$$^-$), and as such it may function as a weak, oxygen-centered nucleophile. We have attempted to use this property of the nitro ligand and activate olefins toward a nucleophilic attack by coordinating them to higher valent group 8 metals such as palladium(II).[4] Initially, we concentrated our

(9) Gaspar, P. P.; Whitsel, B. L.; Jones, M., Jr.; Lambert, J. B. *J. Am. Chem. Soc.* **1980**, *102*, 6108.

(10) Mercury–carbene complexes are not common, but some have been suggested: Wanzlick, H.-W.; Schönherr, H.-J. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 141–142. Schöllkopf, U.; Gerhart, F. *Ibid.* **1967**, *6*, 560–561, 970, 805.

(11) The formation of the metallacycle might imply the production of some CHCl=CBr$_2$ or adducts of CHCl, which we have not as yet found.

(12) It should be emphasized that the second molecule of PhHgCBr$_3$ is not unique in fulfilling this role. The first molecule is necessary to produce CBr$_2$. The second molecule, in its complexation role, can be replaced by other materials. We have found that other PhHgR compounds, which do not produce a carbene, in the presence of decomposing PhHgCBr$_3$ strongly affect [P]/[C].

(13) The reaction of CBr$_2$ with the 2-butenes is stereospecific and without rearrangement: Skell, P. S.; Garner, A. Y. *J. Am. Chem. Soc.* **1956**, *78*, 3409–3411.

(14) The low reactivity of dichloroethene has frustrated the realization of one obvious experiment, the production of CBr$_2$ from a nonmetallic source. We have generated CBr$_2$ by all the common procedures, without observing any reaction with this alkene. Apparently, other components of the mixture (CHBr$_3$, protic solvent, etc.) intercept the carbene before it can react with dichloroethene.

(1) More than 50% of the chemicals needed in industry are prepared by oxidation of petrochemicals. Due to the change in price and availability of the petrochemicals, novel, specific oxidation processes are needed. "Selective Catalytic Oxidation of Hydrocarbons: A Critical Analysis". Catalytica Associates, Inc., Santa Clara, CA, Multiclient Study No. 1077, October 1979.

(2) Tovrog, B. S.; Diamond, S. E.; Mares, F. *J. Am. Chem. Soc.* **1979**, *101*, 270.

(3) Tovrog, B. S.; Diamond, S. E.; Mares, F.; Szalkiewicz, A., submitted; presented in part at the 177th National Meeting of the American Chemical Society, Honolulu, HI, April 1979, and at the First International Symposium on Activation of Molecular Oxygen and Selective Oxidations Catalyzed by Transition Metal Complexes, Bendor, France, May 1979.