Since the lowest antenna of **1** is made up of B (= C) components, compound **3a** served both as the glycosyl donor and, after dibromination and deacylation to **3b**, as the glycosyl acceptor, thereby permitting rapid assembly of the trisaccharide segment **10a**.

The building blocks **9a** and **10a** would now become glycosyl donors. Reductive elimination, carried out most efficiently by sonication overnight with zinc in the presence of tetra-*N*-butylammonium iodide, gave **9b** and **10b**, respectively. Coupling of **2b** gave the tetrasaccharide **11a** (Scheme II) which, after deacylation, was ready for coupling with the pentasaccharide **9b**[10b] to give the protected nonasaccharide **12**.

From Scheme II, it is apparent that once the properly designed monosaccharide precursors are in hand, subsequent synthetic manipulations are confined to liberation of (a) a hydroxyl group or (b) the pentenyl double bond. The fact that these alterations do not tamper with the anomeric center greatly facilitates the use of ^{1}H NMR to monitor the progress. With NIS/Et_3SiOTf as promoter, coupling is immediate, a circumstance which makes for rapid assembly.

It required 3 weeks to prepare 450 mg of pentasaccharide **9a** from mannose,[12] with a total of 8 days being required for the deacetylation steps. We anticipate that with proper attention to logistics it should be possible to assemble the entire nonasaccharide within 2 weeks.

Supplementary Material Available: Listings of experimental procedures for the preparation of compounds **2a,b**, **3a,b**, **8b**, **9a,b**, **10a,b**, **11a,b**, and **12** and their ^{1}H NMR data (9 pages). Ordering information is given on any current masthead page.

(12) We thank Miss Elizabeth Naisang, an undergraduate summer research assistant, for carrying out this experiment.

A Transition-State Model for the Rhodium Porphyrin-Catalyzed Cyclopropanation of Alkenes by Diazo Esters

Kathlynn C. Brown and Thomas Kodadek*

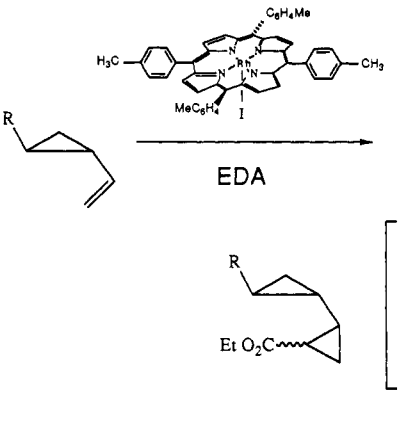
Department of Chemistry and Biochemistry
University of Texas at Austin, Austin, Texas 78712

Received April 13, 1992

A number of metal complexes catalyze the cyclopropanation of alkenes by diazo esters.[1] Rhodium(III) porphyrins are particularly interesting in that they often produce *syn*-cyclopropyl esters preferentially. The syn selectivity increases with the size of the meso substituents, and synthetically useful ratios are achieved with bulky macrocycles.[2] All other metal catalysts exhibit the opposite selectivity, including several recently developed asymmetric catalysts.[3-7] Thus, the porphyrin-catalyzed reactions are of potential utility in organic synthesis, and particularly so if chiral porphyrins could be developed that would render the reaction highly asymmetric. We have recently reported preliminary work directed toward this goal, but high enantiomeric excesses have not yet been realized.[8,9] In order to rationally design more selective catalysts, it would be useful to understand the detailed mechanism of carbene transfer from the putative metallocarbene intermediate[10] to the alkene. The experiments reported here suggest that the exchange occurs without detectable intermediates and has a very early transition state.

The cyclopropanation of *trans*-β-deuterio-*p*-X-styrene (X = H, OCH_3)[11] was examined using RhTTPI[12] as the catalyst and ethyl diazoacetate (EDA) as the carbene donor. In both cases the stereochemistry about the C_α–C_β bond was retained, as deduced by ^{2}H NMR spectroscopy.[13] Furthermore, the ratio of *syn*- to *anti*-cyclopropyl esters produced by the RhTTPI-catalyzed reaction of EDA with a series of para-substituted styrenes is essentially invariant (X = Cl, H, Me, MeO, syn/anti = 0.96 ± 0.05). Finally, when a competitive cyclopropanation reaction was carried out between equimolar amounts of styrene and *p*-methoxystyrene in the presence of EDA and RhTTPI, the ratio of products was 1.0. These data suggest that, for the rhodium porphyrin-catalyzed reactions, cationic species are unlikely to be intermediates in the product-determining step.[14]

Carbon radicals adjacent to a cyclopropyl ring are known to undergo rapid rearrangement to homoallyl radicals. The RhTTPI-catalyzed cyclopropanation of vinylcyclopropane and *anti*-2-phenyl-1-vinylcyclopropane[15] with EDA resulted in the formation of only the dicyclopropane products (eq 1). The possible rearrangement products **1a** and **1b** were not observed by either ^{1}H NMR or GC/MS. The cyclopropane products and unreacted olefin accounted for over 97% of the substrate present, eliminating the possibility that a rearranged radical intermediate is formed, but polymerization occurs rather than cyclization to **1**. Since the rates of rearrangement for both cyclopropylcarbinyl radicals are known (R = H, $k = 1.0 \times 10^8$; R = Ph, $k = 2.1 \times 10^{11}$),[16,17] our data demand that if a radical intermediate is formed, it must close very rapidly.



(1)

The secondary kinetic isotope effect for the cyclopropanation of styrene and styrene-d_8 by EDA was determined in a competitive

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(9) Maxwell, J. L.; O'Malley, S.; Brown, K. C.; Kodadek, T. *Organometallics* **1992**, *11*, 645.
(10) The active intermediate is assumed to be a rhodium–carbene complex. For evidence in favor of this model, see: Maxwell, J. L.; Brown, K. C.; Bartley, D.; Kodadek, T. *Science* **1992**, *256*, 1544.
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(12) RhTTPI is an abbreviation for iodorhodium(III) tetra-*p*-tolylporphyrin.
(13) ^{2}H NMR data for labeled ethyl 2-*p*-X-phenylcyclopropanecarboxylates: X = OCH_3 5.20 (D_a), 1.55 (D_c), 1.25 ppm (D_b); X = H 4.95 (D_a), 1.60 (D_c), 1.30 ppm (D_b). Chemical shifts reported are relative to $CDCl_3$ (7.24 ppm). All resonances are broad singlets due to proton–deuterium coupling. The detection limit is ≥5%. NMR data are available as supplementary material.
(14) For a carbene-transfer reaction in which similar probes have detected carbocation intermediates, see: Brookhart, M.; Kegley, S. E.; Husk, G. R. *Organometallics* **1984**, *3*, 650.
(15) (a) Fischetti, W.; Heck, R. *J. Organomet. Chem.* **1985**, 391. (b) Castellino, A.; Bruice, T. *J. Am. Chem. Soc.* **1988**, *110*, 7512.
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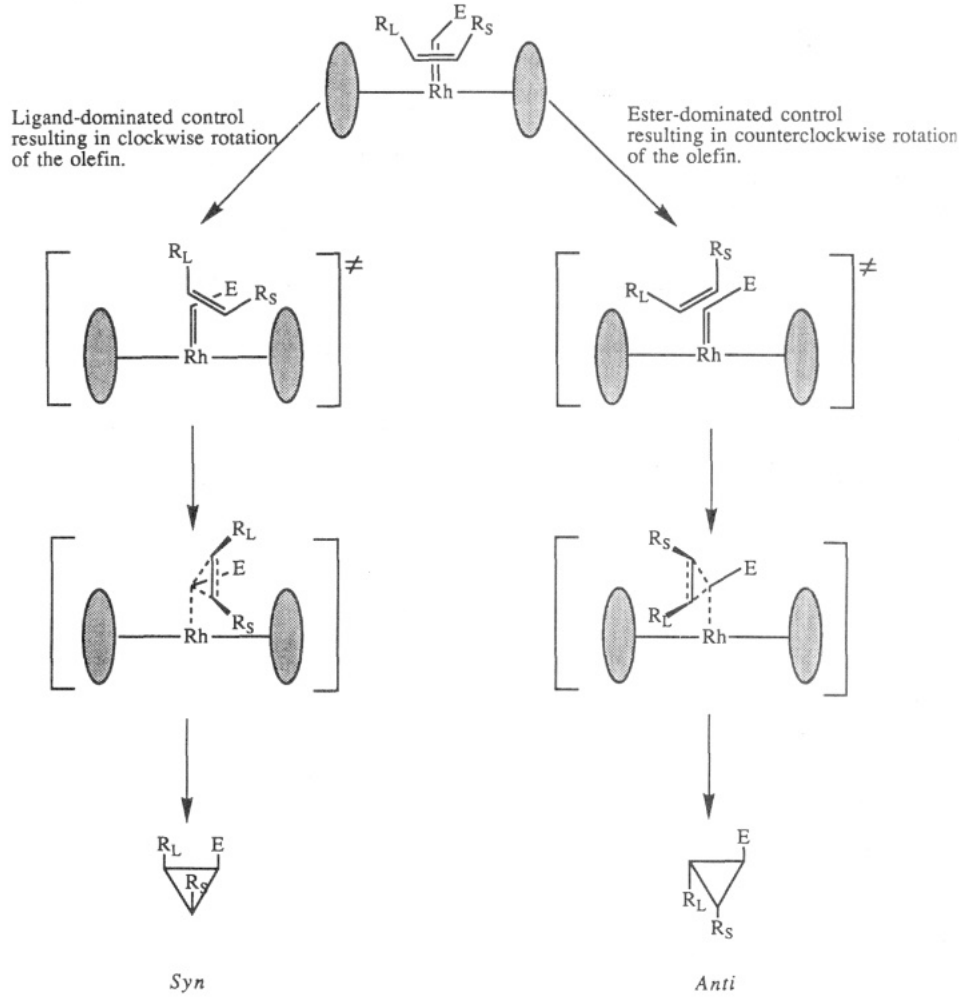

Figure 1. Proposed reaction coordinate model for carbene transfer from a porphyrin rhodium carbene complex to an unsymmetrical alkene. R_L and R_S represent the sterically larger and smaller alkene substituents, respectively. The porphyrin ligand is represented as a line. The *meso*-phenyl rings of a tetraarylporphyrin are shown as shaded ovals. See text for discussion.

reaction using $RhTTPCH_3$ as the catalyst.[18] No detectable secondary isotope effect was observed ($k_H/k_D = 1.0 \pm 0.07$). We conclude that there is little rehybridization of the alkene in the transition state of the carbene-transfer step. Taken together, all of these data suggest that the rhodium porphyrin catalysts transfer the carbene fragment to the substrate in a concerted fashion and that the transition state for this process is very early.

These results, combined with earlier studies,[9] provide sufficient information to construct a model of the reaction coordinate for carbene transfer from the metal to the alkene (Figure 1). Following a model proposed previously by Doyle for rhodium acetate-catalyzed cyclopropanations,[19] the olefin is pictured approaching perpendicular to the carbene with the large substituent opposite the ester group.[20] On the basis of steric considerations, we assume that an unsymmetrically substituted alkene would approach so as to minimize interactions between the larger substituent and the carbene ester (Figure 1). The olefin can then rotate clockwise or counterclockwise about an axis orthogonal to the rhodium–carbon bond to reach the transition state.[9] In this model, the direction of this rotation is dominated by steric factors. If ligand–substrate interactions dominate, as they would for bulky, bowl-shaped porphyrins, the rotation will be clockwise, leading to the syn product. However, if the ester–substrate interactions are more severe, the rotation of the olefin will be counterclockwise, leading to the anti product. This model is consistent with all of the data reported here. No discrete radical or carbocation-containing intermediates are proposed, and an early transition state is postulated in which the alkene carbons are still largely sp^2-hybridized. The relative orientation of the alkene and the porphyrin in the transition state is appropriate to explain the previously reported shape selectivity of the reaction.[9] This model nicely rationalizes the higher syn/anti product ratios of the porphyrin-catalyzed reaction when the bulk of the meso substituents is increased. As the ligand–R_L interaction becomes more severe, the counterclockwise rotation pathway, which leads to the anti product, will become less important.

Our model is similar in many respects to one proposed previously for the rhodium acetate-catalyzed cyclopropanation of alkenes by EDA.[19] However, that model invokes a stabilizing interaction between the ester carbonyl oxygen of the EDA-derived metal carbene and a developing positive charge on one of the alkene carbons in the transition state. In order for this interaction to be feasible geometrically, an unsymmetrical alkene must approach the carbene with the larger substituent on the same side as the ester. This model has the virtue of rationalizing why rhodium acetate-catalyzed reactions employing EDA provide a modest excess of the anti product, while those including phenyldiazomethane (a carbene source lacking a stabilizing group) sometimes yield predominantly the syn product.[21] There is no need to invoke such an ester–alkene interaction in the porphyrin-catalyzed re-

(18) RhTTPMe: methylrhodium(III) tetra-*p*-tolylporphyrin. RhTTPMe was used instead of RhTTPI to avoid complications due to differential binding of styrene and styrene-d_8 to the porphyrin. RhTTPI has been observed to form olefin π complexes whereas RhTTPMe does not.[10]

(19) Doyle, M. P.; Dorow, R. L.; Burho, W. E.; Griffin, J. H.; Tamblyn, W. H.; Trudell, M. L. *Organometallics* **1984**, *3*, 44.

(20) This allows for maximum overlap between the HOMO of the alkene and the LUMO of the metallocarbene.

(21) Doyle, M. P.; Griffin, J. H.; Bagheri, V.; Dorow, R. L. *Organometallics* **1984**, *3*, 53.

actions, since the *syn*-cyclopropyl ester is the dominant product with bulky porphyrins. Furthermore, the lack of substituent and secondary isotope effects in the porphyrin-catalyzed reaction argues against a transition state in which there is considerable charge buildup on, or rehybridization of, the alkene carbons, as implied by the ester stabilization model.

In conclusion, the mechanism proposed here adequately explains all of the results obtained in the rhodium porphyrin-catalyzed reactions of alkenes with simple diazo esters and provides some level of stereochemical predictive power. This knowledge will aid in the design of asymmetric porphyrin cyclopropanation catalysts, which is an ongoing project in our laboratory.

Acknowledgment. This work was supported by a grant from the donors of the Petroleum Research Fund, administered by the American Chemical Society. T.K. is the recipient of a Junior Faculty Research Award from the American Cancer Society.

Supplementary Material Available: ^{1}H NMR spectrum of cyclopropane products (1 page). Ordering information is given on any current masthead page.