

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**¹⁰ 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 ¹H NMR to monitor the progress. With NIS/Et₃SiOTf 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 deacylation 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 ¹H NMR data (9 pages). Ordering information is given on any current masthead page.

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

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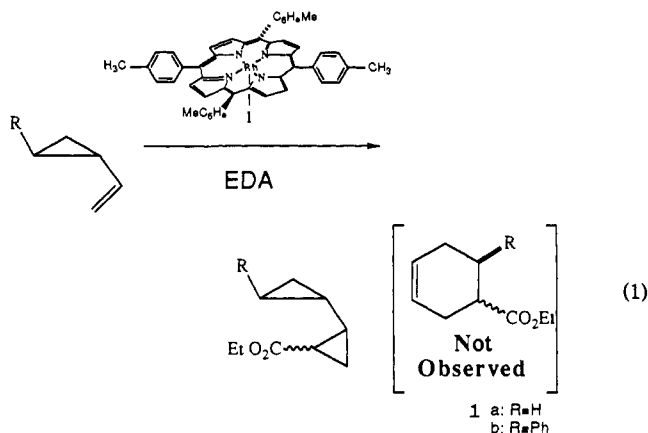
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A number of metal complexes catalyze the cyclopropanation of alkenes by diazo esters.¹ Rhodium(III) porphyrins are particularly interesting in that they often produce *syn*-cyclopropyl esters preferentially. The *syn* selectivity increases with the 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 intermediate¹⁰ 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, OCH₃)¹¹ was examined using RhTTPI¹² 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 ²H 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 \pm 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-vinylcyclopropane¹⁵ 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 ¹H 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 10⁸; R = Ph, *k* = 2.1 \times 10¹¹),^{16,17} our data demand that if a radical intermediate is formed, it must close very rapidly.



The secondary kinetic isotope effect for the cyclopropanation of styrene and styrene-*d*₈ by EDA was determined in a competitive

(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.

(11) (a) Corey, E.; Fuchs, P. *Tetrahedron Lett.* 1972, 36, 3769. (b) Salaun, J. *J. Org. Chem.* 1977, 42, 28.

(12) RhTTPI is an abbreviation for iodorrhodium(III) tetra-*p*-tolylporphyrin.

(13) ²H NMR data for labeled ethyl 2-*p*-X-phenylcyclopropane-carboxylates: X = OCH₃, 5.20 (D_a), 1.55 (D_b), 1.25 ppm (D_c); X = H 4.95 (D_a), 1.60 (D_b), 1.30 ppm (D_c). Chemical shifts reported are relative to CDCl₃ (7.24 ppm). All resonances are broad singlets due to proton-deuterium coupling. The detection limit is \geq 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.

(16) Newcomb, M.; Glenn, A. *J. Am. Chem. Soc.* 1989, 111, 275.

(17) Newcomb, M.; Manek, M. *J. Am. Chem. Soc.* 1990, 112, 9662.

(1) Doyle, M. P. *Chem. Rev.* 1986, 86, 919.

(2) Callot, H. J.; Metz, F.; Piechocki, C. *Tetrahedron* 1982, 38, 2365.

(3) Aratani, T. *Pure Appl. Chem.* 1985, 57, 1839.

(4) Fritsch, H.; Leutenegger, U.; Pfaltz, A. *Angew. Chem., Intl. Ed. Engl.* 1986, 25, 1005.

(5) Lowenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* 1990, 42, 6005.

(6) Evans, D. A.; Worpel, K. A.; Hinman, M. M. *J. Am. Chem. Soc.* 1991, 113, 726.

(7) Doyel, M. P.; Brandes, B. B.; Kazala, A. P.; Pieters, R. J.; Jarstfer, M. B.; Watkins, L. M.; Eagle, C. T. *Tetrahedron Lett.* 1990, 46, 6613.

(8) O'Malley, S.; Kodadek, T. *Organometallics* 1992, 11, 2299.

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.

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