this research. We are also indebted to Janet L. Carlson for the refinement of several of the procedures described here.

References and Notes

(1) For a recent paper in the series, see W. S. Johnson, R. S. Brinkmeyer, V. M. Kapoor, and T. M. Yarnell, J. Am. Chem. Soc., **99**, 8341 (1977).
(2) For a review see W. S. Johnson, *Bioorg. Chem.*, **5**, 51 (1976).
(3) W. S. Johnson, M. B. Gravestock, and B. E. McCarry, *J. Am. Chem. Soc.*, **93**, 4332 (1971).
(4) The tricyclic material was not characterized in this example; however, in a closely related cyclization just such a product has been isolated and characterized. See the Ph.D. Dissertation of B. E. McCarry, Stanford University, 1972.
(5) G. Büchi and H. Wuest, *J. Org. Chem.*, **34**, 1122 (1969).
(6) This substance was evaporatively distilled using a Büchi Kugelrohrofen. The temperature used ranged from 120 to 210 °C and the pressure from 0.15 to 1.15 mmHg.
(7) The NMR and IR spectra were consistent with the assigned structure and a satisfactory combustion analysis was obtained for this compound.
(8) W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T.-t. Li, D. J. Faulkner, and M. R. Petersen, *J. Am. Chem. Soc.*, **92**, 741 (1970).
(9) This product was purified by column chromatography on Florisil.
(10) R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, **35**, 4000 (1977).
(11) W. S. Johnson and G. E. DuBois, *J. Am. Chem. Soc.*, **98**, 1038 (1976); see note 12.
(12) D. F. Morrow, T. P. Culbertson, E. L. Wittle, M. E. Butler, and M. M. Creger, *J. Med. Chem.*, **7**, 537 (1964).
(13) This ratio of *trans*- to *cis*-hydrindan ring systems is similar to that observed in an ethylacetylenic terminated cyclization to form one new ring: P. T. Lansbury and G. E. DuBois, *Chem. Commun.*, 1107 (1971); P. T. Lansbury, T. R. Demmin, G. DuBois, and V. R. Haddon, *J. Am. Chem. Soc.*, **97**, 394 (1975).
(14) L. R. Hughes, W. S. Johnson, and J. L. Carlson, *J. Am. Chem. Soc.*, following paper in this issue.

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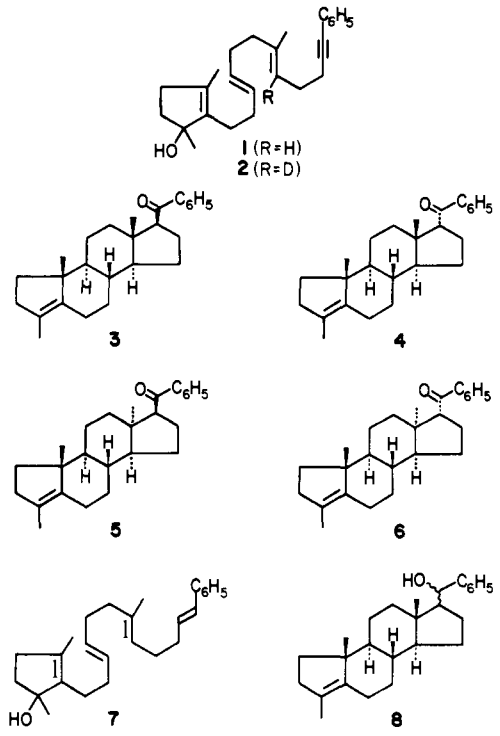
Biomimetic Polyene Cyclizations.[1] A Comparison of the Phenylacetylenic and Styryl Terminators in Influencing the Stereoselectivity of Processes Leading to Steroidal Products

Sir:

It has been observed in our laboratory that certain polyene cyclizations in which an acetylenic terminator is used to form the D ring of the steroid nucleus are not always highly stereoselective, yielding tetracyclic products that contain up to 20% 13α isomers having the unnatural C/D cis configuration.[1a] Thus, cyclization of the substrate **1** gives a good yield of tetracyclic products **3, 4, 5,** and **6;** however, the ratio of C/D trans (**3** + **4**) to C/D cis isomers (**5** + **6**) is 4:1. Since this ratio is not affected significantly either by changing reaction conditions or by the introduction of electro-divergent substituents in the phenyl group,[2] we have been prompted to undertake critical examination of the stereochemical outcome of cyclizations involving other types of terminators in the hope of realizing improved stereoselectivity. The present paper describes such a study of the effect of the styryl terminator via a plan which envisaged cyclization of the substrate **7** followed by oxidation of the resulting[3] benzylic alcohols **8** to the known ketones (**3, 4, 5,** and **6**) and determination of the proportion of these compounds in this mixture.

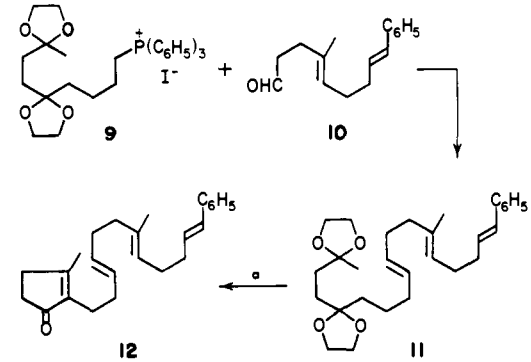
The styryl substrate **7** was prepared by a convergent synthesis (see Scheme I) involving the condensation of the known aldehyde **10**[3a] with the previously described phosphonium salt **9**.[4] Using the Schlosser modification[5] of the Wittig reaction a 50% yield of the bisketal **11**[6-8] was obtained. Hydrolysis to the corresponding dione,[6-8] followed by base-catalyzed cyclodehydration, produced the cyclopentenone **12**,[6-8] in 82% yield (94:6 trans:cis isomers by LC). Treatment of **12** with excess methyllithium gave the unstable cyclopentenol **7.** According



to a procedure developed in these laboratories by F. W. Hobbs, a solution of the crude alcohol **7** (derived from 25 mg of enone **12**) in 7 mL of methylene chloride was added dropwise to a solution of 55 μL of trifluoroacetic acid in 15 mL of methylene chloride maintained at −25 °C. The resulting trifluoroacetates were hydrolyzed with sodium hydroxide in THF and filtered through Florisil to give, in ~80% yield, a mixture of benzylic alcohols **8.** The crude product was then dissolved in hexane and treated with excess activated manganese dioxide[9] to generate the corresponding phenyl ketones.[10] The mixture was analyzed by VPC without further purification and each of the base-line separated peaks identified by coinjection with authentic samples of the tetracyclic ketones **3, 4, 5,** and **6.** In this manner it was possible to show that the 13α (C/D cis) isomers **5** and **6** accounted for <2% of the total ketonic product. Thus, in contrast to the phenylacetylenic terminator, acid-catalyzed cyclization of the substrate **7** containing the styryl terminator appears to be highly stereoselective.[11]

Mechanistic Considerations. The formation of a significant amount of a 13α (C/D cis) isomer has been observed previously in the acid-catalyzed cyclization of **13.** In that case it was demonstrated that the 13α (C/D cis) isomer arose almost exclusively from the acid-catalyzed cyclization of an intermediary tricyclic hydrocarbon **14,** whereas no such partially cyclized intermediate was involved in the formation of the 13β

Scheme I[a]



[a] a, 1:3 5% HCl–acetone, 23 °C, 24 h; 5:6:2 5% NaOH–MeOH–THF, 70 °C, 3 h.

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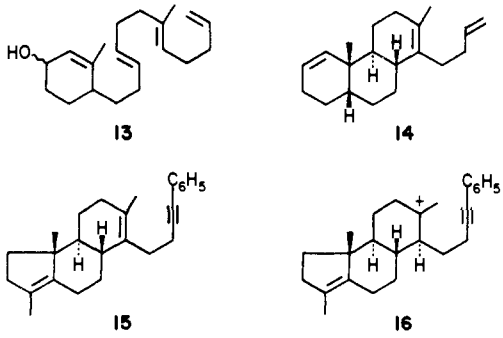

(C/D trans) isomers.[12] To test whether an intermediary tricyclic hydrocarbon, namely **15**, was similarly involved in the formation of the 13α (C/D cis) isomers produced in the cyclization of the substrate **1**, the substance **2**, with a deuterium label at *pro* C-14, was prepared.[13] The tetracyclic products **3** and **5** from the cyclization of the substrate **2** were separated and analyzed by mass spectrometry which showed that both isomers had retained >97% of their deuterium label. This result precludes the possibility of the intermediacy of **15** in the formation of the 13α (C/D cis) isomer.

In attempting to rationalize the fact that the phenylacetylenic terminator favors formation of 13α (C/D cis) isomers relative to the styryl terminator, we have entertained the possibility that the lower steric requirement of the former facilitates axial approach to the tricyclic cation **16**. A difference in the angle of attack on the sp^1 vs. the sp^2 carbon by the cationic center may also be a factor.[14]

Conclusions. In polyene cyclization of the type under consideration here, we feel that high stereoselectivity to form 13β (C/D trans) products having natural configuration will be realized with olefinic terminators, provided that these bonds are sufficiently nucleophilic to react with the incipient cationic center of the tricyclic species (cf. formula **16**) faster than deprotonation occurs to form a tricyclic olefin (which, as shown above in the case of **14**, leads to 13α isomers by a reprotonation mechanism).[15] In addition to the styryl group, a number of other olefinic terminators appear to give highly stereoselective cyclizations and we plan to report on these subsequently.

Acknowledgement. We thank the National Institutes of Health and the National Science Foundation for support of this research.

References and Notes

(1) For recent papers in this series, see (a) W. S. Johnson, L. R. Hughes, J. A. Kloek, T. Niem, and A. Shenvi, *J. Am. Chem. Soc.*, preceding paper in this issue; (b) W. S. Johnson, R. S. Brinkmeyer, V. M. Kapoor, and T. M. Yarnell, *ibid.*, **99**, 8341 (1977).
(2) In work to be described later, substrates **1** with a *p*-methoxyl and with a *p*-fluoro substituent in the phenyl group have been synthesized. These on cyclization gave tetracyclic products with isomer distributions almost identical with those found for the unsubstituted case.
(3) (a) W. S. Johnson and L. A. Bunes, *J. Am. Chem. Soc.*, **98**, 5597 (1976); (b) W. S. Johnson, *Bioorg. Chem.*, **5**, 72 (1976).
(4) W. S. Johnson, M. B. Gravestock, and B. E. McCarry, *J. Am. Chem. Soc.*, **93**, 4332 (1971).
(5) Modification of a previously reported procedure (W. S. Johnson and G. E. DuBois, *J. Am. Chem. Soc.*, **98**, 1038 (1976), note 12) was employed. Thus, after the addition of the anhydrous ether, the solution was warmed slowly to 0 °C and stirred at this temperature for 3 h. Finally the mixture was quenched with excess methanol prior to isolation of the product.
(6) This substance was purified by column chromatography on Florisil.
(7) This substance was evaporatively distilled using a Büchi Kugelrohrofen at a temperature ranging from 200 to 210 °C at pressures in the range 0.02–0.1 mmHg.
(8) The NMR and IR spectra were consistent with the assigned structure; a satisfactory combustion analysis was obtained for this specimen.
(9) Cf. A. J. Fatiadi, *Synthesis*, 65 (1976).
(10) To ensure that the ratio of 13β (C/D trans) to 13α (C/D cis) isomers shown by analyzing the ketonic mixture was an accurate representation of the proportions in the initial cyclized product, the following control experiments were performed. Each of the pure phenyl ketones **3**, **4**, **5**, and **6** was reduced with lithium aluminum hydride to give the corresponding alcohols. These alcohols were then individually oxidized with activated manganese dioxide[9] in hexane to regenerate the starting ketones in virtually quantitative yield.
(11) Indeed the process may be 100% stereoselective as the small amount of 13α product may have arisen from an isomeric contaminant in the cyclization substrate **7** having the *Z* configuration of the trisubstituted olefinic bond.
(12) K. E. Harding, E. J. Leopold, A. M. Hudrlik, and W. S. Johnson, *J. Am. Chem. Soc.*, **96**, 2540 (1974).
(13) The allylic alcohol $CH_2{=}C(CH_3)CH(OH)(CH_2)_2C{\equiv}CC_6H_5$, which is an intermediate in the preparation of **10** (see ref 1a), was oxidized with Jones reagent and the resulting α,β-unsaturated ketone was then reduced with lithium aluminum deuteride. The product was converted (via the ortho-acetate Claisen reaction) into deuterio-**10** which was then employed in a sequence analogous to that shown in Scheme I.
(14) J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 734 (1976).
(15) Examples of inadequately nucleophilic sp^2 terminators that lead to cis-fused products are the terminal vinyl group (as in **13**) and probably the chlorovinyl group. The latter was involved in a cyclization (to form one new ring) which yielded trans- to cis-fused products in a ratio of 3:2 as shown by P. T. Lansbury, T. R. Demmin, G. E. DuBois, and V. R. Haddon, *J. Am. Chem. Soc.*, **97**, 394 (1975).

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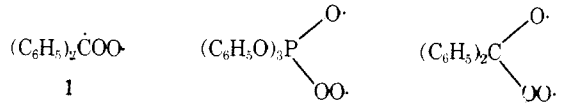
Epoxidation of Olefins with Carbonyl Oxides

Sir:

We report that carbonyl oxides, e.g., **1**, produced via singlet oxygen oxidation of diazo compounds, can epoxidize olefins. The oxidation of the diazo compound can be carried out by both photosensitized and triphenyl phosphite ozonide methods.



1 2 3

This method of producing carbonyl oxides and studying their reactions with olefins avoids many of the complicating factors of olefin ozonolysis, including the strong competition of aldehydes for carbonyl oxides. These results confirm the earlier suggestion of Kwart and Hoffman[1] that carbonyl oxides obtained under nonozonolysis conditions will act as epoxidizing agents.

Hamilton has suggested[2] that certain reactions catalyzed by the monooxygenase enzymes (MOX) occur via an oxygen atom transfer mechanism which he termed an oxenoid mechanism. Hamilton and co-workers subsequently showed[3] that carbonyl oxides, produced by oxidizing 9-diazofluorene and diphenyldiazomethane, serve as models for MOX in that they are capable of oxidizing hydrocarbons to alcohols and carbonyl compounds. In addition, there have now been several reports[1,4-11] of olefin epoxidation with carbonyl oxides. In all of these cases, the carbonyl oxides were produced under ozonolysis conditions. Wasserman and Miller[12] have invoked epoxidation via a carbonyl oxide in order to explain an epoxide product in the photosensitized oxygenation of a pyrrole. Use of the nonozonolysis source of carbonyl oxides has permitted us to show that such epoxidations are a general reaction. This observation and our earlier report[13] that carbonyl oxides, similarly produced, can oxidize an aromatic hydrocarbon add further support to the suggestion of Hamilton[3-5] that these intermediates serve as useful chemical models for the MOX.

The suggestion that photooxidation of diazo compounds could produce carbonyl oxides was first made by Kirmse et al.[14] The possibility was subsequently confirmed by Bartlett and Traylor[15] and Hamilton and Giacin.[3] We earlier had shown[16,17] that carbonyl oxides so produced can be trapped

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