Lewis Acid Promoted Decomposition of Unsaturated α-Diazo Ketones. 3. Stereochemical Consequences of Polyolefinic Cyclizations Initiated by the α-Diazo Ketone Functionality

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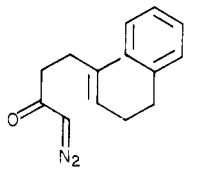
Abstract: This report presents the stereochemical consequences of polyolefinic cyclizations initiated by Lewis acid decomposition of α-diazo ketones. Three diazo ketones (**1**, **2**, and **5**) were examined; each was found to undergo a nonstereospecific process leading either to tri- or bicyclic products which exclusively possessed a cis-fused ring juncture. To verify the stereochemical outcome in the case of **1** and **2**, cyclopropyl ketones **3a** and **4a** were subjected to the Stork–Grieco stereospecific cyclization protocol. Formation of cis-fused products is accounted for by a stepwise (i.e., nonconcerted) process involving initial complexation of the Lewis acid on the oxygen of the diazo ketone functionality.

Introduction

In the preceding papers[2,3] we demonstrated that the α-diazo ketone functionality can function effectively as an initiator of both mono- and polyene cyclization when subjected to Lewis acid promoted decomposition. The terminal nature of the participating olefins, however, precluded any information concerning the role of olefinic geometry in determining the stereochemical outcome of the cyclization process. Of particular interest was whether diazo ketones possessing a trans olefin would undergo stereospecific cyclization to trans-fused products according to the Stork–Eschenmoser hypothesis.[4,5]

In this, the third full account of our work in this area, we document the stereochemical consequences of polyene cyclizations initiated by Lewis acid decomposition of α-diazo ketones. To explore this question, we initially selected two diazo ketones (**1** and **2**) and submitted them to our cyclization protocol; in both



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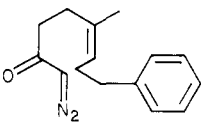

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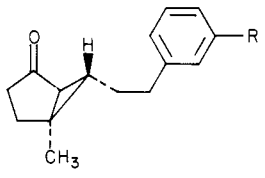
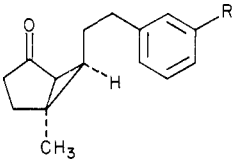


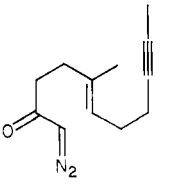
3a, R = H
b, R = OCH_3



4a, R = H
b, R = OCH_3

cases the resultant tricyclic products were shown to possess exclusively the cis-fused ring juncture. To verify this stereochemical outcome, we subjected cyclopropyl ketones **3a** and **4a** to the highly stereospecific Stork–Grieco[6] cyclopropane cyclization process.

Finally, in an attempt to improve the stereospecificity of the cyclization process initiated by the α-diazo ketone functionality we examined the decomposition of diazo ketone **5**, which possesses



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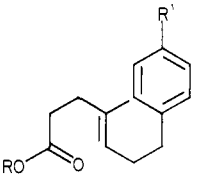
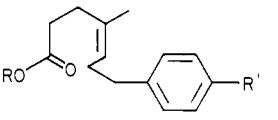
the highly effective acetylene terminator group introduced by Johnson.[7] Again, cis-fused ring products predominated. Product formation in each case is accounted for by a stepwise process involving initial complexation of BF_3 on the oxygen of the diazo ketone functionality.

Preparative Experiments

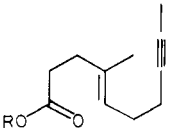
The required diazo ketones (**1**, **2**, and **5**) were prepared in nearly quantitative yields from the corresponding unsaturated acids (**6a** and **8a**) via the standard sequential treatment with oxalyl chloride



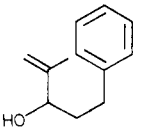
6a, R = R′ = H
b, R = OEt; R′ = H
c, R = H; R′ = OMe



7a, R = R′ = H
b, R = OMe; R′ = H
c, R = H; R′ = OMe



8a, R = H
b, R = Et



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(1) Camille and Henry Dreyfus Teacher Scholar, 1978–1983; National Institutes of Health (National Cancer Institute) Career Development Awardee, 1980–1985.
(2) Part 1: A. B. Smith, III, B. H. Toder, S. J. Branca, and R. K. Dieter, *J. Am. Chem. Soc.*, preceding paper in this issue.
(3) Part 2: A. B. Smith, III, and R. K. Dieter, *J. Am. Chem. Soc.*, preceding paper in this issue.
(4) G. Stork and A. W. Burgstahler, *J. Am. Chem. Soc.*, **77**, 5068 (1955).
(5) A. Eschenmoser, L. Ruzicka, O. Jeger, and D. Arigoni, *Helv. Chim. Acta*, **38**, 1890 (1955).
(6) G. Stork and M. Gregson, *J. Am. Chem. Soc.*, **91**, 2373 (1969); G. Stork, M. Gregson, and P. A. Grieco, *Tetrahedron Lett.*, 1391 (1969); G. Stork, P. A. Grieco, and M. Gregson, *ibid.*, 1393 (1969).
(7) For a review see W. S. Johnson, *Bioorg. Chem.*, **5**, 51 (1976).

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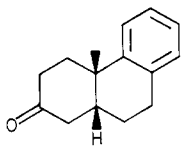
and excess diazomethane. The acids in turn were obtained by alkaline hydrolysis of the respective esters **6b–8b**. Ester **8b** is known,[8] while ester **6b** was prepared by the ortho-Claisen rearrangement strategy developed by Johnson.[8] To this end, reaction of the Grignard reagent prepared from β-phenethyl bromide with methacrolein afforded allylic alcohol **9**, which when treated with propionic acid in excess triethyl ortho acetate at 140 °C for 1 h gave **6b**, both in high yield and of high configurational purity.

The corresponding cis olefinic acid (**7a**), on the other hand, was prepared in analogy to that of Stork and co-workers[6] for the synthesis of the methoxy derivative **7c**. In our case, the product mixture was found by NMR[9] to contain a moderate amount (ca. 25%) of the trans olefinic acid **6a** in addition to the expected cis isomer **7a**. Esterification of the mixture with diazomethane followed by preparative vapor-phase chromatography (VPC) provided the cis olefinic ester **7b**, which upon subsequent alkaline hydrolysis afforded the pure cis acid **7a**. Finally, cyclopropyl ketones **3a** and **4a**, respectively, were prepared from diazo ketones **1** and **2** via treatment with a suspension of copper powder and copper sulfate in cyclohexane.[10]

Results

Having previously ascertained that 1.1 equiv of $BF_3 \cdot Et_2O$ in freshly distilled nitromethane at 0–5 °C constituted the optimal conditions to effect polyolefinic cyclizations initiated by the α-diazo ketone functionality, we submitted diazo ketone **1** to this protocol. Kugelrohr distillation after a conventional workup afforded a 70% yield of volatile material, which after purification by thin-layer chromatography (TLC) on silica gel gave two major components: **10** and **11** in 44% and 18% yields, respectively.



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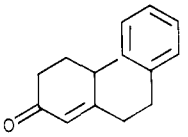

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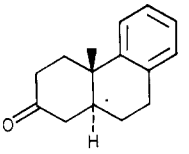

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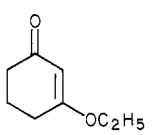
Indicative of polyene cyclization, the major component displayed a carbonyl group absorption at 1720 cm^{-1} in the IR and a quaternary methyl singlet at δ 1.35 as well as a multiplet at δ 6.92–7.42 for four aromatic protons in the 60-MHz NMR. Significant here was the fact that the chemical shift of the methyl singlet was inconsistent with that reported by Wenkert[11] for *trans*-phenanthrenone **12**. Structure **10**, tentatively assigned on this basis, was latter confirmed by alternate synthesis (vide infra).

The minor component, on the other hand, was readily identified to be 4-methyl-3-phenethyl-2-cyclohexenone (**11**). In particular, the 220-MHz NMR spectrum exhibited a doublet at δ 1.18 (3 H) for a secondary methyl group, a singlet at δ 5.73 (1 H) for an olefinic proton, and a multiplet at δ 6.97–7.41 (5 H) for the aromatic ring protons. The absence of a vinyl methyl absorption and the presence of five aromatic protons suggested that only partial cyclization had taken place. Consistent with a product arising from partial cyclization was the strong carbonyl absorption at 1670 cm^{-1} and a moderate C=C stretching vibration at 1630 cm^{-1} indicative of an α,β-unsaturated ketone.[12]

Structure **11** was confirmed by an alternate synthesis. To this end, alkylation of 3-ethoxy-2-cyclohexen-1-one (**13**)[13] with methyl iodide and subsequent reaction with the Grignard reagent derived from phenethyl bromide (i.e., **14**) afforded upon acidic workup a compound which was identical in all respects (i.e., IR, high-field NMR, TLC, and VPC) with **11**.



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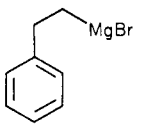

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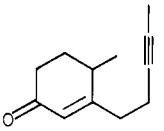
Turning next to the Lewis acid promoted decomposition of the cis isomer (i.e., **2**), *cis*-phenanthrenone **10** and cyclohexenone **11** were again formed; in this case the yields were 38% and 15%, respectively. The structure, including the stereochemistry, of **10** was confirmed by direct comparison with authentic samples of tricyclic ketones **10** and **12**, prepared respectively by acid-catalyzed cyclization of cyclopropyl ketones **4a** and **3a**.[6] In particular, reaction of cyclopropyl ketone **4a** with stannic chloride in benzene containing a trace of water afforded phenanthrene **10** (42%) as well as cyclohexenone **11** (43%), while cyclopropyl ketone **3a** under these conditions afforded *trans*-phenanthrenone **12** and cyclohexenone **11** in 15% and 85% yields, respectively. The structure of the latter (i.e., **12**) was confirmed by comparison of the melting point and IR and NMR spectra with those originally obtained by Wenkert.[11,14]

Exclusive formation of trans tricyclic ketone **12** from **3a** and cis ketone **10** from **4a** is in full accord with the results of Stork and Gregson[6] for cyclization of cyclopropyl ketones **3b** and **4b**, respectively. However, the major product from both **3a** and **4a** proved to be cyclohexenone **11**. This result is in sharp contrast to that of Stork's wherein only tricyclic products were reported.

To explore further the stereospecificity of the cyclization process initiated by the α-diazo ketone functionality as well as the ability of an acetylene to terminate the cyclization process, we investigated decomposition of diazo ketone **5**. Initially this diazo ketone led, under a variety of conditions, predominantly to cyclohexenone **15**; the latter was identified both on the basis of its spectroscopic



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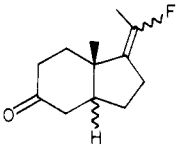


16a,b

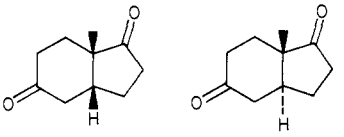
properties and by analogy with the formation of cyclohexenone **11** as observed in the case of diazo ketones **1** and **2**. However, after considerable experimentation, it was discovered that decomposition of **5** in freshly distilled dichloromethane (ca. 1 mg of diazo ketone/mL of solvent) with greater than 5 equiv of boron trifluoride etherate constituted the optimal conditions to effect polyolefinic cyclization. Careful analysis of the resultant product mixture by combined gas chromatography–mass spectrometry[15] revealed no less than 11 compounds, many of which contained either a chlorine or fluorine substituent. However, two major components were observed to be present.

That these components (**16a** and **16b**, 13% and 22%, respectively) were isomeric and possessed a fluorine substituent was revealed by the presence in each case of a parent molecular ion at *m/e* 196 (M^+) in the low-resolution mass spectrum. The 220-MHz ^1H NMR spectra of both isomers exhibited singlets at δ 1.32 (3 H) for tertiary methyl substituents. In addition, doublets at δ 1.85 (J = 18 Hz) and δ 1.93 (J = 19 Hz), respectively, for the major and minor isomer indicated the presence of a vinyl methyl group. The large coupling constants [i.e., 18 and 19 Hz, respectively] were indicative of vicinal hydrogen–fluorine coupling at an sp^2 hybridized center, and thereby suggested the part

(8) W. S. Johnson, M. B. Gravestock, and B. E. McCarry, *J. Am. Chem. Soc.*, **93**, 4332 (1971).
(9) R. B. Bates and D. M. Gale, *J. Am. Chem. Soc.*, **82**, 5749 (1960).
(10) G. Stork and J. Ficini, *J. Am. Chem. Soc.*, **83**, 4678 (1961).
(11) E. Wenkert, A. Afonso, P. Beak, R. W. J. Carney, P. W. Jeffs, and J. D. McChesney, *J. Org. Chem.*, **30**, 713 (1965).
(12) R. T. Conley, "Infrared Spectroscopy", 2nd ed., Allyn and Bacon, Boston, 1972, pp 101–121; J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds", Prentice-Hall, Englewood Cliffs, NJ, 1965, pp 49–52.
(13) W. F. Gannon and H. O. House, "Organic Syntheses", Collect. Vol. V, Wiley, New York, 1973, p 539.
(14) We are grateful to Professor Ernest Wenkert for providing the IR and NMR spectra of authentic **12**.
(15) We are grateful to Drs. N. F. Golob and G. Preti for use of the Hitachi-Perkin Elmer RMU-61 low-resolution mass spectrometer at the Monell Chemical Senses Center.

structure C=C(CH_3)F.[16] Finally, the presence of a carbonyl group in a six-membered ring was indicated by the observation of a strong IR absorption at 1715 cm^{-1}.

To establish rigorously the stereochemistry of the ring fusion in **16a** and **16b**, the major structural point in question, both isomers were individually subjected to RuO_4 oxidation (i.e., ruthenium dioxide–sodium periodate in aqueous acetone).[17] Under these conditions a single diketone, identified in both cases as *cis*-7a-methylhexahydro-1*H*-indene-1,5-dione (**17**) by comparison of the IR and NMR (220 MHz) spectra as well as VPC retention time with those of an authentic sample,[18] was obtained.



17 18

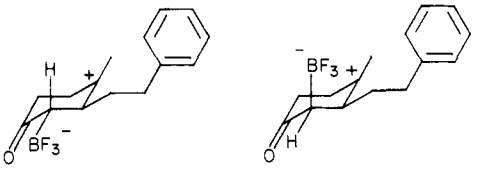
Collectively, the above data demonstrate that the two major components derived from cyclization of diazo ketone **5** each possess a cis ring fusion and are isomeric about the double bond (i.e., **16a,b**). That the major isomer has the fluorine substituent anti to the tertiary methyl group is suggested by recent observations of Johnson.[19] It should be noted, however, that the configuration of the olefin in either case has not been established rigorously.

Finally, to provide stereochemical information on the remainder of the cyclization material, we subjected the entire reaction mixture, without purification, to RuO_4 oxidation. This oxidation resulted in a 5.6:1 mixture of cis and trans diketones **17** and **18**. Bicyclic ketone **18** was identified by comparison of the IR and NMR (220 MHz) spectra as well as VPC retention time with those of an authentic sample.[18]

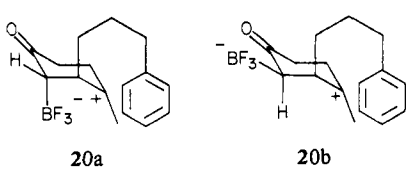
Discussion

The goal in this investigation was to establish the role of olefin geometry in determining the stereochemical outcome of polyene cyclizations initiated by the α-diazo ketone functionality. As presented above the cyclization of diazo ketones **1** and **2** was found to be a nonstereospecific process and therefore cannot proceed via a concerted pathway. That is, since *cis*-phenanthrenone **10** is formed from both diazo ketones **1** and **2** with equal facility, the reaction must proceed via a stepwise process. Indeed, the observation that **1** and **2** lead to identical products in comparable yields is suggestive of a common intermediate.

The nature of this intermediate, however, is unclear. For example, as noted in the accompanying papers, complexation of BF_3 could occur either at the oxygen or the carbon atom of the diazo ketone functionality. Let us first consider complexation on carbon. In this case, trans diazo ketone **1** should initially yield carbonium ions **19a** and **19b**, whereas the cis diazo ketone (**2**)



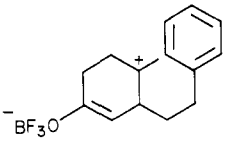
19a 19b



20a 20b

should lead to carbonium ions **20a** and **20b**. On the basis of conformational arguments employed by Harding,[20] it is expected that **19a** and **19b** will cyclize stereospecifically to *trans*-phenanthrenone **12**. Carbonium ions **20a** and **20b** on the other hand, contain an axial side chain and would therefore be expected to undergo stereospecific cyclization to *cis*-phenanthrenone **10**, assuming, of course, that the cyclization process is faster than equilibration to the more stable equatorial carbonium ions **19a** and **19b**, respectively. Carbonium ions **19a** and **19b** could be the anticipated common intermediates. However, they would be expected to show a high degree of selectivity for equatorial bond formation leading to *trans*-phenanthrenone **12**. The view that carbonium ions **19a** and **19b** will stereospecifically afford a trans-fused tricyclic ketone while **20a** and **20b** will stereospecifically afford a cis-fused tricyclic ketone finds analogy in the work of Goldsmith and Phillips.[21] *Collectively, these considerations suggest that if the cyclization of diazo ketones **1** and **2** were to proceed through carbon-complexed intermediates, the reaction should be highly stereospecific or at least yield substantial amounts of trans-fused products.*[22] Our experimental results, however, clearly indicate that only the *cis*-phenanthrenone (**10**) was obtained from the cyclization of diazo ketones **1** and **2**.

The other possibility is that complexation occurs at the oxygen atom of the diazo ketone functionality. Such complexation of diazo ketones **1** and **2** would afford carbonium ion **21**,[23] also a viable



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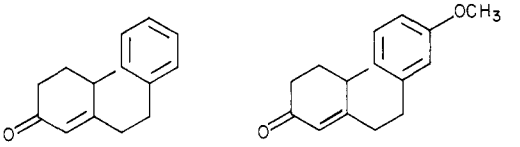
candidate for the proposed common intermediate. Furthermore, its nearly planar geometry would be expected to favor formation of *cis*-phenanthrenone **10**.

As described above, authentic samples of *cis*-phenanthrenone **10** and *trans*-phenanthrenone **12** were prepared by the stereospecific cyclization of cyclopropyl ketones **4a** annd **3a**, respectively. Several aspects of these transformations are noteworthy.

First, the yield of tricyclic ketones from **3a** and **4a** (15% and 42%, respectively) is considerably lower than the yields reported by Stork for the corresponding methoxy derivatives (ca. ~80%).[6] In addition, the major product isolated from both **3a** and **4a** was cyclohexenone **11**. The corresponding cyclohexenone (**22**) was



11 22

not isolated by Stork and Gregson in the cyclization of **3b** and **4b**. Collectively, these results demonstrate that the yields of tricyclic ketones are markedly dependent upon the nucleophilicity of the participating aromatic ring. This observation, coupled with the stereospecificity of the cyclization in our case, is further strong support for a concerted reaction pathway[6] in the cyclization of unsaturated cyclopropyl ketones.

Second, in our case formation of cyclohexenone **11** undoubtedly involves an intermediate carbonium ion such as **23**. This car-

(16) M. Y. DeWolf and J. D. Baldeschwieler, *J. Mol. Spectrosc.*, **13**, 344 (1965).

(17) R. Pappo, D. S. Allen, Jr., R. U. Lemieux, and W. S. Johnson, *J. Org. Chem.*, **21**, 478 (1956).

(18) We are grateful to Dr. Keith H. Baggaley for providing us with authentic samples of diones **17** and **18**.

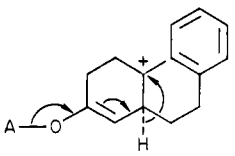
(19) See footnote 4 on p 76 of ref 7.

(20) K. E. Harding, *Bioorg. Chem.*, **2**, 248 (1973).

(21) D. J. Goldsmith and C. F. Phillips, *J. Am. Chem. Soc.*, **91**, 5862 (1969).

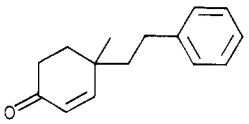
(22) Although the initial site of BF_3 complexation is unknown, this analysis suggests that the intermediate leading directly to tricyclic ketone **10** is not a carbon-complexed intermediate. Due to the possibility of equilibrium processes, initial complexation of BF_3 with the α-carbon atom of the diazo ketone cannot be ruled out.

(23) The conformation of carbonium ion **21** arising from diazo ketone **1** is slightly different than that of the carbonium ion arising from dizo ketone **2**. This small difference in conformation is, however, negligible at the temperatures employed to effect cyclization.



23

bonium ion could give rise to cyclohexenone **11** by proton loss and subsequent migration of the β,γ olefinic bond into conjugation with the carbonyl. However, the complete absence of the β,γ-unsaturated isomer (<1%) precludes this reaction pathway. That is, it is well-known that equilibration of 3,4-dialkyl-2- and 3-cyclohexenones results in a mixture of both the α,β and β,γ isomers. Alternatively, **11** could arise directly from **23** via a 1,2 hydride shift as illustrated in structure **23**. Significant in this regard is the fact that Stork and co-workers have observed similar hydride migrations in connection with the decomposition of closely related cyclopropyl ketones.[24] In addition, we observed in the decomposition of **4a** what was tentatively assigned to be cyclohexenone **24**, the latter arising via a 1,2 alkyl shift of the phenethyl group. This product, however, due to the small amount of available material (<1%), was not fully characterized.



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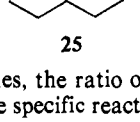
The above considerations explain, we believe, a preplexing problem. In particular, carbonium ion **23** is strikingly similar to carbonium ion **21** which we propose to be the intermediate in the formation of **10**. It is therefore surprising that **10** was not observed in the decomposition of cyclopropyl ketone **3a** which afforded cyclohexenone **11** in 85% yield. It is conceivable, however, that under the conditions employed to effect cyclization of cyclopropyl ketone **3a** (i.e., $SnCl_4$, H_2O, benzene), carbonium ion **23** undergoes a hydride shift faster than cyclization.

Finally, the results obtained from cyclization of cyclopropyl ketones **3a** and **4a** are *vastly different* than those obtained from cyclization of diazo ketones **1** and **2**. This observation is significant in that *it effectively eliminates from consideration an acid-catalyzed cyclopropanation mechanism for cyclizations initiated by the α-diazo ketone functionality.*[25]

To examine further the stereochemical consequences of polyolefinic cyclization initiated by the α-diazo ketone functionality, we explored the cyclization of diazo ketone **5**. The results obtained, however, were somewhat ambiguous. In particular, cyclization of **5** afforded a 5.6:1 ratio of cis- to trans-fused products. It is interesting to note in this regard that Lansbury[26] has shown that acid-catalyzed cyclization of **25** affords a mixture of cis- and



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trans-fused hydrindanones, the ratio of cis to trans being 0.4:1 to 1.4:1, depending on the specific reaction conditions. However, when the cyclohexanone ring was part of a trans-fused decalin system, the ratio of cis- to trans-fused products was roughly 4:1. Johnson,[8] on the other hand, has found that acetylene participation in biomimetic cyclizations led exclusively to trans-fused products. Whether the small amount of trans-fused product arising from diazo ketone **5** in our case is formed in a concerted cyclization or a stepwise process is currently unknown. The cylindrical-linear nature of the acetylene π cloud may be sterically less demanding than the phenyl substituent and thereby be more conducive to a concerted process. That is, although no trans-fused products were observed in the cyclization of diazo ketones **1** and **2**, it is conceivable that the formation of trans-fused products from diazo ketone **5** occurs in a concerted manner.

(24) G. Stork and P. A. Grieco, *Tetrahedron Lett.*, 1807 (1971); G. Stork and M. Marx, *J. Am. Chem. Soc.*, **91**, 2371 (1969).

(25) Further evidence for the fact that the Lewis acid initiated cyclizations of α-diazo ketones do not involve the intermediacy and cleavage of a cyclopropane derives from the fact that cyclopropanes **3** and **4** were stable to anhydrous $SnCl_4$. Only addition of a small amount of water (i.e., generation of HCl) initiated the cyclization process. For related evidence see: G. L. Closs, R. A. Moss, and S. H. Goh, *J. Am. Chem. Soc.*, **88**, 364 (1966); G. L. Closs and S. H. Goh, *J. Org. Chem.*, **39**, 1717 (1974). W. F. Erman and L. C. Stone, *J. Am. Chem. Soc.*, **93**, 2821 (1971); W. F. Erman and L. C. Stone, *J. Agric. Food Chem.*, **19**, 1093 (1971).

(26) P. T. Lansbury, T. R. Demmin, G. E. DuBois, and V. R. Haddon, *J. Am. Chem. Soc.*, **97**, 394 (1975).

Summary

In conclusion, this investigation demonstrates that polyolefinic cyclizations initiated by the α-diazo ketone functionality proceed in a nonstereospecific fashion. This result is believed to be a reflection of the stepwise nature of the cyclization process and, possibly, the site of Lewis acid complexation with the diazo ketone group. In the latter regard, the interesting possibility exists that by the appropriate choice of acid catalyst and/or solvent system, one might alter the site of complexation. That is, if conditions were found that favored complexation at the α-diazo carbon atom rather than at the carbonyl oxygen, cyclization might well occur with a high degree of stereoselectivity. Such a result is, of course, speculation and will have to await further experimentation.

Experimental Section

Materials and Equipment. Solvents used for the cyclization studies were Mallinckrodt nitromethane and Mallincrodt analytical reagent grade dichloromethane. Nitromethane was distilled at atmospheric pressure and dichloromethane was distilled from phosphorus pentoxide prior to use. Tetrahydrofuran was distilled from sodium and benzophenone. Diazomethane was prepared as an ethereal solution from *N,N'*-dimethyl-*N,N'*-dinitrosoterephthalamide (Aldrich, 70% in mineral oil). β-Phenethyl bromide was obtained from Aldrich. All vapor-phase chromatography (VPC) was done by using a Varian Aerograph Model 920 with one of the following columns: A, 25% Carbowax 20M, 10 ft × $^3/_8$ in.; B, 6% Carbowax 20M, 20 ft × $^1/_4$ in.; C, 6% Carbowax, 20M, 50 ft × $^1/_4$ in.; D, 1.5% OV-101, 5 ft × $^1/_4$ in.; D, 12.5% OV-101, 10 ft × $^3/_8$ in. The oven was operated at 160–230 °C, and the helium carrier gas flow rate was 50–100 mL/min. Precoated alumina GF (Analtech) or silica GF (Analtech) plates were used for thin-layer chromatography (TLC). Plates with 1000–2000-μm thickness were used for preparative separations. Melting points were obtained by using a Thomas-Hoover or a Fisher-Johns apparatus and are corrected. Unless otherwise noted, both IR and NMR spectra were obtained for carbon tetrachloride solutions, the former on a Perkin-Elmer Model 337 spectrophotometer and the latter on a Varian Model A-60 (60 MHz) or HR-220 (220 MHz) spectrometer. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane (δ 0.00). Gas chromatographic (column F, 1% SF-96)–mass spectral analyses were obtained by using a Hitachi-Perkin Elmer RMU-6L low-resolution spectrometer with a Watson-Biemann fritted-glass separator. The yields of cyclization products were determined from VPC calibration curves and are based upon the starting acid.

3-Hydroxy-2-methyl-5-phenyl-1-pentene (9). To 1.44 g (60.0 mmol) of magnesium shavings in 100 mL of dry ether was added dropwise 11.0 g (59.5 mmol) of β-phenethyl bromide in 10.0 mL of dry ether. The exothermic reaction was controlled by means of an ice–water bath, and following completion of the addition the solution was stirred at room temperature until all the magnesium shavings had reacted (2.0 h). The solution was cooled to 0–5 °C, and 4.5 g (75.0 mmol) of methacrolein in 5 mL of dry ether was added dropwise. The resulting clear solution was warmed to room temperature, stirred for 10 h, and then poured into saturated aqueous ammonium chloride. The aqueous phase was extracted with ether and the combined organic phase was washed with saturated aqueous ammonium chloride, saturated aqueous sodium bicarbonate, water, and brine and dried. Removal of solvent in vacuo gave 10.15 g (97%) of crude material which was used without further purification.

Purification by TLC on silica (hexane–ether, 1:1 v/v) and final VPC purification on column D gave analytically pure **9**: IR 3620 (s), 3475 (br, m), 3085 (m), 3067 (m), 3028 (s), 2940 (s), 2860 (m), 1800 (w), 1740 (w), 1678 (w), 1650 (m), 1610 (m), 1500 (m), 1455 (s), 1380 (m), 1030 (m), 903 (vs), 695 (vs) cm^{-1}; NMR (60 MHz) δ 1.30 (s, 1 H), 1.72 (br s, 3 H), 1.57–2.03 (m, 2 H), 2.50–2.98 (m, 2 H), 4.00 (t, J = 7 Hz,

1 H), 4.82 (vbr s, 1 H), 4.93 (vbr s, 1 H), 7.15 (br s, 5 H).

Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.40; H, 9.09.

Ethyl 4-Methyl-7-phenyl-*trans*-hept-4-enoate (6b). To 10.15 g (57.5 mmol) of crude allylic alcohol **9** was added 58.32 g (360.0 mmol) of triethyl orthoacetate and 0.444 g (6.0 mmol) of propanoic acid. The mixture was heated to 140 °C for 1.5 h, and the generated ethanol was allowed to distill off. The solution was cooled to room temperature, poured into ether, washed with 10% aqueous hydrochloric acid (5 × 50 mL), saturated aqueous sodium bicarbonate, water, and brine, and dried. Removal of solvent in vacuo gave 12.7878 g (99%) of crude material which afforded 9.6801 (70% yield from β-phenethyl bromide) of material upon distillation [bp 105–120 °C (0.05 mmHg)].

VPC purification on column E gave analytically pure **6b**: IR 3083 (m), 3062 (m), 3025 (s), 2975 (vs), 2930 (vs), 2855 (s), 1728 (vs), 1605 (m), 1490 (m), 1450 (s), 1370 (s), 1340 (m), 1300 (s), 1258 (s), 1160 (vs), 1095 (m), 1030 (s), 930 (w), 853 (m), 693 (vs) cm^{-1}; NMR (60 MHz) δ 1.21 (t, J = 7 Hz, 3 H), 1.54 (br s, 3 H), 2.04–2.86 (m, 8 H), 4.05 (q, J = 7 Hz, 2 H), 5.21 (t, J = 6 Hz, 1 H), 7.11 (br s, 5 H).

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.02; H, 8.80.

Methyl 4-Methyl-7-phenyl-*cis*-hept-4-enoate (7b). 4-Methyl-7-phenyl-*cis*-hept-4-enoic acid prepared according to the procedure of Stork et al.[6] was added to a rapidly stirring ethereal solution of excess diazomethane. Concentration on a steam bath followed by Kugelrohr distillation afforded the desired methyl ester contaminated with a small amount of the trans isomer. VPC purification on column E gave pure **7b**: IR 3085 (m), 3065 (m), 3028 (s), 2950 (vs), 2860 (s), 1740 (vs), 1610 (m), 1495 (m), 1440 (vs), 1360 (m), 1260 (s), 1200 (s), 1170 (vs), 1090 (s), 1030 (m), 985 (m), 897 (m), 840 (m), 695 (vs) cm^{-1}; NMR (60 MHz) δ 1.66 (d, J = 1 Hz, 3 H), 2.03–2.85 (m, 8 H), 3.57 (s, 3 H), 5.18 (br t, J = 7 Hz, 1 H), 7.12 (br s, 5 H).

Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.74; H, 8.79.

5-Methyl-exo-6-phenethylbicyclo[3.1.0]hexan-2-one (3a). To 2.12 g (33.4 mmol) of copper powder and 1.10 g (6.90 mmol) of copper sulfate in 150 mL of refluxing cyclohexane was added dropwise 9.95 g (3.95 mmol) of diazo ketone **1** in 30 mL of cyclohexane over a period of 1 h. The solution was heated at reflux for an additional 2 h, cooled to room temperature, filtered, washed with water and brine, and dried. Removal of solvent in vacuo gave 0.8241 g (98%) of crude material which afforded 570.1 mg (68%) of volatile material upon Kugelrohr [bp 140–160 (0.6 mmHg)] distillation.

TLC purification on silica (R_f 0.35–0.53; hexane–ether, 1:1 v/v) followed by final VPC purification on column D gave analytically pure **3a**: IR 3085 (w), 3065 (w), 3028 (w), 2974 (m), 2930 (s), 2865 (m), 1722 (vs), 1500 (m), 1460 (m), 1425 (m), 1390 (m), 1300 (m), 1272 (m), 1250 (m), 1184 (s), 1160 (m), 1133 (m), 1105 (m), 1068 (m), 1028 (m), 892 (m), 692 (s) cm^{-1}; NMR (60 MHz) δ 1.13–1.38 (m, 2 H), 1.22 (s, 3 H), 1.50–2.20 (m, 6 H), 2.72 (t, J = 7 Hz, 2 H), 7.13 (br s, 5 H).

Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 83.93; H, 8.36.

5-Methyl-*endo*-6-phenethylbicyclo[3.1.0]hexan-2-one (4a). Similarly, 141.6 mg (0.585 mmol) of diazo ketone **2** was decomposed with 294.4 mg (4.65 mmol) of copper powder and 160.9 mg (1.0 mmol) of copper sulfate in 22 mL of cyclohexane to yield 122.1 mg (98%) of crude material.

TLC purification on silica (R_f 0.41–0.66; hexane–ether, 1:1 v/v) gave 65.5 mg (52%) of pure material. Final VPC purification on column D gave analytically pure **4a**: IR 3085 (m), 3065 (m), 3028 (m), 2945 (s), 2925 (s), 1720 (vs), 1605 (m), 1495 (m), 1418 (m), 1385 (m), 1290 (m), 1190 (m), 1162 (m), 1122 (m), 1087 (m), 1045 (m), 1032 (m), 942 (m), 932 (m), 905 (m), 891 (m), 696 (vs) cm^{-1}; NMR (60 MHz) δ 1.08–1.45 (m, 1 H), 1.23 (s, 3 H), 1.52–2.50 (m, 7 H), 2.72 (t, J = 7 Hz, 2 H), 7.20 (br s, 5 H).

Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.25; H, 8.55.

Preparation of Diazo ketones. The diazo ketones were prepared from the corresponding esters. Hydrolysis was effected by stirring a 95% ethanol solution of the ester with an equal volume of 5% aqueous sodium hydroxide (2.0 equiv) at room temperature for 24 h. The solution was poured into water and washed three times with ether. The aqueous phase was acidified with 10% aqueous hydrochloric acid and extracted with ether. The ether extracts were washed with water and brine and dried. Removal of solvent in vacuo afforded the desired acids. Reaction of the acids with 1.2 equiv of oxalyl chloride in benzene at room temperature gave the acid chlorides which afforded the desired diazo ketones upon treatment with an ethereal solution of excess diazomethane.

Decomposition of 1-Diazo-5-methyl-8-phenyl-*trans*-oct-5-en-2-one (1). To a solution of 0.7666 g (3.18 mmol) of diazo ketone **1** in 80 mL of freshly distilled nitromethane cooled to 0–5 °C under nitrogen was added 0.5 mL (0.578 g, 4.0 mmol) of boron trifluoride etherate. The solution immediately turned dark, and after a few seconds a vigorous evolution of nitrogen was observed. The solution was stirred at 0–5 °C for 30 min and then poured into saturated aqueous sodium bicarbonate solution and extracted with ethyl acetate. The extracts were washed four times with saturated aqueous sodium bicarbonate, water, and brine and dried. Removal of solvent in vacuo gave 0.7081 g (100%) of crude material which yielded 0.6863 g (70%) of volatile material upon Kugelrohr distillation [bp 150–200 °C (1.0 mmHg)]. Preliminary TLC purification on silica (hexane–ether, 1:1 v/v) gave two principal fractions.

Fraction I (R_f 0.23–0.41) gave, after final purification by TLC on silica (hexane–ether, 1:1 v/v), pure 4-methyl-3-phenethyl-2-cyclohexen-1-one (**11**): 18% yield; IR 3085 (m), 3065 (m), 3025 (m), 2963 (s), 2930 (s), 2860 (m), 1670 (vs), 1620 (m), 1490 (m), 1450 (s), 1415 (m), 1380 (m), 1345 (m), 1328 (m), 1255 (s), 963 (vs) cm^{-1}; NMR (220 MHz) δ 1.18 (d, J = 7 Hz, 3 H), 1.59–1.89 (m, 1 H), 1.89–2.64 (m, 6 H), 2.64–3.00 (m, 2 H), 5.73 (s, 1 H), 6.95–7.41 (m, 5 H), NMR (60 MHz) δ 1.17 (d, J = 7 Hz, 3 H), 1.40–3.05 (m, 9 H), 5.73 (br s, 1 H), 7.13 (br s, 5 H).

Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.00; H, 8.34.

Fraction II (R_f 0.41–0.54) gave, after final TLC purification on silica (hexane–ether, 1:1 v/v) pure *cis*-3,4,4a,9,10,10a-Hexahydro-4a-methyl-2(1*H*)-phenanthrenone (**10**):[27] 44% yield; IR 3065 (m), 3020 (m), 2970 (vs), 2870 (s), 1720 (vs), 1490 (m), 1450 (s), 1425 (m), 1380 (m), 1350 (m) 1279 (m), 1000 (m), 720 (m), 692 (m) cm^{-1}; NMR (220 MHz) δ 1.36 (s, 3 H), 1.55–1.93 (m, 2 H), 1.98–2.68 (m, 7 H), 2.73–3.05 (m, 2 H), 6.93–7.39 (m, 4 H); NMR (60 MHz) δ 1.35 (s, 3 H), 1.42–2.65 (m, 9 H), 2.66–3.07 (m, 2 H), 6.92–7.42 (m, 4 H).

Decomposition of 1-Diazo-5-methyl-8-phenyl-*cis*-oct-5-en-2-one (2). Decomposition of 161.1 mg (0.665 mmol) of diazo ketone **2** with 100 μL (115.4 mg, 0.81 mmol) of boron trifluoride etherate in 10 mL of nitromethane, as described above, gave 175.9 mg of crude material. Preliminary VPC purification on column D gave two fractions.

Fraction I gave a pure product (15%), identical with **11** by comparison of IR and NMR (220 MHz) spectra, R_f, and VPC retention time (column D).

Fraction II gave, after final TLC purification (hexane–ether, 1:1 v/v), a pure product (38%), identical with **10** by comparison of IR and NMR (220 MHz) spectra, R_f, and VPC retention time (column D).

Decomposition of 5-Methyl-*exo*-6-phenethylbicyclo[3.1.0]hexan-2-one (3a). To 0.570 g (2.66 mmol) of cyclopropyl ketone **3a** and 25 μL of water in 8 mL of benzene under nitrogen was added 250 μL (532 mg, 2.05 mmol) of stannic chloride, and the resulting dark colored solution was stirred at room temperature for 15 h. The mixture was poured into ether, washed with 10% aqueous hydrochloric acid, water, and brine, and dried. Removal of solvent in vacuo gave 600.9 mg (100%) of crude material which afforded 0.5260 g (93%) of volatile material upon Kugelrohr [bp 130–160 °C (0.5 mmHg)] distillation. Preliminary TLC purification on silica ($CHCl_3$) gave two principal fractions.

Fraction I (R_f 0.20–0.63) gave, after TLC purification on silica ($CHCl_3$) and final purification on column D, a product (85%) identical with **11** by comparison of IR and NMR (220 MHz) spectra, R_f, and VPC (column D) retention time.

Fraction II (R_f 0.63–0.66) gave, after recrystallization from petroleum ether, pure *trans*-3,4,4a,9,10,10a-Hexahydro-4a-methyl-2(1*H*)-phenanthrenone (**12**): 15% yield: mp 105–106 °C; IR 3100 (w), 3060 (m), 3015 (m), 2935 (vs), 2865 (s), 2838 (m), 1715 (vs), 1485 (m), 1450 (m), 1415 (m), 1375 (m), 1248 (m), 1182 (m), 1138 (m), 1045 (m), 937 (m), 718 (m), 680 (m) cm^{-1}; NMR (220 MHz) δ 1.30 (s, 3 H), 1.52–2.11 (m, 4 H), 2.14–2.64 (m, 5 H), 2.77–3.05 (m, 2 H), 6.89–7.11 (m, 3 H), 7.13–7.32 (m, 1 H); NMR (60 MHz, $CDCl_3$) δ 1.30 (s, 3 H), 1.43–3.20 (m, 11 H), 7.00–7.55 (m, 4 H) [lit.[11] mp 107–108 °C; NMR (60 MHz, $CDCl_3$) δ 1.29 for the methyl resonance].

Decomposition of 5-Methyl-*endo*-6-phenethylbicyclo[3.1.0]hexan-2-one (4a). Similar decomposition of 56.8 mg (0.265 mmol) of cyclopropyl ketone **4a** in 1.0 mL of benzene and 5 μL of water with 25 μL (55.6 mg, 0.214 mmol) of stannic chloride gave 59.4 mg (100%) of crude material. TLC purification on silica (hexane–ether, 1:1 v/v) gave two fractions. Fraction I (R_f 0.27–0.42) gave, after the final TLC purification on silica (hexane–ether, 1:1 v/v), a pure product (42%) identical with **11** by comparison of IR and NMR (220 MHz) spectra, R_f, and VPC (column D) retention time.

Fraction II (R_f 0.42–0.53) gave, after final VPC purification on column D, a product (43%) identical with **10** by comparison of IR and NMR (220 MHz) spectra, and R_f, and VPC retention time.

(27) E. Wenkert and J. W. Chamberlin, *J. Org. Chem.*, **25**, 2027 (1960), and references cited therein.

4-Methyl-3-phenethyl-2-cyclohexen-1-one (11). To 80.3 mg (3.34 mmol) of magnesium in 7.0 mL of dry ether was added dropwise 620.6 mg (3.28 mmol) of β-phenethyl bromide in 2.0 mL of dry ether. The reaction was initiated with a warm water bath and then stirred at room temperature until the magnesium shavings had reacted (1.5 h). The dark solution was cooled to 9-5 °C, and 499.7 mg (3.25 mmol) of 3-ethoxy-6-methyl-2-cyclohexen-1-one[13] was added dropwise in 5 mL of dry ether. The solution became clear and was stirred for 10 h at room temperature whereupon 5.0 mL of 10% aqueous hydrochloric acid and 5.0 mL of ether were added to the solution, and the mixture was stirred for 1 h at room temperature, poured into water, and extracted three times with 50 mL of ether. The ether extracts were washed with 10% aqueous hydrochloric acid, saturated aqueous sodium bicarbonate, water, and brine and dried. Removal of solvent in vacuo gave 581.0 mg (83%) of crude material. Kugelrohr distillation [bp 160-190 °C (1.0 mmHg)] afforded 499.1 mg (71%) of volatile material. Preliminary TLC purification on silica (hexane-ether, 1:1 v/v) gave, after final VPC purification on column D, a product identical with **11** by comparison of IR and NMR (220 and 60 MHz) spectra, R_f, and VPC retention time.

Decomposition of 1-Diazo-5-methyl-*trans*-5-decen-9-yn-2-one (5). To a solution of 488.1 mg (2.4 mmol) of diazo ketone **5** in 300 mL of dry dichloromethane cooled to 0-5 °C under nitrogen was added in one addition 3.07 mL (3.550 g, 25 mmol) of boron trifluoride etherate. The solution immediately turned dark, and after a few seconds a vigorous evolution of nitrogen was observed. The solution was allowed to slowly warm to 10 °C over a period of 30 min and poured into saturated aqueous sodium bicarbonate. The organic phase was washed with saturated aqueous sodium bicarbonate, water, and brine and dried. Removal of solvent in vacuo gave 474.9 mg of crude material. VPC (column B) and gas chromatographic (column F)-mass spectral analyses indicated a very complex reaction mixture. Two principal fractions (**16a,b**) were, however, isolated by VPC on column B.

Fraction I [**16a**: 13% yield; mass spectrum, *m/e* 196 (M^+), for a fluorine compound; IR 1715 (vs) cm^{-1}; NMR (220 MHz) δ 1.32 (s, 3 H), δ 1.85 (d, J = 18 Hz, 3H)] was oxidized in the following manner. To a solution of 17.2 mg (0.129 mmol) of ruthenium dioxide, 266.4 mg (1.25 mmol) of sodium periodate in 5 mL of water, and 11 mL of acetone was added 20.2 mg of fraction I. The bright yellow solution immediately turned dark and was stirred at room temperature for 4 h. Isopropyl alcohol (4 mL) was added, and the solution was stirred for 30 min at room temperature, filtered, poured into water, and extracted with ether. The ether extracts were washed with saturated aqueous sodium bicarbonate, water, and brine and dried. Removal of solvent in vacuo and VPC purification on column B gave a product identical with *cis*-7a-methyl-2,3,3a,6,7,7a-hexahydro-1*H*-indene-1,5-dione (**17**)[18] by comparison of IR and NMR (220 MHz) spectra and VPC retention time.

Fraction II [**16b**: 22% yield; mass spectrum, *m/e* 196 (M^+), for a fluorine compound; NMR (220 MHz) δ 1.32 (s, 3H), 1.93 (d, J = 19 Hz, 3H)] was oxidized as described above. To a solution of 16.5 mg (0.124 mmol) of ruthenium dioxide, 215.0 mg (1.0 mmol) of sodium periodate in 5 mL of water, and 11 mL of acetone was added 14.7 mg of fraction II. Again, VPC purification on column B gave a product identical with *cis*-7a-methyl-2,3,3a,6,7,7a-hexahydro-1*H*-indene-1,5-dione (**17**) by comparison of IR and NMR (220 MHz) spectra and VPC retention time.

Oxidation of 150.5 mg of the crude reaction mixture with 106.7 mg (0.78 mmol) of ruthenium dioxide and 1.5379 g (7.2 mmol) of sodium periodate in 20 mL of water and 45 mL of acetone, as described above, gave 110.3 mg of product. VPC purification on column B gave two fractions, A and B, in a ratio of 5.6:1, respectively. Fraction A was identical with *cis*-7a-methyl-2,3,3a,6,7,7a-hexahydro-1*H*-indene-1,5-dione (**17**) by comparison of IR and NMR (220 MHz) spectra and VPC retention time. Fraction B was identical with *trans*-7a-methyl-2,3,3a,6,7,7a-hexahydro-1*H*-indene-1,5-dione (**18**)[18] by comparison of IR and NMR (220 MHz) spectra and VPC retention time.

Decomposition of diazo ketone **5** in dichloromethane under the optimal conditions (1 mg/mL, >5.0 equiv boron trifluoride etherate, 5-10 °C) led to a 41% yield of bicyclic products. Under a variety of other conditions 4-methyl-3-(3′-pentynyl)-2-cyclohexen-1-one (**15**) was isolated as a moderate to major product: IR 2960 (m), 2930 (s), 2860 (m), 1675 (vs), 1622 (m), 1445 (m), 1250 (m), 1200 (m) cm^{-1}; NMR (220 MHz) δ 1.21 (d, J = 7 Hz, 3 H), 1.75 (s, 3 H), 1.67-1.85 (m, 1 H), 1.85-2.53 (m, 8H), 5.68 (s, 1 H).

Acknowledgment. It is a pleasure to acknowledge the support of this investigation by the National Institutes of Health through Grant No. GM-24680, by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and by Research Corp. In addition, we thank Mr. S. T. Bell of the Rockefeller University for the microanalysis and the Middle Atlantic Regional NMR Facility (NIH Grant No. RR542) at the University of Pennsylvania, where the 220-MHz NMR spectra were recorded.

Double-Bond Deformation in Two Crystalline Derivatives of *syn*-Sesquinorbornene ($\Delta^{4a,8a}$-Octahydro-1,4,5,8-dimethanonaphthalene)

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Abstract: The cycloaddition of maleic anhydride to isodicyclopentadiene (**1**) leads under a variety of conditions to similar amounts of the *anti*-sesquinorbornene *endo*-anhydride **2** and the *syn*-sesquinorbornene *exo*-anhydride **3**, the structures being established by X-ray crystallography. Whereas the double-bond system of **2** is planar, that of the *syn*-sesquinorbornene derivatives **3** and **6** has a dihedral angle of 162-164° between the planes of the two rings sharing the double bond, the bending being such as to spread the methylene bridges apart. Phenyl azide reacts with **3** but not with **2**. An X-ray study confirms the structure **7** of the adduct obtained by Paquette and co-workers from phenyl azide and *syn*-sesquinorbornene. The results of X-ray crystallographic studies of **2**, **3**, **6**, and **7** are presented.

Although *syn*-[2] and *anti*-sesquinorbornenes[3] have only recently been prepared and characterized, the ring system has been of interest ever since Alder and co-workers[4] in 1956 added maleic anhydride to "isodicyclopentadiene" (**1**) in ether and reported that the single product added phenyl azide to yield an *N*-phenyltriazoline. Of the four possibilities (**2-5**) the structure **2**, an *anti*-sesquinorbornene *endo*-anhydride, was assigned to the product of the Diels-Alder reaction. Reservations about this assignment[5] were strengthened by the observation of Sugimoto et al.[6] that methyl acrylate and methyl propiolate added to **1** on the endo side to give products with the *syn*-sesquinorbornene ring system.

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0002-7863/81/1503-2022$01.25/0