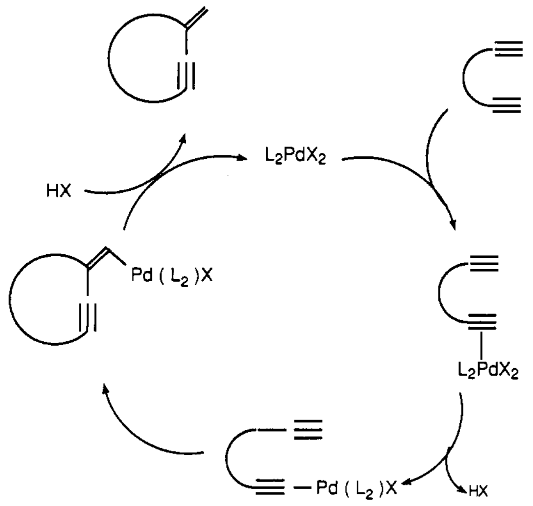
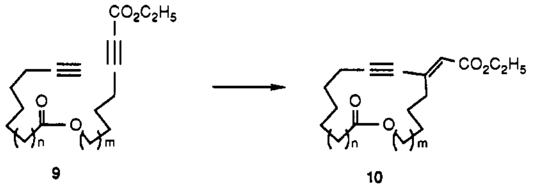
Scheme II. A Catalytic Cycle



To test the chemoselectivity in terms of the synthesis of macrolides, the simple esters **9a–d** were prepared and cyclized (eq 3). The sluggishness of the cyclization of diyne **9a** under the above conditions led to an in-depth ligand study in which **9a** was added over 40 min to a refluxing mixture of 5 mol % of palladium acetate, 10 mol % of ligand, and 5 Å molecular sieves, with a 0.02 M final substrate concentration. The effectiveness of the ligands for palladium decreased in the order TDMPP > tris(*o*-methoxyphenyl)phosphine ~ triphenylphosphine ~ tris(2,4,6-trimethoxyphenyl)phosphine > tris(*o*-tolyl)phosphine > tris(2-furyl)phosphine > tris[3-(trifluoromethyl)phenyl]phosphine (see table in supplementary material). A combination of both steric and electronic effects appears important.

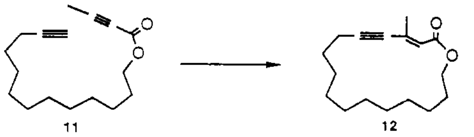


(3)

9 **10**

a) m=1, n=2 b) m=1, n=1 c) m=1, n=6 d) m=8, n=6

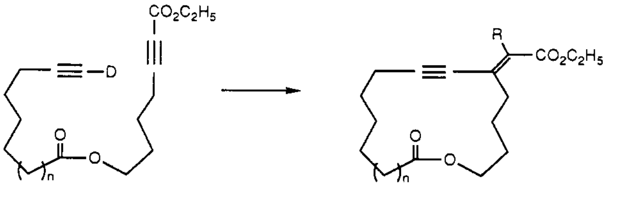
When the above conditions were used with TDMPP as ligand, in addition to the 15-membered-ring lactone **10a**[8] (57% yield) were also obtained 14-membered-ring lactone **10b**,[8] 19-membered-ring lactone **10c**,[8] and 26-membered-ring lactone **10d**,[8] in 67%, 57%, and 70% yields, respectively. The *E* geometry of the exocyclic double bond derives from the strong deshielding of the allylic methylene group (e.g., δ 2.81 for **10a**), consistent with this group being cis to the ester group. Having the acceptor acetylene endocyclic with respect to the forming ring, as in diyne **11**, still permits cyclization to the cycloalkenyne **12** (eq 4, 38% yield).



(4)

11 **12**

Scheme II outlines a reasonable proposal for the catalytic cycle. Insertion into the acetylenic hydrogen appears to be fast and reversible relative to cyclization, as evidenced by H–D exchange in terminal alkynes being competitive with alkyne dimerization. Further, cyclization of the deuterated substrate **13** led to the cyclization product **14**, retaining only 39% of the deuterium. The remarkable chemoselectivity associated with cyclization of **3** then arises from a kinetic preference for the palladium acetylide to add to the alkyne of a propargyl alcohol compared to a simple terminal alkyne. Since electron-withdrawing groups clearly activate the acceptor acetylene, the inductive effect of the propargyl hydroxyl group may account for part of its activation. The fact that the *p*-methoxybenzyl and *tert*-butyldimethylsilyl ethers of **3** produce complex mixtures whereas the acetate cyclizes even more efficiently supports this contention. The geometry of cyclization products supports the clean cis addition. An alternative catalytic cycle in which the acetic acid moiety remains bonded to palladium throughout the cycle (i.e., invoking a Pd^{4+} species) cannot be discounted. Clearly, much work needs yet to be done to define the mechanism more fully, but the scheme serves as a convenient working hypothesis for predictive purposes. The ability to form macrocycles with such versatile functionality by a simple isomerization, however, should prove to be a useful new strategy. Further, the prospects for developing alternative tandem annulations may provide opportunities for new types of polycyclizations.



13 **14** R=H+D

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Supplementary Material Available: General experimental procedure, table of ligand effects on macrocyclization of diyne **9a**, and characterization for **2–8** and **10a–d** (4 pages). Ordering information is given on any current masthead page.

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(10) Cyclodecyne has been calculated to have about 10 kcal/mol of strain energy. See: Allinger, N. L.; Meyer, A. Y. *Tetrahedron* **1975**, *31*, 1807. However, see: Turner, R. B.; Jarrett, A. D.; Goebel, P.; Mallon, B. J. *J. Am. Chem. Soc.* **1973**, *95*, 790. Oxidative dimerization of a diacetylene produced the 10-membered ring in only 6–9% yield; see: Wolovsky, R.; Sondheimer, F. *J. Am. Chem. Soc.* **1966**, *88*, 1525. For a cycloalkylation approach, see: Deslongchamps, P.; Lamothe, S.; Lin, H. J.; Ho, S. *Can. J. Chem.* **1987**, *65*, 1298.

Orbital Symmetry Control of Epimeric Rates of Generation of an Allylic Cation from Sterically Unbiased Precursors

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The concept of orbital symmetry control of stereochemistry[2] has proved to be one of the most fruitful ideas to emerge in physical organic chemistry in recent decades. Its use to date has been restricted to the several groups of reactions collectively described as pericyclic; however, it is in principle applicable not merely to reactions involving cyclic arrays of p orbitals but to all processes featuring the interconversion of trigonal and tetragonal carbon. The question that occurred to us is whether the face selection that characterizes these reactions depends on orbital symmetry.

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(1) (a) Present address: Plastics Research Department, Rohm and Haas Company, Box 219, Bristol, PA 19007. (b) Natural Sciences and Engineering Research Council of Canada Postdoctoral Fellow.

(2) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie/Academic Press: New York, 1971.

0002-7863/89/1511-8746$01.50/0

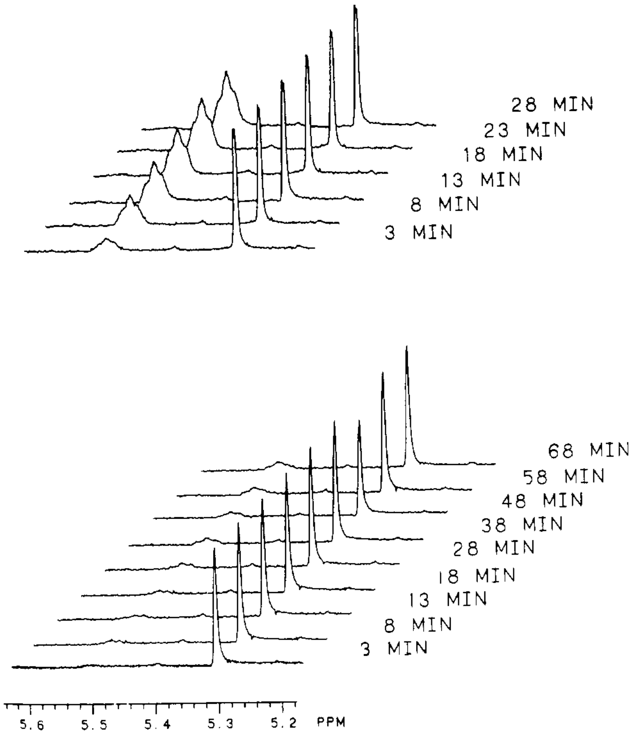
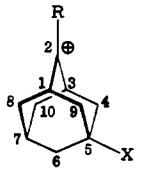


Figure 1. Rate of growth of the vinyl C-H signal of **8** from (*E*)- and (*Z*)-**5** (top and bottom, respectively). Compared with CH_2Cl_2 as internal standard. The initial rate constants at 22 °C were estimated at 4.6×10^{-4} s^{-1} and 9.8×10^{-6} s^{-1}, respectively. The initial concentrations were 0.034 and 0.032 for the *E* and *Z* substrates, respectively. The sulfuric acid concentration was 5×10^{-4}; both rate plots show substantial curvature due to dilution of the acid by water as the dehydration proceeds. A mixture of (*E*)- and (*Z*)-**5** under these conditions also showed that the *E* isomer quickly vanishes before the *Z* isomer has reacted to any significant degree.

Heterolysis is a particularly promising candidate for study in this connection; epimeric rate ratios as well as face selectivities in the capture of carbocations tend to be especially large. We are not aware of previous searches for this phenomenon, in spite of the huge amount of work done on solvolysis. The reason for this may be that the large epimeric rate ratios so often observed have long remained controversial;[3] furthermore, the assumption is usually made that allylic and benzylic ions are too stable to show any face selectivity. However, we recently found that such selectivity persists even in propargyl[4] and in cumyl cations[5] and that it could unequivocally be attributed to σ delocalization.[6] In these studies, we used 5-substituted 2-adamantyl cations **1** as our probe; alternative explanations such as those based on steric bias and ion-pair mediation could be ruled out by means of them.[6] In harmony with previous results, we recently reported[7] that (*Z*)-5-fluoro-2-adamantyl tosylate **2** hydrolyzes 200 times faster than the *E* isomer; we now address the question of whether the rate ratio is reversed in an appropriate, conformationally rigid vinylog.



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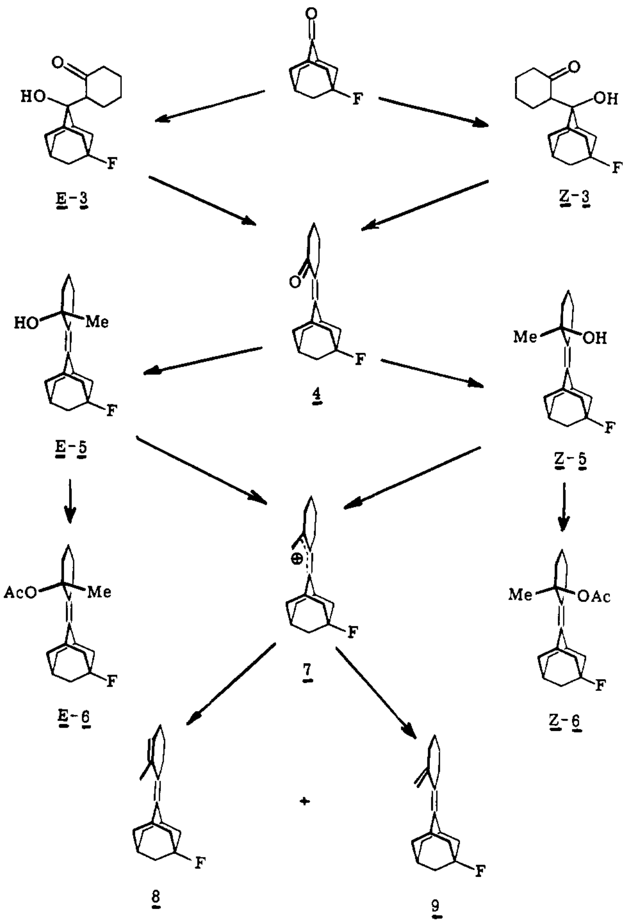
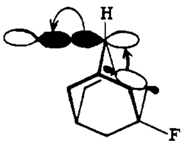
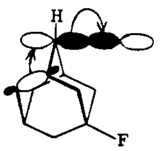
Scheme I





E-**2**‡



Z-**2**‡

Condensation of the imine produced from *n*-butylamine and cyclohexanone with 5-fluoro-2-adamantanone gave *E* and *Z* keto alcohols **3** in the normal[6] ratio, about 2:1 (85%); the mixture was dehydrated with acetic anhydride to give racemic enone **4** (Scheme I). Treatment of **4** with methyllithium afforded a 50/50 mixture of "*E*" and "*Z*" alcohols **5**.[8] These alcohols were separated chromatographically and, in part, converted to acetates **6** by means of acetic anhydride; the tosylates are unstable and not isolable.

The configuration of (*E*)-**6** was determined by means of measurements of the ^{13}C chemical shifts in the presence of Eu(fod)$_3$:[9] carbons 4, 5, and 9, easily recognized by virtue of their large ^{19}F couplings, are shifted downfield much less than carbons 7, 8, and 10. Treatment of either (*E*)- or (*Z*)-**5** solution with a dilute $CDCl_3$ solution of sulfuric acid irreversibly gave identical mixtures of dienes **8** and **9** in a 10:1 ratio; **9** was prepared independently via a Wittig reaction of **4**. The rates of dehydration

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(3) Brown, H. C. *The Nonclassical Ion Problem*, with comments by Schleyer, P.v.R.; Plenum: New York, 1977.

(4) le Noble, W. J.; Chiou, D.-M.; Okaya, Y. *Tetrahedron Lett.* **1978**, 1961.

(5) Lin, M.-H.; Cheung, C.-K.; le Noble, W. J. *J. Am. Chem. Soc.* **1988**, *110*, 6562.

(6) Cheung, C. K.; Tseng, L. T.; Lin, M.-h.; Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 1598.

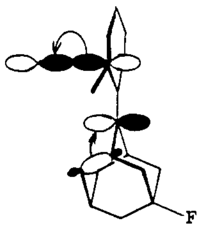
(7) Xie, M.; le Noble, W. J. *J. Org. Chem.* **1989**, *54*, 3839.

(8) For convenience, we use the *E* designation for the racemic mixture *RR* (shown in Scheme I) and *SS*, and *Z* for that of *RS* and *SR*. Melting points: *E*, 104-6 °C; *Z*, 74-6 °C. Both alcohols exhibited clean 17-signal ^{13}C NMR spectra (see supplementary material) and, in the MS, high-resolution parent peaks within 2 ppm of the theoretical values.

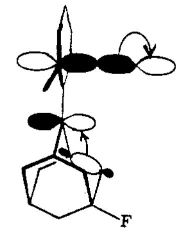
(9) Slow decomposition of **6** occurred in the presence of Eu(fod)$_3$, but this did not interfere. The ^1H NMR spectrum was also observed, but the induced shifts were not helpful in the assignment of configuration.

of the epimeric alcohols **5** via cation **7** were measured separately but under identical conditions by means of ^{1}H NMR; the rate of growth of the vinyl proton signal of **9** was monitored, with the proton signal of added methylene chloride as the standard. The contrast between the two is easily visible in Figure 1; the *E* alcohol forms the olefins 43 times faster than the *Z* isomer does. Thus, the face selection observed in the reactions of **2** has been reversed by an overall factor of roughly 10^4.

It should be noted that (*E*)- and (*Z*)-**5** would be enantiomers but for the presence of the 5-fluoro substituent. That is to say, the rates would be identical in the unsubstituted alcohols; hence, the observed rate ratio must be attributed to the fluorine atom. We can conceive of no explanation for this reversal other than that based on the change in symmetry of the orbital being vacated, when the ionization processes of isomers **2** are compared with those of isomers **5**. In both cases, the mechanism of the directive effect is the induction by the fluorine atom, which differentiates the vicinal carbon-carbon bonds flanking C_2. The possibility that our observation is related to the stability or basicity of the initial alcohols seems remote, as we have to date not encountered any instance in which 5-fluoro substitution led to substantial deviations from 50/50 *equilibrium* populations of epimers. Thus, when a 50/50 mixture of (*E*)- and (*Z*)-5-fluoroadamantan-2-ols is treated with various amounts of Eu(fod)$_3$, the NMR signals undergo virtually identical shifts, so that such an explanation is ruled out as the basis of the rate ratio for (*E*)- and (*Z*)-**2**.



E-5



Z-5

If our present interpretation is correct, it will be of interest to study whether similar reversals of stereochemistry are characteristic of the vinylogs of the host of solvolysis substrates in which σ,[10] σ-π,[11] and π[12] assistance have been claimed. Similarly, the question arises whether and to what extent the capture of nucleophiles by carbonyl compounds,[6] the attack of electrophiles on olefins,[13] and pericyclic reactions[14,15] will reverse stereochemistry when vinylogs are considered. Examples may already be in the literature; we regard Smith's observation of anti cuprate methylation to 5-methoxy-2-cyclopentenone as one possibility.[16]

Acknowledgment. We acknowledge with thanks the support of this work by the NSF and by the donors of the Petroleum Research Fund, administered by the American Chemical Society. Cherry Keaise contributed the basicity measurement of (*E*)- and (*Z*)-**2**.

Supplementary Material Available: Details of the preparation of compounds **3-6** and **9** and listings of their ^{13}C NMR signals and the shift reagent results of (*E*)-**6** (7 pages). Ordering information is given on any current masthead page.

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[10] Winstein, S.; Trifan, D. S. *J. Am. Chem. Soc.* **1952**, *74*, 1147, 1154.

[11] Tanida, H.; Tsuji, T.; Irie, T. *J. Am. Chem. Soc.* **1967**, *89*, 1953. Battiste, M. A.; Deyrup, C. L.; Pincock, R. E.; Haywood-Farmer, J. *J. Am. Chem. Soc.* **1967**, *89*, 1954. Coates, R. M.; Kirkpatrick, J. L. *J. Am. Chem. Soc.* **1970**, *92*, 4883.

[12] Winstein, S.; Shatavsky, M.; Norton, C.; Woodward, R. B. *J. Am. Chem. Soc.* **1955**, *77*, 4183.

[13] Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 5874. Johnson, C. R.; Tait, B. D.; Cieplak, A. S. *J. Am. Chem. Soc.* **1987**, *109*, 5875.

[14] Chung, W.-S.; Turro, N. J.; Srivastava, S.; Li, H.; le Noble, W. J. *J. Am. Chem. Soc.* **1988**, *110*, 7882.

[15] Lin, M.-h.; le Noble, W. J. *J. Org. Chem.* **1989**, *54*, 997.

[16] Smith, A. B.; Dunlap, N. K.; Sulikowski, G. A. *Tetrahedron Lett.* **1988**, *29*, 439. Smith, A. B.; Trumper, P. K. *Tetrahedron Lett.* **1988**, *29*, 443. A different view of this observation has just appeared; see: Corey, E. J.; Hannon, F. J.; Boaz, N. W. *Tetrahedron* **1989**, *45*, 545.

Synthesis of Benzene from Methane over a Ni(111) Catalyst

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We report the synthesis of C_6H_6 from CH_4 over a Ni(111) catalyst under ultrahigh vacuum (UHV) conditions. The gas phase hydrocarbon selectivity of this synthesis for benzene production is 100%. This is the first observation of a reaction of CH_4 to form a gas-phase, higher hydrocarbon over a metallic catalyst at the low pressures ($<10^{-4}$ Torr) commensurate with a UHV environment. Since CH_4 is normally unreactive under these conditions, this synthesis is effected by molecular beam techniques to activate CH_4 via a new mechanism: collision-induced dissociative chemisorption.[1,2] A monolayer of CH_4 physisorbed on Ni(111) at 47 K is exposed to a beam of Kr atoms. The collision of the incident Kr with the physisorbed CH_4 distorts the CH_4 from its tetrahedral configuration, thereby lowering the barrier to dissociation into an adsorbed methyl radical and an adsorbed hydrogen atom. As the surface temperature is raised to 230 K, all the adsorbed CH_3 dissociates to CH and the CH recombines to form adsorbed C_2H_2[3] via a mechanism established and discussed elsewhere.[4] Some of the C_2H_2 trimerizes to adsorbed C_6H_6,[5,6] and at 410 K and 425 K, respectively, the atomically adsorbed hydrogen desorbs as H_2 and some of the chemisorbed C_6H_6 desorbs. The progress of this reaction is monitored, and the adsorbed intermediates are identified by high-resolution electron energy loss spectroscopy. The gas-phase products are detected mass spectrometrically in a thermal desorption experiment.

The key to benzene formation is the attainment of a sufficiently high C_2H_2 coverage to allow C_2H_2 to trimerize without having to diffuse over a large area. In separate studies using C_2H_2 as the initial reactant,[6] C_2H_2 below 0.1 monolayer (ML) dehydrogenates at 440 K without undergoing the trimerization to and desorption as C_6H_6 which takes place at temperatures as low as 300 K for a C_2H_2 saturation coverage of 0.25 ML. Therefore, to effect trimerization at the lower surface temperatures where there is no C_2H_2 dehydrogenation, the C_2H_2 coverage must be high. The difficulty with the attainment of high C_2H_2 coverage is that the three adsorbed hydrogen atoms produced from the dissociative chemisorption of each CH_4 molecule block sites for the dissociation of additional CH_4. The hydrogen must be removed by maintaining the surface at a sufficiently high temperature to desorb it. Unfortunately, temperatures above 395 K also result in partial dehydrogenation of the C_6H_6 product to C_6H_5 or C_6H_4.[6] The following procedure, carried out in an apparatus described previously,[1c,2] is designed to achieve a high C_2H_2 coverage by providing sites for CH_4 dissociation while minimizing the dehydrogenation of the C_6H_6 product.

The Ni(111) crystal is maintained at 47 K in an ambient atmosphere of 3.5×10^{-6} Torr of CH_4. Under these conditions,

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[†] NSERC Postdoctoral Fellow.

[‡] Dreyfus Teacher-Scholar.

[1] (a) Beckerle, J. D.; Yang, Q. Y.; Johnson, A. D.; Ceyer, S. T. *J. Chem. Phys.* **1987**, *86*, 7236. (b) Beckerle, J. D.; Johnson, A. D.; Yang, Q. Y.; Ceyer, S. T. *J. Vac. Sci. Technol., A* **1988**, *6*, 903. (c) Ceyer, S. T. *Annu. Rev. Phys. Chem.* **1988**, *39*, 479.

[2] Beckerle, J. D.; Johnson, A. D.; Ceyer, S. T. *J. Chem. Phys.*, in press.

[3] (a) Ceyer, S. T.; Lee, M. B.; Yang, Q. Y.; Beckerle, J. D.; Johnson, A. D. *Methane Conversion*; Bibby, D., Chang, C., Howe, R., Yurchak, S., Eds.; Elsevier Science: Amsterdam, 1988; p 51. (b) Yang, Q. Y.; Ceyer, S. T. *J. Vac. Sci. Technol., A* **1988**, *6*, 851.

[4] (a) Yang, Q. Y.; Johnson, A. D.; Ceyer, S. T., in preparation. (b) Yang, Q. Y. Ph.D. Thesis, Massachusetts Institute of Technology, 1989.

[5] Bertolini, J. C.; Massardier, J.; Dalmai-Imelik, G. *J. Chem. Soc., Faraday Trans. 1* **1978**, *74*, 1720.

[6] Maynard, K. J.; Johnson, A. D.; Yang, Q. Y.; Ceyer, S. T., in preparation.

0002-7863/89/1511-8748$01.50/0