these important molecules to be prepared simply and stereospecifically. Also this method yields the nitrogen function in a protected form and allows the preparation of the hydrazine analogues. In addition, the dihydrooxadiazine intermediates show the promise of stereoselective opening with non-oxygen-based nucleophiles. Further studies on the scope of the reactions of these cycloadducts will be reported in due course.

Acknowledgment. We thank Dr. M. Bernstein for performing variable temperature—^{1}H NMR on the glycosides. N.C. thanks NSERC (Canada) for an Undergraduate Student Research Award.

A Metal-Catalyzed Cyclization of Enallenes

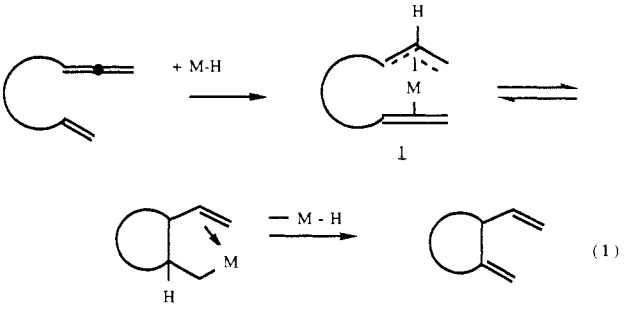
Barry M. Trost* and James M. Tour

Department of Chemistry, Stanford University
Stanford, California 94305

Received March 28, 1988

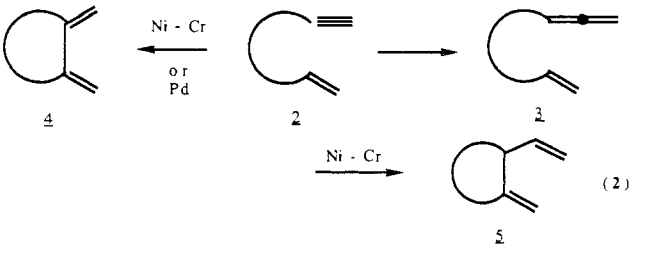
The development of chemical processes which involve a set of reactants that corresponds exactly to the empirical formula of the desired product avoids the development of chemical wastes that require disposal. Such a process for ring construction involves isomerizing an acyclic system. Cyclizations involving catalytic intramolecular carbametalations represent a type of reaction that meets such a goal.[1-6] The greatest success has focussed upon the acetylenic linkage. We wish to report that allenes can serve as an excellent functional group for cyclizations via isomerizations with use of a novel nickel–chromium bimetallic catalyst.[5,7]

The concept for the cyclization derives from our postulating that a metal hydride,[8] which was involved in the isomerization of enynes to five- and six-membered rings with a nickel–chromium catalyst,[5] may initiate the sequence of events outlined in eq 1.[7,9-11]



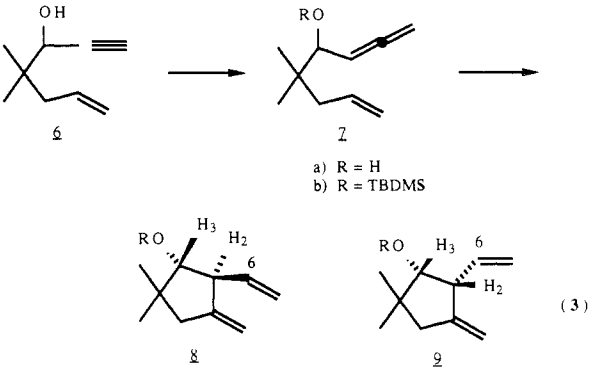
(1)

The existence of such a process would significantly extend the value of the catalytic intramolecular carbametalation. As shown in eq 2, the enynes **2**, which are easily transformed into the enallenes **3**,[12] then serve as common precursors to either 1,3-dienes like **4**[4,5] or 1,4-dienes represented by **5**.



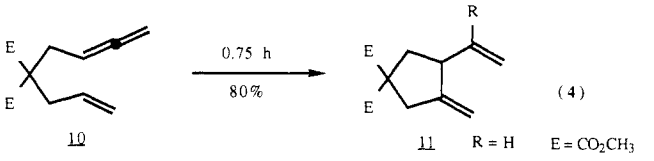
(2)

To probe the process, the allene **7a**, easily available from the corresponding acetylene **6** [$(CH_2O)_n$, $(i\text{-}C_3H_7)_2NH$, CuBr, dioxane, reflux, 59%], was exposed to 10 mol% of (*p*-diphenylphosphinopolystyrene)nickel dichloride and 30 mol% chromous chloride in 4:1 THF–ethanol at ambient temperature (eq 3).



(3)

These standard conditions effected cyclization to a 3.4:1 mixture of **8a**[13] and **9a**[13] in 55% isolated yield. Upon the basis of both proton coupling constants ($J_{2,3}$ = 10.2 Hz for **8a** and 5.5 Hz for **9a**) and ^{13}C NMR data (δ_{C_6} = 138.97 for **8a** and 136.30 for **9a**), the major product is assigned as trans. Performing the same reaction on the *tert*-butyldimethylsilyl ether **7b** increases the yield to 78% and the diastereoselectivity to >99:1 by capillary VPC.



(4)

(1) For stoichiometric intramolecular carbametalations of enynes, see: Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 2788. Negishi, E.; Swanson, D. R.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1987**, *28*, 917; Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829. Negishi, E. Holmes, S. J.; Tour, J. M.; Miller, J. A. *J. Am. Chem. Soc.* **1985**, *107*, 2568. For reviews, see: Negishi, E. *Acc. Chem. Res.* **1987**, *20*, 65. Yasuda, H.; Nakamura, A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 723.

(2) For metalloene reactions and other main group intramolecular carbametalations, see: Oppolzer, W.; Schneider, P. *Helv. Chim. Acta* **1986**, *69*, 1817 and earlier references in the series. Felkin, H.; Kwart, L. D.; Swierczewski, G.; Umpleby, J. D. *J. Chem. Soc., Chem. Commun.* **1975**, 242. Courtois, G.; Masson, A.; Miginiac, L. *C. R. Acad. Sci. Paris Ser. C* **1978**, *286*, 265. Jousseaume, B.; Douboudin, J. G. *Synth. Commun.* **1979**, *9*, 53. Crandall, J. K.; Battioni, P.; Wehlacz, J. T.; Bindra, R. *J. Am. Chem. Soc.* **1975**, *97*, 7171. Hill, E. A. *J. Organomet. Chem.* **1975**, *91*, 123. Richey, H. G.; Rothman, A. M. *Tetrahedron Lett.* **1968**, 1457.

(3) For Pd catalyzed intramolecular additions of allyl acetates to olefins, see: Oppolzer, W.; Gaudin, J.-M. *Helv. Chim. Acta* **1987**, *70*, 1477. Trost, B. M.; Luengo, J., to be published.

(4) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781. Trost, B. M.; Lautens, M. *Tetrahedron Lett.* **1985**, *26*, 4887. Trost, B. M.; Chen, S. F. *J. Am. Chem. Soc.* **1986**, *108*, 6053.

(5) (a) Trost, B. M.; Tour, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 5268. (b) Also, see: Bogdanovic, B. *Adv. Organomet. Chem.* **1979**, *17*, 105.

(6) Takacs, J. M.; Anderson, L. G.; Creswell, M. W.; Takacs, B. E. *Tetrahedron Lett.* **1987**, *28*, 5627. Takacs, J. M.; Anderson, L. G. *J. Am. Chem. Soc.* **1987**, *109*, 2200.

(7) Surprisingly, there has been little work involving nickel-catalyzed reactions of allenes. See: Jolly, P. W.; Wilke, G. *The Organic Chemistry of Nickel*; Academic Press: 1975; Vol II, Chapter 2. Jolly, P. W. *Comp. Organomet. Chem.* **1982**, *8*, 649.

(8) Jolly, P. W. *Comp. Organomet. Chem.* **1982**, *6*, 37.

(9) Jolly, P. W. *Comp. Organomet. Chem.* **1982**, *8*, 671.

(10) dePasquale, R. J. *J. Organomet. Chem.* **1971**, *32*, 381. Otsuka, S.; Tani, K.; Yamagata, T. *J. Chem. Soc., Dalton Trans.* **1973**, 2491. Jolly, P. W.; Kruger, C.; Salz, R.; Sckutowski, J. C. *J. Organomet. Chem.* **1979**, *165*, C39. Hene, B.; Jolly, P. W.; Salz, R.; Stobbe, S.; Wilke, G.; Benn, R.; Mynott, R.; Seevogel, K.; Goddard, R.; Kruger, C. *J. Organomet. Chem.* **1980**, *191*, 449.

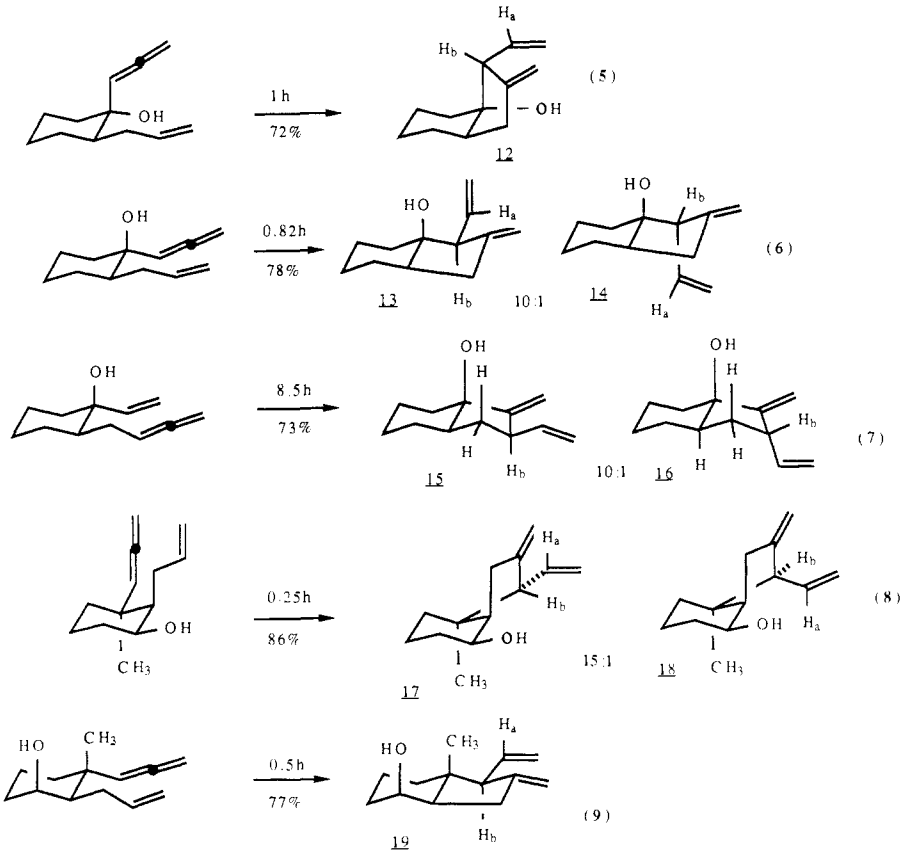
(11) For addition of a π-allylnickel to norbornene, see: Gallazzi, M.-C.; Porri, L.; Vitulli, G. *J. Organomet. Chem.* **1975**, *97*, 131. The cooligomerization of dienes with olefins presumably involves such a process. See: ref 5b, 9, and Jolly et al. (Jolly, P. W.; Wilke, G. *The Organic Chemistry of Nickel*; Academic Press: 1975; Vol II, Chapter 1, pp 26–39).

(12) Searles, S.; Li, Y.; Nassim, B.; Lopes, M.-T. R.; Tran, P. T.; Crabbé, P. *J. Chem. Soc., Perkin Trans. 1* **1984**, 747. We have found that significant improvement in our yields resulted when (1) the temperature was maintained at 70 °C for 1 h before raising it to reflux and (2) approximately 0.5 mol% of BHT was added.

(13) This compound has been fully characterized spectroscopically, and elemental composition has been established by high resolution mass spectroscopy and/or combustion analysis.

0002-7863/88/1510-5231$01.50/0

Scheme I



Similarly, the diester **10** cyclized to the methylenecyclopentane **11** in 80% isolated yield (eq 4). The importance of site isolation effected by employing a polymer bound nickel chromium catalyst is emphasized by the absence of any monomeric product when bis(triphenylphosphine)nickel dichloride and chromous chloride are employed in a homogeneous system.

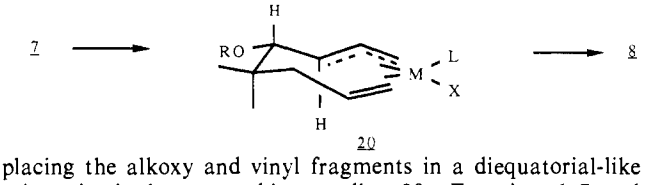
The use of this approach for annulations is of particular interest. We focussed on the effect of various substitution patterns on formation of the important perhydroindanes. Equations 5–9 demonstrate that both *cis*- and *trans*-perhydroindanes form with equal ease. The presence of a free hydroxyl group α to the allene or alkene poses no problem in the cyclization. Placing either the allene or alkene on a quaternary carbon also has no effect. Good (>10:1) to excellent (>99:1) diasteroselectivity characterized all these cyclizations. The stereochemistry of **12–14** is assigned based upon $Eu(fod)_3$ induced shifts. For **12**, addition of 30 μL of 0.096 M $Eu(fod)_3$ solution to 3 mg of **12** in $CDCl_3$ caused the signal for H_a to shift from δ 5.72 to 6.40 ($\Delta\delta$ = 0.68), whereas H_b shifted somewhat less from δ 3.17 to 3.69 ($\Delta\delta$ = 0.52). For the isomer epimeric at the carbon bearing the vinyl group, dramatic differences in the reverse order should have been expected. Similar results are seen in the case of cyclopentane **13** [60 μL of $Eu(fod)_3$ and 3 mg of **13**, $\Delta\delta$ for Ha, 0.33; for H_b, 0.27]. For the epimeric compound **14**, the dramatic differences in the reverse direction are observed [20 μL of $Eu(fod)_3$ and 3 mg of **14**, $\Delta\delta$ for Ha, 0.17; for H_b, 0.56].

Assignment of stereochemistry to **15** and **16** was derived from the vicinal coupling constants of H_b to the protons of the adjacent methylene group. MM2 calculations suggest vicinal coupling constants for H_b of 8.2 and 9.8 Hz for **15** and 7.7 and 1.0 Hz for **16**. The experimental values of 8.2 Hz for both vicinal couplings for **15** and 9.2 and <1 Hz for **16** are in good agreement with the calculations.

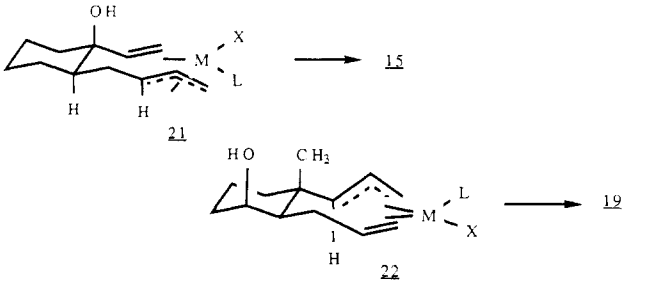
Difference NOE provides the basis for assigning the stereochemistry of **17–19**. For **17**, the NOE between the methyl group and the bis-allylic hydrogen (H_b) should be larger than that between the methyl group and the vinylic hydrogen H_a (obsd 7% for H_b versus 4% for H_a). For **18**, the reverse should be the case as is observed (8% for H_a and 3.5% for H_b). The 17% NOE between the methyl group and the vinylic hydrogen H_a of **19** compared to 1% NOE for the doubly allylic hydrogen H_b supports the depicted assignment.

To probe the mechanism, the cyclization of **10** (eq 4) was performed in CH_3OD/THF (1:4). While mass spectroscopy indicated only 17% monodeuteriation with no detectable dideuteriation, 86% of the label appeared at the internal vinyl position by ^2H NMR (**11**, R = D), in accord with the original rationale. The low incorporation presumably arises from the low rate of exchange of the polymeric nickel (or chromium) hydride intermediate with the solvent.[14]

The stereochemistry can be understood on the basis of a chairlike conformation for the reactive intermediate. Thus, preferential formation of **8** (eq 3) can be understood based upon

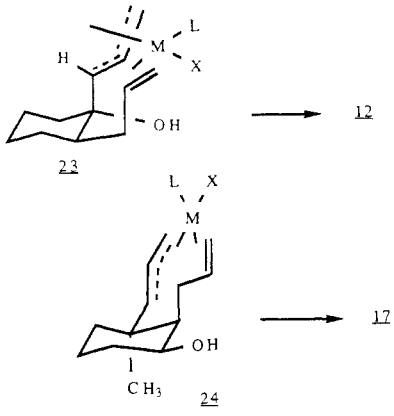


placing the alkoxy and vinyl fragments in a diequatorial-like orientation in the proposed intermediate **20**. Equations 6, 7, and



(14) Cf. Kanai, H.; Kushi, K.; Sakanoue, K.; Kishimoto, N. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2711.

9 illustrate that formation of the *trans*-perhydroindanes preferably to exclusively places the vinyl group at C(8) or C(9) cis to the bridgehead substituent. Folding the proposed syn-π-allylmetal complex in a chairlike array as depicted in **21** and **22** nicely rationalizes the observations. This conformational picture also accommodates the dramatically opposite results in the two *cis*-perhydroindane cases (eq 5 and 8). A chair folding with the syn-π-allylmetal unit in an axial orientation as in **23** places the vinyl substituent on the exo face in the product as in **12**. On the



other hand, a chair folding with the syn-π-allylmetal unit in an equatorial position as in **24** orients the vinyl group on the endo face in the product as in **17**. The 15:1 preference for the contra-steric product in the latter case provides a measure of the conformational bias for a chairlike transition state in the cyclication.

The extraordinary reactivity of the allenes toward this catalyst is underscored by the current requirement that the vinyl group be unsubstituted in order to effectively capture the proposed π-allylmetal intermediate in preference to intermolecular capture by another allene. The facile addition of π-allylnickel complexes to allenes has previously been noted.[15] Nevertheless, the fact that the strain associated with forming the *trans*-perhydroindane even with a bridgehead methyl group does not deter the process demonstrates that strain effects are not as important as steric effects. The failure to effect related cyclizations using a catalyst derived from palladium(0) and a carboxylic acid, presumably a hydridopalladium carboxylate, emphasizes the importance of the nickel–chromium catalyst.[16]

The ability to use allenes as partners in intramolecular carbametalations opens a new dimension to cyclization via isomerization. The excellent chemo- and diasteroselectivity makes the process very useful synthetically. At a minimum, flexibility to generate either 1,2-dimethylenecyclopentanes or 2-vinyl-1-methylenecyclopentanes according to eq 2 from the same enyne now exists. To underscore this point, each of the allenes of eq 3–9 were synthesized in one step from the corresponding acetylene via the novel homologation of Crabbé.[12]

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health for their generous support of our programs. J.M.T. thanks the National Institutes of Health for a postdoctoral fellowship for a portion of his stay in these laboratories. Mass spectra were gratefully provided by the Mass Spectrometry Facility, University of California—San Francisco, supported by the NIH Division of Research Resources.

Supplementary Material Available: Details of the preparation of **11** (2 pages). Ordering information is given on any current masthead page.

(15) Baker, R.; Copeland, A. H. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2560.
(16) Matsuda, K., unpublished work in these laboratories. See: Trost, B. M.; Rise, F. *J. Am. Chem. Soc.* **1987**, *109*, 3161.

A Biomimetic Synthesis of (±)-Petiodial. A Novel Palladium-Catalyzed Enallene Cyclization

Barry M. Trost* and Koyo Matsuda

Department of Chemistry, Stanford University
Stanford, California 94305

Received April 11, 1988

Extracts of the marine algae of the family Udoteaceae have shown a variety of biological activities which include antimicrobial, cytotoxic, and ichthyotoxic properties.[1] Petiodial (**1**), an unusual cyclopentanoid diterpene which shares a carbon skeleton only with udoteatriol,[2] is one of the biologically active secondary metabolites whose structure, except for stereochemistry, has been suggested on the basis of spectral data.[1,3] We wish to record a synthesis of this compound and, on the basis of this synthesis, suggest a relative stereochemistry. The route involves an unexpected and novel palladium-catalyzed cyclization of an enallene.

In considering a synthesis of (±)-petiodial, the development of a strategy patterned after its biosynthesis from a suitable geranyl–geraniol derivative (cf. eq 1) raises the question of specific functionalization of C(19) rather than C(8) during the course of cyclization. An expedient solution to this subtle selectivity question derives from our earlier observations in the complementary behavior observed in the thermal versus Pd^{2+}-catalyzed ene reactions of enyne **2** (eq 2) which we have shown derives from the presence of the terminal double bond, which serves as a remote binding site during the course of the transition-metal-catalyzed process.[4] The intrinsic selectivity of this metal-catalyzed reaction and the existence of a similarly situated double bond in the geranyl–geraniol system suggested a route outlined in Scheme I in which the ring-forming step relies on a chemo- and regiocontrolled Pd^{2+} enyne cyclization (**4** → **5**).[4,5]

As outlined in Scheme I, **4** is readily available from farnesyl bromide.[6,7] Cyclization of **4a** with palladium acetate in warm benzene (65 °C) gives a 2.5–3.3:1 ratio of the silylated and unsilylated cyclized products **10** and **5b** in a sluggish reaction (eq 3). By using benzene-d_6, the reaction may be monitored by ^1H NMR spectroscopy which shows the buildup of an intermediate which we postulate to be an allene, such as **11**, based upon the appearance of an additional vinyl absorption at δ 5.01.

Because palladium-catalyzed enallene cyclization is, to our knowledge, unprecedented, we explored the cyclization of the allene **12** which forms exclusively upon desilylation of the silylacetylene **4a** [$AgNO_3$, ethanol–water, room temperature, 20 min then KCN,[8] room temperature, 20 min, 89%]. Under the cyclization conditions for enyne **4a** in which the enyne reacts sluggishly, enallene **12** cyclizes completely within 1 h to give only **5b** in 82% (eq 3). Addition of *N,N'*-dibenzylideneethylenediamine as a ligand for palladium[9] improves the yield slightly. The extraordinary selectivity for the terminal methylene isomer in contrast to a positional olefinic isomer is to be noted. It is outside the scope of this communication to speculate upon the mechanism of this new enallene cyclization; nevertheless, it is interesting to contrast this reaction to a recently discovered Ni–Cr-catalyzed enallene cyclization which produces a totally different type of product (eq 4).[10] Attempts to cyclize substrates like **12** under the Ni–Cr conditions failed.

(1) Paul, V. J.; Fenical, W. *Tetrahedron* **1984**, *40*, 2913 and earlier references cited therein.
(2) Nakatsu, T.; Ravi, B. N.; Faulkner, D. J. *J. Org. Chem.* **1981**, *46*, 2435. Whitesell, J. K.; Fisher, M.; Jardine, P. D. S. *J. Org. Chem.* **1983**, *48*, 1556.
(3) Fattorusso, E.; Magno, S.; Mayol, L.; Novellino, E. *Experentia* **1983**, *39*, 1275.
(4) Trost, B. M.; Lautens, M. *Tetrahedron Lett.* **1985**, *26*, 4887.
(5) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781.
(6) VanTamelen, E. E.; Nadeau, R. G. *Bioorg. Chem.* **1982**, *11*, 197.
(7) Enders, D.; Eichenauer, H. *Chem. Ber.* **1979**, *112*, 2933.
(8) Corey, E. J.; Kirst, K. A.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 6314.
(9) Trost, B. M.; Jebaratnam, J. *Tetrahedron Lett.* **1987**, *28*, 1611.
(10) Tour, J. M., unpublished work in these laboratories.

0002-7863/88/1510-5233$01.50/0