The calculated geometries of **1** agree well with the X-ray structure (Table I).[19] The relative bowl depths from LDF (C hub plane to C rim plane) for **1**, **7**, and **8** are 0.91 (0.89 Å X-ray), 0.88, and 0.86 Å, respectively. LDF predicts the eclipsed conformation about the C_{sp^3}–C_{sp^3} bonds in **7** and **8** with average H–C–C–H torsion angles of ca. 12° and 8°. Unlike coronene, which shows distinct bond shortening solely in the rim bonds,[20] **1** shows bond alternation within each ring; the spoke and rim bonds are shorter than the hub and flank bonds.

In the ground-state bowl conformation of **7** and **8**, the geminal hydrogens are diastereotopic with an exo/endo relationship; bowl inversion renders these sites equivalent. Thus, variable-temperature NMR studies on mixtures enriched in **7** and **8** allow us to probe the bowl inversion process and assign approximate free energies of activation to the inversion in **7** (8.5 ± 0.5 kcal/mol) and **8** (6–7 kcal/mol).[21,22] This demonstrates the flexible nature of these bowls, a property one can relate to the analogous carbon fragments leading up to buckminsterfullerene.[4]

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Supplementary Material Available: Listings of spectral data for compounds **2–15** (6 pages). Ordering information is given on any current masthead page.

(15) Calculations on the barrier to inversion in **1** have been reported using empirical force field,[16] SCF-MO,[17] and ab initio[18] methods.
(16) Kao, J.; Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 975.
(17) Gleicher, G. J. *Tetrahedron* **1967**, *23*, 4257.
(18) Schulman, J. M.; Peck, R. C.; Disch, R. L. *J. Am. Chem. Soc.* **1989**, *111*, 5675.
(19) Hanson, J. C.; Nordman, C. E. *Acta Crystallogr.* **1976**, *B32*, 1147.
(20) Fawcett, J. K.; Trotter, J. *Proc. R. Soc.* **1966**, *A289*, 366.
(21) (a) Sandstrom, J. *Dynamic NMR Spectroscopy*; Academic Press: New York, 1982; p 97. (b) Gutowsky, H. S.; Holm, C. H. *J. Chem. Phys.* **1956**, *25*, 1228.
(22) The barrier to inversion for a derivative of corannulene has been measured to be 10.2 ± 0.2 kcal/mol. See: Scott, L. T.; Hashemi, M. M.; Bratcher, M. S. *J. Am. Chem. Soc.*, preceding paper in this issue.

Palladium-Catalyzed Alkylative Cyclization of 1,6- and 1,7-Enynes

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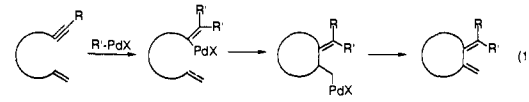
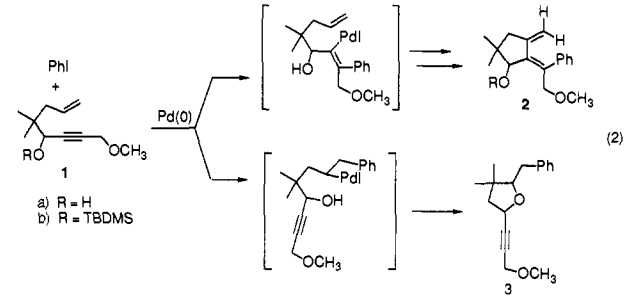
1,2-Bis(alkylidene)cycloalkanes are valuable building blocks for further structural elaboration as well as interesting substances in their own right. The discovery that Pd(0) in the presence of acetic acid catalyzes the cycloisomerization outlined in eq 1 (R′ = H)[1] with generation of the *E* dienes suggested the feasibility of an alkylative cycloaddition which would provide an unprecedented entry to substituted bis(alkylidene)cycloalkanes possessing the R′ stereospecifically *Z* as depicted in **1**, a stereochemical outcome that is of great interest for further cyclization if R′ is an unsaturated group or for itself as in the case of vitamin D.[2] A key unanswered question for the success of an alkylative cyclization concerns the chemoselectivity of carbapalladation of an olefin versus an acetylene.[3-5]



The reaction of iodobenzene with enyne **1** was chosen to test the feasibility of the process. Enyne **1a** followed by iodobenzene is added to a suspension consisting of 2 mol % $Pd(OAc)_2$, 4 mol % Ph_3P (TPP), and 1 equiv of silver carbonate (method A). Heating eventually to 75 °C led to the desired alkylated cycloadduct **2a**.[7] The stereochemistry is assigned as depicted on the basis of a positive NOE between one of the vinyl protons and the aromatic ring protons. Decomposition accompanying isolation of **2a** led to preparative cyclization of the silyl ether **1b** to give diene **2b**[7] in 60% yield after purification. Switching the catalyst to 2 mol % $(dba)_3Pd_2{\cdot}CHCl_3$ and 4 mol % tri-*o*-tolylphosphine (TOT) (method B) gives the furan **3** as a major product in addition to the diene **2a**.[6] The two products appear to derive from the selectivity of the initial carbapalladation as illustrated in eq 2.



The use of vinyl bromides proves most interesting. Reacting enyne **1b** with β-bromostyrene using method A but replacing silver carbonate with triethylamine leads to the bicyclic product **5**[7] as a single diastereomer, as determined by both chromatographic and spectroscopic analysis (eq 3), apparently as a result of electrocyclic cyclization of the initial hexatriene **4**. The unusual

(1) Trost, B. M.; Lautens, M.; Chan, C.; Jebaratnam, D. J.; Mueller, T. *J. Am. Chem. Soc.* **1991**, *113*, 636. Trost, B. M. *Janssen Chim. Acta* **1991**, *9*, 3. Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34.
(2) For two excellent recent leading references, see: Posner, G. H.; Nelson, T. D. *J. Org. Chem.* **1991**, *113*, 6958. For some reviews, see: Georghiou, P. E. *Chem. Soc. Rev.* **1977**, *6*, 83. Lythgoe, B. *Chem. Soc. Rev.* **1990**, *9*, 449. Kametani, T.; Furayama, H. *Med. Res. Rev.* **1987**, *7*, 147.
(3) For a review of the Heck reaction, see: Heck, R. F. *Org. React. (N.Y.)* **1982**, *27*, 345. For examples of polycyclizations, see: Zhang, Y.; Wu, G.; Agnel, G. Negishi, E. *J. Am. Chem. Soc.* **1990**, *112*, 8590. Grigg, R.; Dorrity, M. J.; Malone, J. F.; Sridharan, V.; Sukirthalingam, S. *Tetrahedron Lett.* **1990**, *31*, 1343. Kucera, D. J.; Overman, L. E. *Abstracts of Papers*, 200th National Meeting of the American Chemical Society, Washington, DC; American Chemical Society: Washington, DC, 1990; ORGN 128. Carpenter, N. E.; Kucera, D. J.; Overman, L. E. *J. Org. Chem.* **1989**, *54*, 5864. Abelman, M. M.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 2328. Zhang, Y.; Negishi, E. I. *J. Am. Chem. Soc.* **1989**, *111*, 3454.
(4) For some examples of Heck reactions involving acetylenes, see: Fournet, G.; Balme, G.; Van Hemelryck, B.; Gore, J. *Tetrahedron Lett.* **1990**, *31*, 5147. Negishi, E.; Noda, Y.; Lamaty, F.; Vawter, E. J. *Tetrahedron Lett.* **1990**, *31*, 4393. Grigg, R.; Dorrity, M. J.; Malone, J. F.; Sridharan, V.; Sukirthalingam, S. *Tetrahedron Lett.* **1990**, *31*. 1343. Lee, G. C. M.; Tobias, B.; Holmes, J. M.; Harcourt, D. A.; Garst, M. E. *J. Am. Chem. Soc.* **1990**, *112*, 9330. Silverberg, L. J.; Heck, R. F. *J. Organomet. Chem.* **1991**, *409*, 411.
(5) Cf.: Trost, B. M.; Burgess, K. *J. Chem. Soc., Chem. Commun.* **1985**, 1084. Grigg, R.; Sukirthalingam, S.; Sridharan, V. *Tetrahedron Lett.* **1991**, *32*, 2545.
(6) Cf.: Fournet, G.; Balme, G.; Gore, J. *Tetrahedron* **1990**, *46*, 7763.
(7) New compounds have been characterized spectrally and their elemental compositions established by combustion analysis and/or high-resolution mass spectrometry. All yields are for isolated pure product unless otherwise indicated.

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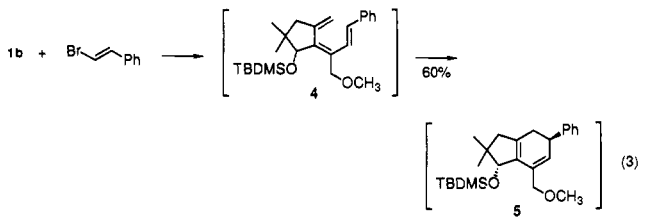
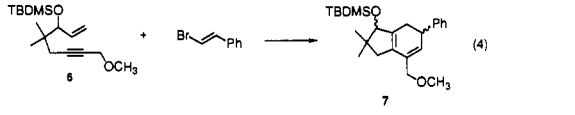
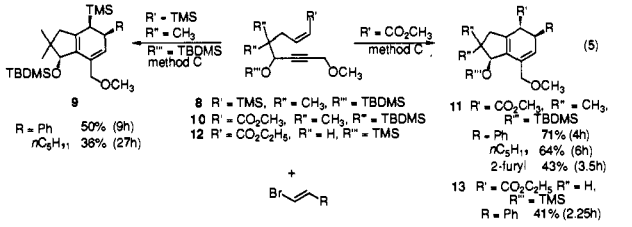


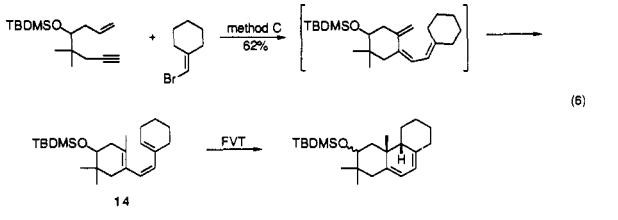
rotoselectivity[8] of the triene derives from the interaction of the siloxy and methoxymethyl substituents since the isomeric enyne **6** produces the expected diastereomeric mixture (eq 4). The tentative stereochemical assignment of **5** derives from mechanistic considerations.



Equation 5 illustrates the ability to introduce both electron-donating and electron-withdrawing substituents on the terminal olefinic carbon of the enyne and to vary the substituent on the vinyl bromide. All reactions were performed using 5 mol % $Pd(OAc)_2$, 15 mol % TPP, and 1 equiv of triethylamine in refluxing toluene (method C) without optimizing conditions in any example. In spite of increasing the reactivity of the olefin toward carbametalation by incorporating an ester, kinetic carbapalladation of the acetylene still dominates. Chromatographic and spectroscopic analyses indicate that each product is a single diastereomer. The 4,5-stereochemistry of **9**[7] (R = Ph and n-C_5H_{11}) as *Z* derives from J = 5.5 Hz for H_4–H_5; the stereochemistry of **11**[7] (R = Ph, n-C_5H_{11}, and C_4H_3O) as *E* derives from J = 12.3 ± 0.3 Hz for H_4–H_5. While the latter result is in accord with that anticipated from a mechanism invoking *cis*-carbapalladation, *cis*-β-hydrogen insertion, and disrotatory cyclization of the presumed hexatriene, the former is not. Clearly, the mechanistic details of this process must yet be established.



Cyclization of enyne **12** with β-bromostyrene explores the effects of ring substitution (eq 5). The more modest yield of bicycle **13**[7] compared to **9** (R = Ph) in eq 5 may derive from the higher sensitivity of the product toward decomposition during workup. The alkylative cyclization depicted in eq 6 illustrates the successful extension to six-membered rings. In this case, the hexatriene **14** may be isolated (71% yield) or flash vacuum thermolyzed to the tricycle.



The reaction has good chemoselectivity, as illustrated by the compatibility with free alcohols, esters, vinyl- and allylsilanes, dienes, and furans. The sequence of alkylative cyclization–electrocyclic reaction constitutes an equivalent of a [2 + 2 + 2] bicyclization minus HBr.

(8) For consideration of rotoselectivity in 4e cases, see: Trost, B. M.; McDougal, P. G. *J. Org. Chem.* **1984**, *49*, 458. Kallel, E. A.; Wang, Y.; Spellmeyer, D. C.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 6759.

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Registry No. 1a, 122917-11-7; **1b**, 138572-83-5; **2a**, 138572-81-3; **2b**, 138572-99-3; **3**, 138572-82-4; **5**, 138572-84-6; **6**, 138572-85-7; *cis*-**7**, 138572-86-8; **8**, 138572-87-9; **9** (R = Ph), 138572-88-0; **9** (R = n-C_5H_{11}), 138572-93-7; **10**, 138572-89-1; **11** (R = Ph), 138572-90-4; **11** (R = n-C_5H_{11}), 138572-94-8; **11** (R = 2-furyl), 138572-95-9; **12**, 138605-35-3; **13**, 138572-91-5; **14**, 138572-92-6; (*E*)-BrCH=CHPh, 588-72-7; PhI, 591-50-4; *trans*-**7**, 138573-00-9; (*E*)-BrCH=CH-n-C_5H_{11}, 53434-74-5; (*E*)-BrCH=CH-2-furyl, 138572-96-0; H_2C=$CHCH_2CH$(OTBDMS)-$C(CH_3)_2CH_2C$≡CH, 138572-97-1; (bromomethylene)cyclohexane, 1121-49-9; 2,2-dimethyl-3-((dimethyl-*tert*-butylsilyl)oxy)-1,2,3,4,4a,4b,5,6,7,8-decahydrophenanthrene, 138572-98-2.

Supplementary Material Available: Characterization data for **2a**,**b**, **5**, **9**, **11**, **13**, and **14** (3 pages). Ordering information is given on any current masthead page.

New Strategy for the Total Synthesis of 1α-Hydroxyvitamin D Derivatives

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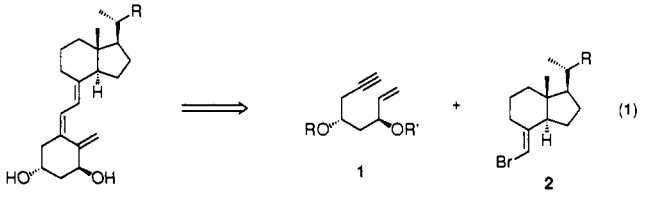
The increasing number of potential clinical applications of 1α-hydroxyvitamin D analogues enhances interest in simplifying their syntheses.[1] Two strategies are currently employed: one based on a biomimetic path from a normal steroid precursor[2] and one based on a convergent approach of attaching a preformed ring-A system to a CD fragment (Grundmann ketone or an analogue thereof).[3,4] We wish to record a new convergent strategy in which ring A is created from an acyclic unit as a result of the method of attachment of this unit to a Grundmann's ketone derivative utilizing a Pd-catalyzed alkylative enyne cyclization[5] as outlined in eq 1.



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