(Figure 1) with terminal carbonyl ligands and ethyl substituents. Crystallographic evidence that the interstitial atom is Ni(i) rather than Ge(i) (which differ by only four electrons) was provided from separate least-squares refinements, which gave a more reasonable equivalent isotropic thermal parameter when the interstitial atom was designated as Ni(i). The central atom was unambiguously determined to be Ni(i) by LD/FTMS, which revealed the parent-ion peak and its isotopic distribution pattern as well as the fragment-ion pattern to be entirely consistent with the compound's composition.[15]

The following structural-bonding implications emerge from an examination in Table I of the mean molecular parameters in **2** and related clusters: (*1*) The closely similar geometries of **3** and **4** indicate that replacement of terminal CO with PPh_3 ligands does not markedly affect their electronic structures. (2) A consequence of each capping Ge atom in **2** having a 0.16-Å-larger covalent radius[16] than each P atom in **3** is that its Ni(s)-E distances are greater by 0.18 Å; thus, the nonbonding Ni(i)···E distances of 2.76 Å in **2** (E = Ge) are 0.3 Å larger than the corresponding cube center-E distances in **3** (E = P). It follows that the nonbonding trans P···P distances of 4.9 Å in **3** are probably too small to accommodate a Ni(i) within the $Ni_8(\mu_4\text{-}P)_6$ cage to give a cluster analogous to **7**. The unusually short eight Ni(i)-Ni(s) distances of 2.31 Å in **2** imply strong radial interactions between the Ni(i) AOs and appropriate cage Ni(s) orbitals. (3) Although **2** and **5** contain similar-sized E atoms and have the same number (124) of CVEs, their cage geometries are very different. Whereas the distances in **2** suggest that the Ni(i)-centered $Ni_8(\mu_4\text{-}Ge)_6$ cage is stabilized by both radial bonding Ni(i)-Ni(s) and tangential (edge-bridged) bonding Ni(s)-Ni(s′) interactions, those in **5** signify no edge-bridged bonding Pd(s)-Pd(s′) interactions but instead indicate that the Pd(i) is involved in radial bonding interactions with the six capping As atoms as well as with the eight Pd(s) atoms. These geometrical differences are partly attributed to the less contracted valence Pd AOs forming stronger bonding interactions at longer distances. Although similarly large bond-length differences are observed between the Pd(i)-centered $Pd_8(\mu_4\text{-}Sb)_6$ cage of the 124-electron **6** and the Ni(i)-centered $Ni_8(\mu_4\text{-}Te)_6$ cage of the 130-electron **7**,[17,18] their different electron counts prevent an unambiguous qualitative bonding analysis. (4) Both the radial bonding Ni(i)-Ni(s) and edge-bridged bonding Ni(s)-Ni(s′) interactions are presumed to be considerably smaller in **7** than in **2** on account of the 0.2-Å-longer distances in **7**. (5) From bonding considerations under O_h symmetry, it is proposed that the four "extra" electrons in the 124-electron **2** occupy an additional doubly-degenerate pair of antibonding radial MOs originating from the 3d (e_g) AOs of the interstitial Ni(i); the stronger radial interactions of the 3d (t_{2g}) Ni(i) AOs with the cage Ni(s) orbitals are presumed to produce *occupied* bonding but *empty* antibonding MOs. This structural-bonding analysis of **2** shows that general electron-counting rules[9] will need to be revised for $M_8(\mu_4\text{-}E)_6$ cubic-caged clusters containing late first-row transition metals as interstitial atoms.

Work is in progress to characterize other compounds from reactions of **1** with $EtGeCl_3$; these include the $[Ni_{11}(GeEt)_2(CO)_{18}]^{2-}$ dianion, which has a nickel-centered icosahedral $Ni_{10}Ge_2$ cage, and the trigonal-bipyramidal Ni(II) $[Ni(GeEtCl_2)_4(CO)]^{2-}$ complex. Fenske-Hall MO calculations are also being carried out[19,20] as operational tests of the bonding interpretations presented herein.

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Supplementary Material Available: A figure showing a mass spectrum of **2** and tables listing atomic parameters, interatomic distances, and bond angles of **2** (7 pages); listing of structure factor amplitudes of **2** (11 pages). Ordering information is given on any current masthead page.

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(17) An EHMO treatment[18] of the corresponding hypothetical 130-electron $[Ni_9(\mu_4\text{-}Te)_6(H)_8]^{8-}$ under O_h symmetry gave triply-degenerate HOMOs (t_{2g}) containing four electrons with closely spaced (<0.1 eV) doubly-degenerate LUMOs (e_g).

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(19) The indicated diamagnetism[13] of **2** is completely consistent with the results of preliminary Fenske-Hall MO calculations[20] for the 124-electron $Ni_9(\mu_4\text{-}GeH)_6(CO)_8$ (in which H atoms are substituted for Et substituents). The filled doubly-degenerate HOMOs are well-separated (ca. 2.9 eV) from the triply-degenerate LUMOs.

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Organoyttrium-Catalyzed Cyclization of Substituted 1,5- and 1,6-Dienes

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Cyclization of dienes, diynes, and enynes promoted by various organometallics represents an extremely powerful means to convert simple, readily accessible substrates to more complex organic molecules.[2] Our interest in utilizing lanthanide reagents for stereoselective organic transformations[3] has prompted us to explore employment of organolanthanide and group 3 organometallic catalysts for selective carbon-carbon bond formation. In this initial effort we report the first use of organoyttrium catalysts in reductive cyclization reactions of 1,5- and 1,6-dienes.

In related work, unsaturated organotitaniums undergo intramolecular olefin insertion,[4] and organoscandiums have been reported to promote cyclization of simple, unfunctionalized 1,5- and 1,6-dienes.[5] However, the former process is not catalytic, and stereochemical issues, functional group compatibility,[6] and a facile catalyst synthesis were not addressed in the latter study. More

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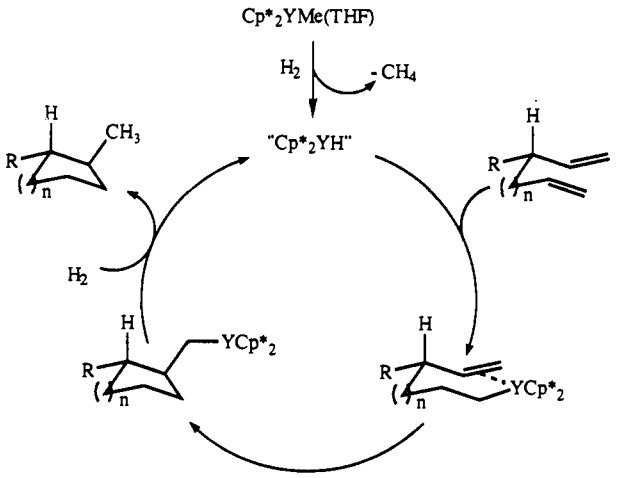
Scheme I



complete development of organolanthanide and group 3 organometallic catalysts which includes resolution of these issues thus becomes of paramount importance for their application in selective organic synthesis. The initial aim of our work was to attain a rapid annulation of 1,5- and 1,6-dienes with high stereochemical control. Furthermore, we wished to study the compatibility of these catalysts with various functional groups. The catalytic cycle investigated is outlined in Scheme I. All of the individual steps of this transformation are well precedented,[7] and precedent exists for the overall process as well.[5]

Cyclization of 1,5-hexadiene was initially explored utilizing $[Cp^*_2YH]_2$ as a catalyst in the presence of H_2.[7d] However, it was subsequently determined that a more convenient protocol for reductive cyclization involved generation of the requisite "organoyttrium hydride" in situ from $Cp^*_2YMe(THF)$.[8] Thus, treatment of 1,5-hexadiene with 5 mol % of $Cp^*_2YMe(THF)$ in 0.5 M benzene under 1–2 atm of H_2 resulted in complete conversion to methylcyclopentane within 45 min at room temperature (Table I).[9] As can be seen in Table I for substrates **1–9**, this process proved general for a variety of 1,5- and 1,6-dienes, and excellent yields and diastereoselectivities[10] were achieved in most cases.

Several features of the reaction are noteworthy. The first is that, in spite of the "extreme Lewis acidity" of the electron-deficient organoyttrium catalyst,[5b,6] functional groups such as ethers, acetals, and dithioacetals survive the reaction intact. The incorporation of bulky alkoxy groups such as the trityl ether moiety into the 1,5-dienes produces products with pronounced regio- and diastereoselectivities. The enhanced regioselectivity can be rationalized by initial reaction of the organoyttrium hydride with the least sterically hindered and most electron rich olefin, with subsequent cyclization resulting in formation of 1,2-disubstituted

Table I. Catalytic $Cp^*_2YMe(THF)$ Cyclization of Substituted Dienes

substrate	Product(s) (% Isolated Yield)[a]		R	diastereoselectivity[b]
1a	2a (91)[c]	(0)	H	
1b	2b (84)	(5)	OBn	6:1
1c	2c (91)	(0)	OTBS	4:1
1d	2d (99)	(0)	$OCPh_3$	21:1
1e	2e (91)	(8)	Ph	>100:1
3a	4a (82)	(5)	OTBS	1.5:1
3b	4b (70)	(25)	$OCPh_3$	>100:1
5	6 (97)	(2)		
7	8 (85)	(5)		
9	10 (53)	(26)		
11	12 (64)			
13a			CN	No Cyclization
13b			CO_2Me	No Cyclization
13c			SO_2Ph	No Cyclization

[a] Isolated by distillation as a mixture of the indicated products. All of these compounds have been fully characterized spectroscopically (^1H NMR, ^{13}C NMR, IR), and elemental composition has been established by high-resolution mass spectrometry and/or combustion analysis. [b] Refers to diastereoselectivity of major product determined on the crude reaction mixture by fused silica capillary gas chromatography. [c] NMR yield.

cyclopentanes in preference to 1,3-disubstituted cyclopentanes. If an alkoxy-directed reaction had occurred,[5b,11] a 1,3-disubstitution pattern would have been expected. The sense of relative asymmetric induction is in line with the predicted chair-like transition structure depicted in Scheme I.

Cyclization of 1,6-dienes is also quite efficient, although the reaction is complicated by reduction of the olefins to form acyclic alkanes (substrates **3a–7**). Significant reduction is seen in a constrained molecule such as *o*-divinylbenzene (**9**), and entropic factors associated with the elongated Si–C bonds in substrate **11** are perhaps responsible for preventing annulation of the intermediate organoyttrium species in that case. Simple reduction again intercedes. Finally, use of selected functional groups (**13a–c**) totally inhibits the reaction. Irreversible reaction of the catalyst with these functional groups is probably responsible for these results, although studies are still underway to determine precisely the reason for failure in these cases.

In summary, promising results have been obtained for the organoyttrium-catalyzed reductive cyclization of substituted 1,5- and 1,6-dienes. The facile process which has been developed provides excellent selectivities and yields in many cases. In view of the fact that the organometallic catalyst is synthesized in a one-pot process, an attractive synthetic method for the construction of functionalized five- and six-membered rings has also been

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(9) The heterogeneous mixture was cooled to −78 °C and purged–filled 3× with hydrogen. After stirring at room temperature the mixture was filtered through 2 g of Florisil and distilled.

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established. Although nominal reduction of 1,6-dienes occurs utilizing the current protocol, further studies designed to optimize the organometallic catalyst by both "ligand tuning" and "metal tuning" are expected to resolve this problem.

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Supplementary Material Available: Complete experimental details and spectral data for all of the cyclization reactions described herein (38 pages). Ordering information is given on any current masthead page.

Novel and Versatile Strategy for the Synthesis of Prostanoids in the E, F, H, and I Series§

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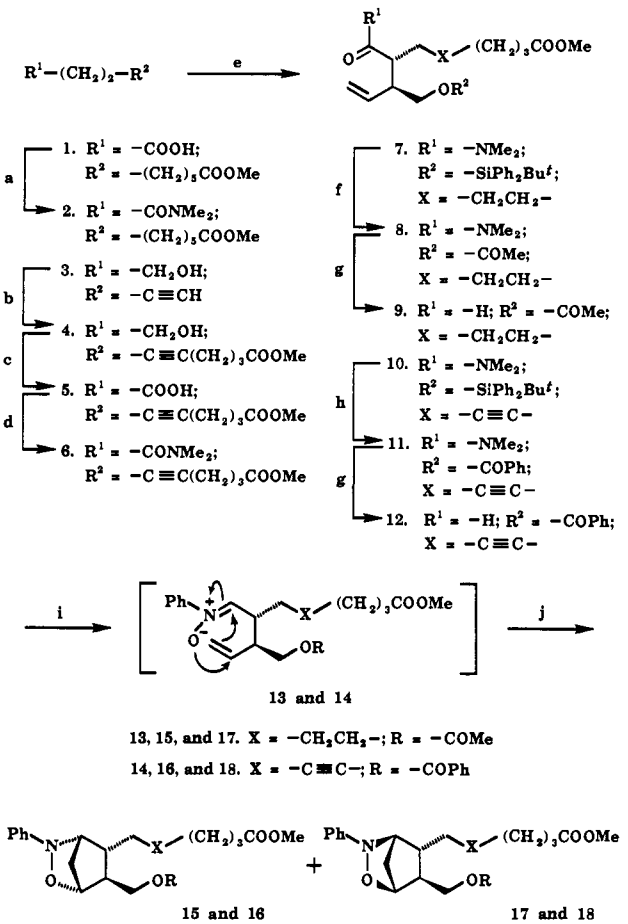
Prostaglandins (PGs) exist in most mammalian tissues.[1] Isolation of PGs from natural biosynthetic sources cannot meet their medicinal demand.[2] Total synthesis thus remains the only means by which sufficient quantities of prostanoids can be made available.[2,3] Herein we report a novel biomimetic, cascade-type synthesis[4] of various prostanoids via common 11α,9α-epoxyimino-PGHs (i.e., **25** and **27**).

Scheme I shows our four-step synthesis of alkenyl aldehyde **9** from the monomethyl ester of azelaic acid (**1**). The key step **2** → **7** involved a [3,3]-sigmatropic rearrangement,[5] by which two contiguous chiral centers were established. In the conversion of **8** to **9**, we were able to reduce a tertiary amide selectively in the presence of a C=C and two ester functionalities to an aldehyde in 50% yield by using MeOTf and L-Selectride in sequence.[6]

We then condensed this readily available aldehyde (**9**) with PhNHOH in the presence of 5A molecular sieves to give the corresponding alkenyl nitrone **13** (Scheme I). Various temperatures (105–180 °C) were used for the thermolysis of nitrone **13** in situ to give [3 + 2] cycloadducts, isoxazolidines **15** and **17**, in 54–75% overall yields. At 180 °C with 1,2-dichlorobenzene as the solvent, the cyclization took only 4 min and gave isoxazolidines **15** and **17** in a ratio of 1:1.

We elongated the ω-chain of **15** to give enone **21** through the procedures shown in Scheme II. For the synthesis of prostanoids

Scheme I[a]



[a] a: (1) $SOCl_2$, 80 °C; (2) Me_2NH, H_2O (87%). b: (1) $LiNH_2$, NH_3, Et_2O; (2) $Br(CH_2)_3C(OMe)_3$, –33 °C (84%).[18,19] c: CrO_3, 4.0 M H_2SO_4 (aq), Me_2CO, room temperature (83%). d: $(COCl)_2$, Me_2NH, room temperature (87%). e: (1) MeOTf, CH_2Cl_2, room temperature; (2) *cis*-$LiOCH_2CH{=}CHCH_2OSiPh_2Bu^t$, THF, Δ (for **2** → **7**, 69%; for **6** → **10**, 72%).[5] f: (1) *n*-Bu_4NF, THF; (2) Ac_2O, Et_3N, room temperature (98%). g: (1) MeOTf, CH_2Cl_2, room temperature; (2) L-Selectride, THF, –78 °C; (3) H_3O^+ (for **8** → **9**, 50% for **11** → **12**, 64%).[6] h: (1) *n*-Bu_4NF, THF; (2) $(PhCO)_2O$, Et_3N, room temperature (98%). i: PhNHOH, 5A molecular sieves, solvent. j: Δ.[4]

in optically active form, enone **21** was reduced asymmetrically with (*S*)-BINAL-H[7,8] to give diastereomeric allylic alcohols (–)-**25** (36% yield, 86% e.e.) and (+)-**28** (38% yield, 78% e.e.) in 74% overall yield. Saponification of (–)-**25** with NaOH in MeOH provided (–)-11α,9α-epoxyimino-PGH_1 sodium salt **26** in 88% yield.

An efficient method for the conversion of epoxyimino-PGH (–)-**25** to (–)-PGE_1 is appealing because PGEs possess therapeutic value[9] and can be further converted to PGA, PGB, and PGC.[3] Thus we oxidized[10,11] (–)-**25** with *m*-CPBA to afford PGE_1 ester (–)-**30** in 65% yield (Scheme II). Finally, a total synthesis of (–)-PGE_1 was accomplished by saponification of ester (–)-**30** with bakers' yeast.[12]

To demonstrate the versatility of 11α,9α-epoxyimino-PGHs as a common precursor for other types of PGs, we also degraded (–)-**25** to a prostanoid in the F series (Scheme II). Thus reductive

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§ Cordially dedicated to Professor James P. Collman on the occasion of his 60th birthday.

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