Alkenylzinc-Mediated Approach to the Vitamin D Skeleton. Application to the Synthesis of 6-Methyl Analogs of Vitamin and Previtamin D

Ana M. García, José L. Mascareñas, Luis Castedo, and Antonio Mouriño*

Departamento de Química Orgánica y Unidad Asociada al CSIC, Universidad de Santiago de Compostela, 15706 Santiago de Compostela, Spain

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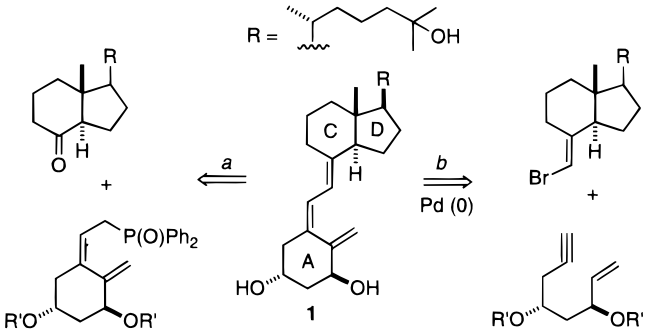
Palladium-catalyzed cross-coupling of alkenylzinc reagents, bearing the C,D-ring/side chain portion, and (*Z*)-1-iodo-1,3-bis-exocyclic dienes (as A-ring precursors), provides a mild, convergent entry to the vitamin D skeleton, that is suitable for the synthesis of thermally labile derivatives such as those bearing substituents on the triene system.

Introduction

An increasing body of evidences suggests that the hormone 1α,25-dihydroxyvitamin D_3 [**1**, 1α,25-$(OH)_2$-D_3; Scheme 1], in addition to its well known functions in calcium and phosphate metabolism,[1] plays a critical role in regulation of the proliferation and differentiation of a large variety of malignant cells.[2] It has also been reported to have a complex role in the immune system[2d] and possibly to be of use in the treatment of multiple sclerosis.[3] These findings have considerably stimulated research aimed at the development of nontoxic vitamin D derivatives suitable for use as drugs for the treatment of hyperproliferative diseases such as psoriasis and cancer and of immunological conditions such as autoimmune diseases and graft rejection.[4]

Although a variety of strategies for the synthesis of the natural hormone **1** and its analogs have been reported, there remains a need for more practical and versatile approaches.[5] The greatest flexibility is offered by convergent strategies in which the C/D-side chain and A-ring fragments are elaborated separately. The classical Lythgoe approach, relying on the coupling between A-ring phosphine oxides and upper-part ketones (route a, Scheme 1), provides an excellent stereoselective entry to the natural triene system.[6] Unfortunately, preparation of the required A-ring fragment usually entails numerous, scarcely flexible steps.[7]

Scheme 1



This problem was to some extent overcome by the introduction of a particularly elegant convergent strategy based on a Pd-catalyzed tandem carbometalation−cyclization (route b, Scheme 1).[8] In this approach, the vitamin D triene system is assembled in a single operation, from relatively simple and readily accessible acyclic A-ring precursors, considerably speeding up the synthetic process and providing a means for the synthesis of diverse analogs modified at the A-ring. A drawback to this approach is that heating is required for achieving the palladium-catalyzed coupling, which restricts its application to the synthesis of thermally stable derivatives.[9]

[⊗] Abstract published in *Advance ACS Abstracts,* August 1, 1997.

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(4) In recent years, a wide range of analogs of **1** with weak calcemic effects have been prepared, some of which have been shown to be promising drugs for the treatment of psoriasis and certain cancers: (a) Ikekawa, N. *Med. Chem. Rev.* **1987**, *7*, 333. (b) Abe, J.; Morikawa, M.; Miyamoto, K.; Kaiho, S.; Fukushima, M.; Miyaura, C.; Abe, E.; Suda, T.; Nishii, Y. *FEBS Lett.* **1987**, *226*, 58. (c) Ostrem, V. K.; Lau, W. F.; Lee, S. H.; Perlman, K.; Prahl, J.; Schnoes, H. K.; DeLuca, H. F. *J. Biol. Chem.* **1987**, *262*, 14164. (d) Shiuey, S. J.; Partridge, J. J.; Uskokovic, M. R. *J. Org. Chem.* **1988**, *53*, 1040. (e) Zhou, J.; Norman, A. W.; Lubbert, M.; Collins, E. D.; Uskokovic, M. R.; Koeffler, H. P. *Blood* **1989**, *74*, 82. (f) Perlman, R. R.; Sicinski, H. K.; Schnoes, H. K.; DeLuca, H. F. *Tetrahedron Lett.* **1990**, *31*, 1823. (g) Figadere, B.; Norman, A. W.; Henry, H. L.; Koeffler, H. P.; Zhou, J.-Y.; Okamura, W. H. *J. Med. Chem.* **1991**, *34*, 2452. (h) Kissmeyer, A.-M.; Binderup. L. *Biochem. Pharmacol.* **1991**, *41*, 1601. (i) Zhou, J.-Y; Norman, A. W.; Akashi, M.; Chen, D.-L.; Uskokovic, M. R.; Aurrecoechea, J. M.; Dauben, W. H.; Okamura, W. H.; Koeffler, H. P. *Blood* **1991**, *78*, 75. (j) Binderup, L. *Biorg. Med. Chem. Lett.* **1993**, *3*, 1891.

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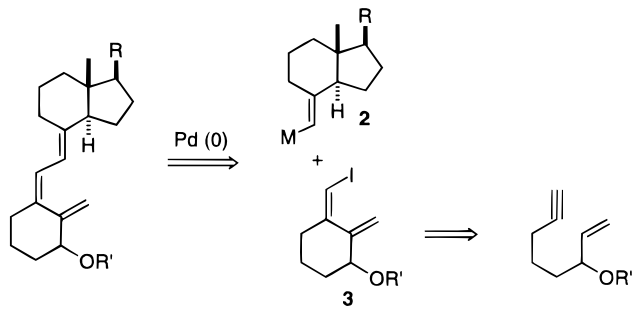
(7) For more recent approaches, see: (a) Vryelink, S.; Vandewalle, M.; García, A. M.; Mascareñas, J. L.; Mouriño, A. *Tetrahedron Lett.* **1995**, *36*, 9023. (b) Acmatowicz, B.; Jankowski, P.; Wicha, J. *Tetrahedron Lett.* **1996**, *37*, 5589.

(8) (a) Trost, B. M.; Dumas, J. *J. Am. Chem. Soc.* **1992**, *114*, 1925. (b) Trost, B. M.; Dumas, J.; Villa, M. *J. Am. Chem. Soc.* **1992**, *114*, 9836.

(9) Most vitamin D derivatives equilibrate with their previtamin isomers under the coupling conditions. It has recently been reported that the Trost methodology was of limited utility for the synthesis of oxa-A-ring analogs : Daniel, D.; Middleton, R.; Henry, H. L.; Okamura, W. H. *J. Org. Chem.* **1996**, *61*, 5617.

S0022-3263(97)00605-1 CCC: $14.00

Scheme 2



We have recently discovered that the conjugated triene system of vitamin D can be efficiently assembled under mild conditions by coupling alkenyl-organometallic reagents bearing the C,D-ring/side chain portion (**2**) with A-ring iododiene units (**3**) derived from acyclic precursors (Scheme 2).[10]

Herein we describe the full details of this approach and its application to the synthesis of 3-deoxy-1α− and 1β-hydroxyvitamin D_3. We also demonstrate its potential for the synthesis of thermally labile derivatives such as those in which the triene system bears substituents. These types of analogs are difficult to make by other approaches and might prove useful for evaluation of the role of the triene system in biological activity,[11] and also for studying the chemistry of vitamin−previtamin isomerization.[12]

Results and Discussion

Zirconocene-Mediated Approach to the A-Ring Iododiene Unit 6b. The key step in the synthesis of the (*Z*)-1-iodovinyl bis-exocyclic A-ring precursors was a zirconium-promoted cyclization-iodonolysis of acyclic 1,7-enynes.[13] The required silylated enyne **4c**[13c,d] was readily prepared by treatment of **4b**[14] with methyllithium and trapping the resulting acetylide with TMSCl. Using the classical conditions developed by Negishi for the cyclization-iodonolysis reaction [(a) Cp_2ZrCl_2, *n*-BuLi; (b) I_2, THF], the desired diiodo derivative **5a** was obtained in yields ranging from 30 to 50%. Systematic modification of different reaction parameters revealed that more reproducible and slightly better yields (57%) can be obtained if the intermediate zirconacycle is slowly added to a cooled (−50 °C) solution of *N*-iodosuccinimide (NIS) in CH_2Cl_2. Using NBS instead of NIS provides the expected dibromo compound **5b**, albeit in a lower 23% yield. Changing the metal from Zr to Ti or using other iodinating agents did not provide better results. The stereochemistry of **5a** was assigned on the basis of previously reported data for the related compound **5c**.[13c,d] In the ^{1}H NMR spectrum of **5a**, in contrast to that of **5c** there was no observable coupling between H-1 and H-2, indicating that both these lay equatorial (Figure 1).[15]

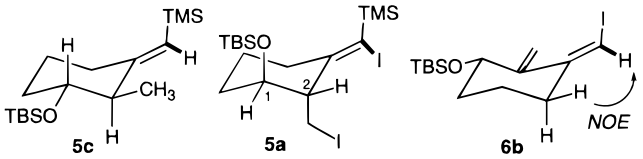
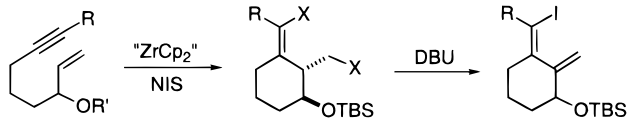


Figure 1.

Scheme 3



4a, R, R' = H
4b, R = H, R' = TBS
4c, R = TMS, R' = TBS

5a, R = TMS, X = I
5b, R = TMS, X = Br
5c, R = TMS, X = H
5d, R = H, X = I

6a, R = TMS
6b, R = H

The exocyclic double bond was efficiently introduced by treatment of **5a** with DBU in CH_2Cl_2 at room temperature for 12 h (90% yield), and the trimethylsilyl group was smoothly removed by reaction of **6a** with Cs_2CO_3 in DMF (84% yield). Compound **6b** can also be obtained by inverting the procedure, treating **5a** firstly with Cs_2CO_3 in DMF (or alternatively stirring it with KF in CH_3CN) to remove the trimethylsilyl group and then with DBU in CH_2Cl_2 (81% yield for both steps). Most interestingly, treatment of compound **5a** with excess of DBU (3 equiv) for five days at room temperature gave the desired vinyl iodide **6b** in a one-pot reaction in 97% yield. The (*Z*)-stereochemistry of compound **6b** was confirmed by ^{1}H NMR spectroscopy and NOE experiments (Figure 1). In summary, the desired A-ring precursor **6b** was obtained from the acyclic enyne **4b** in three steps and 53% overall yield.

Coupling of 6b with a Model Partner. To rapidly establish whether these vinyl iodides could be used as A-ring precursors of a typical vitamin D skeleton, the cross-coupling reaction of **6b** with the vinyltributyltin derivative **7** was attempted under typical Stille conditions.[16] Stirring a solution of **6b** and **7**[17] in DMF in the presence of $(CH_3CN)_2PdCl_2$ for two days at room temperature, followed by desilylation, provided the expected triene **8** in a 50% yield. The structure of this compound

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(11) Although the conjugated triene system of natural vitamin D is believed to be necessary for biological activity, there has been little research into the biological effect of modifying this triene system. However, several substituted derivatives have been synthesized and shown to have interesting activities: (a) Wilhelm, F.; Dauben, W. G.; Kohler, B.; Roesle, A.; Norman, A. W. *Arch. Biochem. Biophys.* **1984**, *233*, 127. (b) Gray, T. K.; Millington, D. S.; Maltby, D. A.; Williams, M. E.; Cohen, M. S.; Dodd, R. C. *Proc. Nat. Acad. Sci. U.S.A.* **1985**, *82*, 8218. (c) Shiina, Y. Y.; Miyaura, C.; Tanaka, H.; Abe, E.; Yamada, S.; Yamamoto, K.; Ino, E.; Takayama, H.; Matsunaga, I.; Nishii, Y.; Suda, T. *J. Med. Chem.* **1985**, *28*, 1153. (d) Steinmeyer, A.; Neef, G. *Tetrahedron Lett.* **1992**, *33*, 4879.

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(14) Compound **4b** was prepared by addition of vinylmagnesium bromide to 5-hexynal, followed by protection of the resulting alcohol with TBSCl, see: Ihle, N. C.; Heathcock, C. H. *J. Org. Chem.* **1993**, *58*, 560.

(15) The greater stability of this conformation is consistent with molecular mechanics calculations (MMX).

(16) (a) Stille, J. K. *Angew. Chem., Int. Ed. Eng.* **1986**, *25*, 508. (b) Stille, J. K.; Groh, B. L. *J. Am. Chem. Soc.* **1987**, *109*, 813. (c) Mitchel, T. N. *Synthesis* **1992**, 803. (d) Farina, V. *Pure Appl. Chem.* **1996**, *68*, 73.

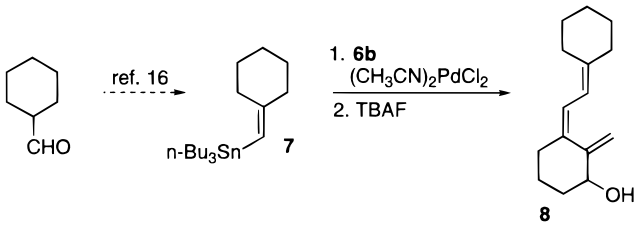
(17) Compound **7** was prepared by a known procedure: Nemoto, H.; Wu, X.-M.; Kurobe, H.; Minemura, K.; Ihara, M.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1185.

Table 1. Palladium-Catalyzed Cross-Coupling of 10 and 6b[a]

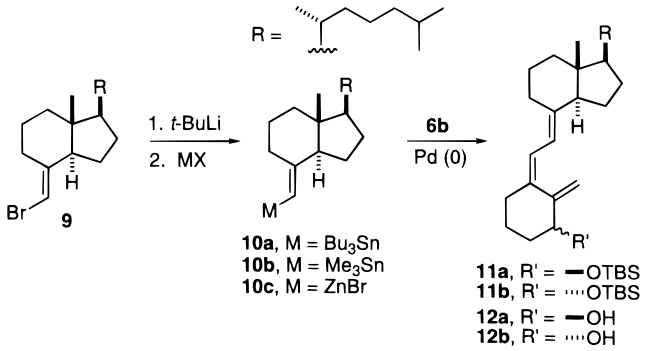
M	catalyst[b]	solvent	temp (°C)	time[c]	**11** (% yield)
n-Bu_3Sn	$(CH_3CN)_2PdCl_2$	DMF	25	3 days	–
n-Bu_3Sn	$(CH_3CN)_2PdCl_2$	DMF	60	1.5 day	–
n-Bu_3Sn	$(PPh_3)_2PdCl_2$/CuI (1:2)	THF	60	1 day	–
n-Bu_3Sn	Pd_2dba_3/TFP (1:2)	NMP[d]	25	3 days	–
Me_3Sn	$(CH_3CN)_2PdCl_2$	DMF	25	4 days	20
Me_3Sn	Pd_2dba_3/TFP (1:2)	NMP	25	2 days	23
Me_3Sn	Pd_2dba_3/TFP (1:2)	NMP	60	2 days	–
Me_3Sn	Pd_2dba_3/TFP/CuI (1:4:4)	DMF	25	4 days	33
BrZn	$Pd(PPh_3)_4$	THF−Et_2O	25	2 h	95

[a] 1.5 equiv of **6b** were used. [b] 5 mol %. [c] Until **6b** disappeared (TLC and NMR monitoring). [d] *N*-Methylpyrrolidinone.

Scheme 4



Scheme 5



was confirmed by comparison of its spectroscopic data with those previously reported.[18] Although a triene such as **8** is known to rapidly equilibrate with their previtamin isomers, the mild thermal conditions used in the coupling reaction allowed isolation of the vitamin type triene (a small amount of the previtamin form was detected in the ^{1}H NMR spectrum), which is not possible using coupling procedures that require thermal activation.[8]

Synthesis of 3-Deoxy-1α- and 1β-Hydroxyvitamin D_3. Following the success of the above experiment we investigated the coupling of vinyl iodide **6b** with stannane **10a**, which bears the C,D ring-side chain of the naturally occurring vitamin D skeleton. Compound **10a** was prepared by treatment of vinyl bromide **9**[8] with *t*-BuLi and trapping the resulting anion with tributyltin chloride. Unfortunately, initial attempts at cross-coupling **10a** and vinyl iodide **6b** using $(CH_3CN)_2PdCl_2$ as catalyst failed, even at temperatures higher than room temperature (Table 1). We then proceeded to study the effects of other catalysts, ligands, and additives. The results are summarized in Table 1. Note that no coupling was observed using additives such as CuI or ligands such as tris(2-furyl)phosphine (TFP), which have recently been reported to accelerate the Stille coupling reaction.[19] However, by using the less sterically demanding trimethyltin derivative **10b** as organometallic partner, we were able to isolate a mixture of protected diastereoisomeric vitamins **11a** and **11b**, albeit in low yield (20−33%).

Since the coupling reaction appeared to be mainly affected by the nature of the organometallic fragment, it was envisaged that use of an even less sterically demanding and more reactive derivative, such as an organozinc halide,[20] might give better results. To our delight, *room temperature* reaction (2 h) of iodide **6b** with **10c** in the presence of 5 mol % $Pd(PPh_3)_4$ gave the expected mixture of protected 1α- and 1β-hydroxy-3-deoxyvitamin D_3 derivatives **11** smoothly and in excellent yield (95%). These diastereoisomers were easily separated by flash chromatography and then deprotected by treatment with TBAF in THF. The structures of **11a** and **11b** were corroborated by comparison of the ^{1}H NMR spectra of their respective deprotected derivatives **12a** and **12b** with those of authentic samples.[21]

Synthesis of Analogs with a Triene-Substituted System. Having developed a mild, efficient approach to the natural vitamin D skeleton, we next examined the feasibility of using the same approach to prepare vitamin D analogs with a substituted triene system, compounds that are difficult to make by classical routes. Little is known about how substituents that can perturb the steric and electronic characteristics of the triene system affect the biological activity.[11,12] Since the presence of a methyl group at position 6 of vitamin D is known to considerably decrease the energetic barrier to its isomerization to the previtamin form,[22] we firstly attempted the synthesis of this type of derivatives, on the assumption that success would give a good indication of the suitability of this approach to the synthesis of thermally sensitive analogs.

In order to facilitate spectroscopic identification of the coupling products, the A-ring iododiene precursor was prepared in an optically active form. Sharpless kinetic resolution of the racemic allylic alcohol **4a** (Scheme 3), by reaction with titanium tetraisopropoxide, dicyclohexyl D-(−)-tartrate and *tert*-butyl hydroperoxide in CH_2Cl_2 at −20 °C,[23] gave the desired (*S*)-(−)-eninol **13a** almost quantitatively (45%, Scheme 6). The optical purity (>97% ee) was established by conversion of the alcohol **13a** to the corresponding (*S*)-(+)-*O*-methylmandelic ester

(18) Condran, P.; Okamura, W. H. *J. Org. Chem.* **1980**, *45*, 4011.
(19) (a) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585. (b) Farina, V.; Kapadia, S.; Krishnan, B.; Wang, C.; Liebeskind, L. S. *J. Org. Chem.* **1994**, *59*, 5905.
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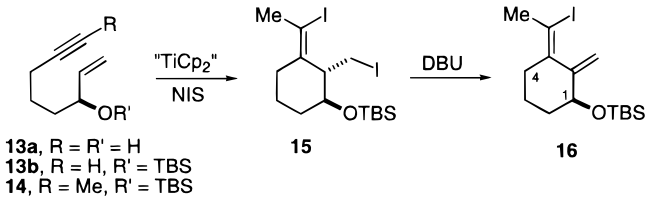
(21) (a) Condran, P.; Hammond, M. L.; Mouriño, A.; Okamura, W. H *J. Am. Chem. Soc.* **1980**, *102*, 6259. (b) Condran, P. Ph.D. Thesis, University of California, Riverside, 1980.
(22) Sheves, M.; Mazur, Y. *J. Chem. Soc., Chem. Commun.* **1977**, 21.
(23) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. K.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

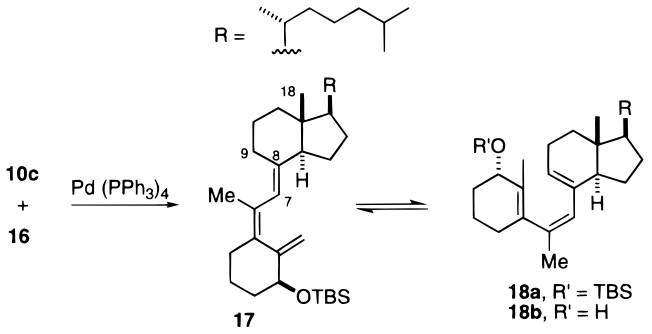
Scheme 6



13a, R = R' = H
13b, R = H, R' = TBS
14, R = Me, R' = TBS

15 **16**

Scheme 7



17 **18a**, R' = TBS
18b, R' = H

and comparison of its ^{1}H NMR spectrum with that of the mixture obtained by esterification of racemic **4a**.[24]

After silylation, treatment of **13b** with *n*-butyllithium and trapping of the resulting acetylide with MeI gave the enyne **14** in 94% yield. Cyclization−iodonolysis of **14** using Cp_2ZrCl_2 as organometallic promoter and NIS as iodine source gave the expected diiodide **15** in low yield (24%). In this case we found that Cp_2TiCl_2 provides slightly better results. Thus treatment of **14** with the titanocene complex obtained by reaction of Cp_2TiCl_2 with *n*-BuLi, followed by slow addition of the resulting mixture to a cooled solution of NIS in CH_2Cl_2, gave the diiodide **15** in 41% yield.

Diodide **15** was easily transformed into the iododiene **16** by treatment with DBU at room temperature (70% yield). The stereochemistry of the double bond was confirmed by the observation of NOE between the methyl group and the pseudoequatorial H-4.

Finally, a solution of iododiene **16** and zincate **10c** (Scheme 7) in THF containing 5 mol % of $(PPh_3)_4Pd$ was stirred at room temperature for 2 h to give the desired vitamin derivative **17** in an excellent 94% yield. The structure of this compound was confirmed by spectroscopic analysis. The ^{1}H NMR spectrum shows, as more relevant, the peaks of the three alkenyl hydrogens of the triene portion, and the singlet at 0.51 ppm due to the C_{18}-CH_3, characteristic of a vitamin D type structure. As previously described by Mazur for 6-methylvitamin D_3,[22] the UV spectrum of the 6-substituted vitamin **17** differs from that of the natural vitamins, in that their absorption maxima appears at considerably shorter wavelength (λ = 242 nm for the methyl derivative **17** as against λ = 264 nm for an unsubstituted vitamin). This shift has been attributed to deviations in the planarity of the conjugated system due to steric interactions between the methyl group and H-9.[22]

As expected, the 6-methylvitamin D analog **17** showed a great propensity to isomerize to the corresponding previtamin D form **18a**. Thus, we found that the isomerization equilibrium lies completely in favor of the previtamin isomer, and were able to calculate a half life of 15.3 h in CD_2Cl_2 at 37 °C. The isomerization was easily followed and quantified by integration of the ^{1}H NMR signal due to the 18-CH_3, which appears at 0.51 ppm for the vitamin D form and at 0.66 ppm for the previtamin D form. The origin of the increased rate of isomerization with respect to that for unsubstituted vitamin D most probably lies in the predisposition of the methyl-substituted vitamin to adopt the 6,7-*cis* conformation required for the [1,7]-sigmatropic hydrogen shift. The deprotected previtamin derivative **18b** was easily obtained by treatment of **18a** with TBAF in THF (65%).

(24) Only one enantiomer could be detected by ^{1}H NMR.

Conclusion

Palladium-catalyzed coupling of acyclic iododienes (as A-ring precursors) with alkenylzinc reagents bearing the C/D ring-side chain of vitamin D_3 provides a new, efficient entry to the vitamin D skeleton. In contrast to other convergent approaches that require high temperatures to assemble the triene system,[8] this coupling reaction proceeds under mild conditions, thus allowing preparation of thermally sensitive vitamin D analogs such as those bearing substituents on the triene system. By way of example, we prepared 3-deoxy-1α-[(*tert*-butyldimethylsilyl)oxy]-6-methylvitamin D_3, a compound that is extremely prone to undergo equilibration to the corresponding previtamin isomer under gentle thermal activation.

Experimental Section

General Procedures. See preceding paper.[25]

3-[(*t*-Butyldimethylsilyl)oxy]-1-octen-7-yne (4b). Vinylmagnesium bromide (76 mL, 76 mmol, 1 M in THF) was added to a solution of 5-hexynal (5 g, 51 mmol) in THF (60 mL) at −78 °C.[14] The reaction mixture was allowed to reach rt and stirred for 12 h. The reaction was quenched with aqueous NH_4Cl (20 mL) and extracted with Et_2O (3 × 15 mL). The combined organic phases were washed with aqueous HCl (5%), dried, and concentrated in vacuo. The residue was filtered through a short pad of silica gel eluting with 10% EtOAc/hexane to give the allylic alcohol **4a** (3.3 g, 52% yield, viscous oil). *t*-Butyldimethylsilyl chloride (5.2 g, 34.6 mmol) and imidazole (5.8 g, 85.1 mmol) were added to a solution of this compound in DMF (30 mL) . The mixture was stirred at rt for 12 h, poured into H_2O (10 mL), and extracted with CH_2Cl_2. The combined organic layers were washed with brine (15 mL), dried, filtered, and concentrated. Flash chromatography of the residue (4% EtOAc/hexanes) gave 5.7 g of the enyne **4b** [46% yield from hexynal, R_f = 0.7 (10% EtOAc/hexanes), colorless oil]. ^{1}H NMR δ: 5.8 (1 H, ddd, J = 17.2, 10.4 and 6.0), 5.15 (1 H, ddd, J = 17.0, 1.6 and 1.5), 5.04 (1 H, ddd, J = 10.0, 1.8 and 1.5), 4.14 (1 H, m), 2.19 (2 H, m), 1.95 (1H, t, J = 2.6), 1.56−1.60 (4 H, m), 0.06, 0.04 (6 H, 2 s); ^{13}C NMR δ: 141.6 (CH), 113.8 (CH_2), 84.4 (C), 73.3 (CH), 68.2 (CH), 37 (CH_2), 25.8 (CH_3), 24 (CH_2), 18.4 (CH_2), 18.3 (C), −4.9, −4.5 (CH_3).

3-[(*t*-Butyldimethylsilyl)oxy]-8-(trimethylsilyl)-1-octen-7-yne (4c). A solution of **4b** (500 mg, 2.09 mmol) in Et_2O (5 mL) was slowly added to MeLi·LiBr (3 mL, 4.5 mmol, 1.5 M in Et_2O) at −20 °C. Freshly distilled TMSCl (0.8 mL, 6.3 mmol) was added, and the mixture stirred at rt for 7 h. The reaction was quenched with aqueous HCl (5 mL, 5%), poured into brine, and extracted with Et_2O. The combined organic layers were dried, filtered, and concentrated. Flash chromatography (hexanes) gave **4c** [572 mg, 88%, R_f = 0.6 (3% EtOAc/hexanes), colorless oil]. ^{1}H NMR δ: 5.79 (1 H, ddd, J = 17.2, 10.4, and 6.0), 5.15 (1 H, ddd, J = 17.1, 1.8, and 1.5), 5.03 (1 H, ddd, J = 10.4, 1.8 and 1.3), 4.12 (1 H, m), 2.23 (2 H, br t, J = 6.5), 1.6 (4 H, m), 0.9 (9 H, s), 0.14 (9 H, s), 0.06, 0.04 (6

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H, 2 s); ^{13}C NMR δ: 141.5 (CH), 113.7 (CH_2), 107.4 (C), 84.5 (C), 73.3 (CH), 37.0 (CH_2), 26.0 (CH_3), 24.0 (CH_2), 19.7 (CH_2), 18.0 (C), 1.0 (CH_3), −4.5, −5 (CH_3); LRMS [*m*/*z* (%)]: 310.2 (M^+, 1), 283 (7), 253.2 (M^+ − *t*-Bu, 9), 179.05 (M^+ − OTBS, 3), 147 (100); HRMS calcd for $C_{17}H_{34}OSi_2$: 310.2148; found: 310.2142.

(1*S, 2*S**, 3*Z*)-1-[(*t*-Butyldimethylsilyl)oxy]-3-[(trimethylsilyl)iodomethylene]-2-(iodomethyl)cyclohexane (5a).** *n*-BuLi (0.8 mL, 1.96 mmol, 2.46 M in hexanes) was added dropwise to a solution of Cp_2ZrCl_2 (290 mg, 0.98 mmol) in THF (6 mL) at −80 °C. The mixture was allowed to warm to −55 °C in 1 h, and a solution of enyne **4b** (200 mg, 0.64 mmol) in THF (4 mL) was added dropwise *via* cannula. The reaction mixture was allowed to warm to rt and stirred for 7 h. The resulting solution was slowly added to a solution of NIS (436 mg, 1.96 mmol) in CH_2Cl_2 at −80 °C. The mixture was stirred for 1 h at −50 °C and 1 h at rt and poured into saturated aqueous NH_4Cl (10 mL). The resulting suspension was filtered through a pad of Celite and extracted with hexanes. The combined organic phases were dried, filtered, and concentrated in vacuo. Flash chromatography (hexanes) yielded the diiodide **5a** [207 mg, 57%, R_f = 0.8 (2% EtOAc/hexanes), glassy solid]. ^{1}H NMR δ: 4.27 (1 H, m), 3.40 (1 H, m), 3.15 (2 H, m), 2.75 (1 H, br d, J = 14.0), 1.90 (1 H, m), 1.80−1.20 (4 H, m), 0.87 (9 H, s), 0.28 (9 H, s), 0.14, 0.06 (6 H, 2 s); ^{13}C NMR δ: 156.3 (C), 109.5 (C), 71.3 (CH), 59.0 (CH), 31.0 (CH_2), 28.0 (CH_2), 26.0 (CH_3), 21.0 (CH_2), 18.0 (C), 4.4 (CH_2), 2.2 (CH_3), −4.9 (CH_3), −4.7 (CH_3); LRMS [*m*/*z* (%)]: 549 (M^+− Me, 0.3), 506.9 (M^+ − *t*-Bu, 20), 307 (27), 184.9 (32), 73 (100); HRMS calcd for $C_{17}H_{34}OI_2Si_2$ − C_4H_9: 506.9533, found: 506.9533.

(1*S, 2*S**, 3*Z*)-1-[(*t*-Butyldimethylsilyl)oxy]-3-[(trimethylsilyl)bromomethylene]-2-(bromomethyl)cyclohexane (5b).** This compound was obtained following a similar procedure to the above described for **5a** [23% yield, oil]. ^{1}H NMR δ: 4.31 (1 H, m), 3.65 (1 H, m), 3.4 (2 H, m), 2.6 (1 H, br d, J = 13.6), 1.96−1.47 (5 H, m), 0.86 (9 H, s), 0.26 (9 H, s), 0.10, 0.06 (6 H, 2 s); ^{13}C NMR δ: 150.2 (C), 126.7 (C), 69.3 (CH), 52.2 (CH), 31.9 (CH_2), 30.3 (CH_2), 28.1 (CH_2), 25.6 (CH_3), 20.7 (CH_2), 17.8 (C), 1.05 (CH_3), −4.9 (CH_3), −4.7 (CH_3); LRMS [*m*/*z* (%)]: 412.9 (M^+ − *t*-Bu, 12), 340.9 (0.3), 331 (5), 259 (70), 73 (100); HRMS calcd for $C_{17}H_{34}OBr_2Si_2$ − C_4H_9: 412.9790, found: 412.9793.

(3*Z*)-1-[(*t*-Butyldimethylsilyl)oxy]-2-methylene-3-(iodomethylene)cyclohexane (6b). DBU (0.8 mL, 5.31 mmol) was added to a solution of **5a** (200 mg, 0.35 mmol) in CH_2Cl_2 (4 mL) at 0 °C . The reaction mixture was stirred at rt for 5 days. The solvent was removed under reduced pressure and the residue diluted with hexanes and washed with H_2O (15 mL). The organic layer was dried, filtered, and concentrated. Flash chromatography (hexanes) gave **6b** [125 mg, 97%, R_f = 0.5 (5% EtOAc/hexanes), colorless oil]. ^{1}H NMR δ: 6.06 (1 H, br s), 5.33 (1 H, t, J = 1.8), 5.05 (1 H, t, J = 1.7), 4.06 (1 H, m), 2.50 (1 H, m), 2.3 (1 H, m), 2.00−1.80 (2 H, m), 1.70−1.40 (2 H, m), 0.90 (9 H, s), 0.40, 0.30 (6 H, 2 s); ^{13}C NMR δ: 150.5 (C), 150.1 (C), 110.9 (CH), 73.1 (CH_2), 72.1 (CH), 38.1 (CH_2), 36.7 (CH_2), 25.8 (CH_3), 23.4 (CH_2), 18.2 (C), −5.1, −4.8 (CH_3); LRMS [*m*/*z* (%)]: 364 (M^+, 0.04), 349 (M^+ − Me, 1), 307 (M^+ − *t*-Bu, 100), 233 (M^+ − OTBS, 8); HRMS calcd for $C_{14}H_{25}OISi$ − C_4H_9: 307.0015; found: 307.0011.

Coupling of 6b and 7. A mixture of iododiene **6b** (60 mg, 0.16 mmol), stannane **7**[17] (40 mg, 0.10 mmol), and $(CH_3CN)_2PdCl_2$ (approximately 4 mg) in DMF (5 mL) was stirred for 48 h at rt. The reaction was quenched with aqueous NH_4OH, poured into brine (10 mL), and extracted with CH_2Cl_2. The combined organic phases were dried and concentrated in vacuo. The residue was dissolved in THF (6 mL) and treated with TBAF (0.15 mL, 0.15 mmol, 1.0 M in THF). After stirring in the dark for 2 h at rt, the mixture was poured into brine (10 mL), extracted with Et_2O, dried, filtered, and concentrated in vacuo. Flash chromatography (5% EtOAc/hexanes) afforded compound **8** [15 mg, 50%].[18] ^{1}H NMR δ: 6.23 and 6.10 (2 H, AB, J = 11.4), 5.28 (1 H, s), 4.93 (1 H, s), 4.16 (1 H, m), 2.38−2.11 (4 H, m), 2.07−1.8 (2 H, m), 1.6 (4 H, m), 1.23 (4H, m), 0.95 (2 H, m).

Procedure for the Preparation of Stannanes 10a and 10b. Exemplified for the preparation of **10b**: *tert*-butyllithium (0.32 mL, 0.63 mmol, 1.95 M in pentane) was added to a solution of bromide **9**[8] (100 mg, 0.29 mmol) in THF (2 mL) at −78 °C. The mixture was stirred for 1 h, and *n*-Bu_3SnCl (75.5 mg, 0.37 mmol) was added. The reaction mixture was stirred for 12 h at rt and quenched with H_2O (10 mL). The resulting mixture was extracted with hexanes, and the combined organic phases were dried, filtered, and concentrated. The oily residue (112 mg, ≈91%) was proved to be primarily the desired stannane **10b** by ^{1}H NMR. This crude was subjected to the coupling reaction without any further purification. ^{1}H NMR δ: 5.26 (1 H, s), 2.2 (1 H, m), 0.92 (3 H, d, J = 5.8), 0.87 (6 H, d, J = 6.1), 0.54 (3 H, s), 0.14 (9 H, s); ^{13}C NMR δ: 158.7 (C), 117.3 (CH), 57.9, 56.6, 45.5, 40.36, 39.5, 37.8, 37.4, 36.1, 29.7, 27.9, 27.5, 24.4, 23.9, 22.8, 22.5, 22.4, 22.2, 18.8, 11.9, −8.6; LRMS [*m*/*z* (%)]: 411.2 (M^+ + H^+ − Me, 100), 410.2 (M^+ − Me, 41), 409.2 (73), 408.2 (31), 407.2 (41). **10a**: ^{1}H NMR δ: 5.20 (1 H, s), 2.17 (1 H, m), 0.52 (3 H, s).

Coupling of Iodide 6b with Trimethylstannane 10b. A mixture of iodide **6b** (31 mg, 0.085 mmol), stannanne **10b** (32 mg, 0.074 mmol), and $(CH_3CN)_2PdCl_2$ (approximately 2 mg) in DMF (2 mL) was stirred at rt for 4 days. The reaction was poured into H_2O (5 mL) and extracted with hexanes. The combined organic layers were dried, filtered, and concentrated in vacuo. Flash chromatography (hexanes) afforded the mixture of protected vitamins **11** [8 mg, 20%, R_f = 0.45 (hexanes)].

Coupling of Iodide 6b with Zincate 10c. Synthesis of 3-Deoxy-1α-[(*t*-butyldimethylsilyl)oxy]vitamin D_3 (11a) and 3-Deoxy-1*β*-[(*t*-butyldimethylsilyl)oxy]vitamin D_3 (11b). *tert*-Butyllithium (0.5 mL, 0.61 mmol, 1.3 M in pentane) was slowly added to a solution of bromide **9** (100 mg, 0.29 mmol) in Et_2O (2.5 mL) at −78 °C. The mixture was stirred for 15 min, and a solution of $ZnBr_2$ (71.8 mg, 0.32 mmol, freshly dried under vacuum) in Et_2O (2 mL) was added. After stirring at −10 °C for 1 h, the reaction mixture was cooled to −78 °C, and a solution of iodide **6b** (70 mg, 0.19 mmol) and $Pd(Ph_3P)_4$ (9 mg, 0.07 mmol) in THF (1 mL) was added. The resulting solution was allowed to reach rt and stirred for 2 h. The reaction was quenched with H_2O (3 mL), and the resulting mixture was extracted with hexanes. The combined organic layers were dried, filtered, and concentrated in vacuo. Flash chromatography (hexanes) afforded **11a** (45 mg) and **11b** (47 mg) [96% overall yield]. **11a**: ^{1}H NMR δ: 6.2 and 6.0 (2 H, AB, J = 11 Hz), 5.23 (1 H, br t, J = 1.8 Hz), 4.8 (1 H, br t, J = 1.8), 4.05 (1 H, m), 2.79 (1 H, br s), 0.93−0.82 (18 H, m), 0.52 (3 H, s), 0.06, 0.05 (6 H, 2 s); ^{13}C NMR δ: 150.1(C), 141.4 (C), 139.5 (C), 121 (CH), 118 (CH), 109.9 (CH_2), 74.3 (CH), 56.7, 56.4, 46.0, 41.0, 39.9, 37.8, 37.5, 36.5, 30.0, 29.3, 28.4, 28.1, 26.2, 24.4 24.2, 24.1, 22.9, 22.7, 22.6, 19.0, 18.0, 12.1, −4.7, −4.9. **11b**: ^{1}H NMR δ: 6.2 and 5.97 (2 H, AB, J = 11), 5.22 (1 H, br t, J = 1.8), 4.78 (1 H, br t, J = 1.5) 4.07 (1 H, m), 2.79 (1 H, m), 0.91−0.82 (18 H, m), 0.51 (3 H, s), 0.06 (6 H, 2 s); ^{13}C NMR δ: 150.1 (C), 141.4 (C), 139.5 (C), 121.1 (CH), 118 (CH), 109.9 (CH_2), 74.3 (CH), 57 (C), 56.7, 46, 40.1, 39.9, 37.8, 37.5, 36.5, 30.1, 29.3, 28.4, 28.1, 26.2, 24.3, 24.2, 23.9, 22.9, 22.7, 19.0, 12.0, −4.7, −4.9.

3-Deoxy-1α-hydroxyvitamin D_3 (12a) and 3-Deoxy-1*β*-hydroxyvitamin D_3 (12b). Exemplified for the deprotection of **11a**: tetrabutylammonium fluoride (0.03 mL, 0.03 mmol, 1 M in THF) was added to a solution of **11a** (14 mg, 0.028 mmol) in THF (1 mL). The reaction mixture was stirred at rt for 12 h and poured into H_2O (6 mL). The aqueous layer was extracted with Et_2O, and the combined organic layers were dried, filtered, and concentrated in vacuo. Flash chromatography gave the alcohol **12a** [8 mg, 80%, R_f = 0.25 (30% EtOAc/hexanes)]. **12a**: ^{1}H NMR δ: 6.27 and 5.98 (2 H, AB, J = 11.3), 5.24 (1 H, br t, J = 1.8), 4.88 (1 H, br t, J = 1.8), 4.04 (1 H, m), 2.81 (1 H, br d, J = 11), 2.13 (2 H, m), 0.91 (3 H, d, J = 6), 0.85 (6 H, br d, J = 6), 0.53 (3 H, s). **12b**: ^{1}H NMR δ: 6.28 and 5.98 (2 H, AB, J = 11.3), 5.23 (1 H, br t, J = 1.7), 4.86 (1 H, br t, J = 1.7), 4.09 (1 H, m), 2.8 (1 H, br d, J = 11), 2.23 (2 H, m), 0.90 (3 H, d, J = 6), 0.85 (6 H, br d, J = 6), 0.52 (3 H, s).

Kinetic Resolution of (±)-1-Octen-7-yn-3-ol (4a). Freshly distilled titanium tetraisopropoxide (1.5 mL, 5 mmol) was added to a stirred suspension of freshly activated powdered molecular sieves (600 mg), racemic **4a** (0.625 g, 5.09 mmol), and (2*S*,3*S*)-(−)-dicyclohexyl tartrate (1.9 g, 6 mmol) in CH_2Cl_2 (20 mL) at −20 °C. After stirring for 30 min, *t*-BuOOH (1.1 mL, 3.3 mmol, 3 M in isooctane) was added to the mixture cooled at −40 °C. The reaction flask was placed in the freezer (−20 °C) for 18 days and then poured into an ice-cooled suspension of $FeSO_4 \cdot 7H_2O$ (3.3 g) and tartaric acid (1 g) in H_2O (10 mL). The mixture was extracted with Et_2O (3 × 15 mL), and the combined organic layers were washed with brine (15 mL), dried, filtered, and concentrated in vacuo. Flash chromatography (15% EtOAc/hexanes) afforded **13a** (280 mg, 45%, >97% ee by ^{1}H NMR analysis of the (S)-(+)-*O*-methylmandelic ester derivative and compared with that of the racemic mixture). $[\alpha]^{20}_D = -10.7$ (*c* 1.2, $CHCl_3$).

(3*S*)-3-[(*t*-Butyldimethylsilyl)oxy]-1-octen-7-yne (13b). Imidazole (178 mg, 2.5 mmol) and TBSCl (0.15 g, 1 mmol) were added to a solution of **13a** (100 mg, 0.8 mmol) in DMF (5 mL). The reaction mixture was stirred for 12 h and poured into H_2O (15 mL). The resulting mixture was extracted with hexanes, and the combined organic phases were dried, filtered, and concentrated in vacuo. The residue was filtered through a short pad of silica gel (hexanes) to give **13b** (185 mg, 98%).

(3*S*)-3-[(*t*-Butyldimethylsilyl)oxy]-1-nonen-7-yne (14). A solution of **13b** (260 mg, 1.09 mmol) in THF (8 mL) was added to *n*-BuLi (0.6 mL, 1.3 mmol, 2.35 M in hexanes) cooled at −78 °C. After stirring for 1 h, MeI (0.2 mL, 3.27 mmol) was added, and the reaction mixture was allowed to warm to rt and stirred for 7 h. The reaction was quenched with H_2O (10 mL), and the aqueous layer was extracted with Et_2O. The combined organic layers were dried, filtered, and concentrated in vacuo. Flash chromatography (1% EtOAc/hexanes) gave **14** [261 mg, 94%, $R_f = 0.5$ (3% EtOAc/hexanes), colorless oil]. ^{1}H NMR δ: 5.79 (1 H, ddd, $J = 17.2$, 10.4, and 6), 5.14 (1 H, ddd, $J = 17.1$, 1.7, and 1.4), 5.03 (1H, ddd, $J = 10.4$, 1.5, and 1.3), 4.11 (1 H, q, $J = 5.8$), 2.12 (2 H, m), 1.77 (3 H, t, $J = 2.6$), 1.54 (4 H, m), 0.9 (9 H, s), 0.04, 0.06 (6 H, 2 s); ^{13}C NMR δ: 141.6 (CH), 113.7 (CH_2), 79 (C), 79 (C), 75 (C), 73.4 (CH), 37.1 (CH_2), 25.8 (CH_3), 24.6 (CH_2), 18.7 (CH_2), 18 (C), 3.3 (CH_3), −5 (CH_3), −4.5 (CH_3); LRMS [*m*/*z* (%)]: 237.1 (M^+ − Me, 5), 207 (6), 195.1 (M^+ − *t*-Bu, 30), 171 (37); HRMS calcd for $C_{15}H_{28}OSi - CH_3$: 237.1674; found: 237.1671.

(1*S*, 2*S*, 3*E*)-1-[(*t*-Butyldimethylsilyl)oxy]-3-(iodoethylidene)-2-(iodomethyl)cyclohexane (15). *n*-Butyllithium (0.96 mL, 2.37 mmol, 2.46 M in hexanes) was added dropwise by syringe to a solution of Cp_2TiCl_2 (300 mg, 1.19 mmol) in THF (6 mL) cooled at −80 °C. The mixture was stirred for 1 h while allowing to warm to −55 °C, and a solution of enyne **14** (200 mg, 0.79 mmol) in THF (4 mL) was added dropwise via cannula. The reaction mixture was allowed to warm to rt and stirred for 7 h. The resulting solution was added slowly (2 h) by syringe to a solution of NIS (535.2 mg, 2.37 mmol) in CH_2Cl_2 (4 mL) cooled at −78 °C. Stirring was continued for 1 h at −50 °C and 1 h at rt. The reaction was quenched with saturated aqueous NH_4Cl (10 mL). The resulting suspension was filtered through a pad of Celite and extracted with hexanes. Drying and concentration in vacuo afforded a residue that was purified by flash chromatography (hexanes) to give the diiodide **15** [164 mg, 41%, $R_f = 0.7$ (2% EtOAc/hexanes), white glassy solid]. $[\alpha]_d = +7.2$ (*c* 1.1, $CHCl_3$). ^{1}H NMR δ: 4.25 (1 H, m), 3.19−3.06 (3 H, m), 2.75 (1 H, m), 2.56 (3 H, s), 1.76−1.4 (5 H, m), 0.87 (9 H, s), 0.14, 0.07 (6 H, 2 s); ^{13}C NMR δ: 140.9 (C), 98 (C), 70.8 (CH), 57.2 (CH), 30.1 (CH_3), 28.4 (CH_2), 25.8 (CH_3), 25.4 (CH_2), 20.2 (CH_2), 17.9 (C) , 5.39 (CH_2), −5, −4.8 (CH_3); LRMS [*m*/*z* (%)]: 448.9 (M^+ − *t*-Bu, 100), 379.05 (M^+ − I, 18), 321.9 (22), 246.9 (33), 214.9 (20); HRMS calcd for $C_{15}H_{28}OI_2Si - C_4H_9$: 448.92947; found: 448.92981.

(1*S*,3*E*)-1-*t*[(*t*-Butyldimethylsilyl)oxy]-2-methylene-3-(iodoethylidene)cyclohexane (16). DBU (0.22 mL, 1.4 mmol) was added to a solution of **15** (86 mg, 0.17 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C. The reaction mixture was stirred at rt for 48 h and poured into H_2O (15 mL). The aqueous layer was extracted with hexanes, and the combined organic phases were dried, filtered, and concentrated in vacuo. Flash chromatography (hexanes) gave the iodide **16** [45 mg, 70%, $R_f =$ 0.7 (1% EtOAc/hexanes)]. ^{1}H NMR δ: 5.26 (1 H, t, $J = 1.9$), 4.92 (1 H, t, $J = 1.8$), 4.06−4.01 (1 H, m), 2.7 (1 H, m), 2.58 (3 H, s), 2.09−1.88 (2 H, m), 1.82-1.65 (1 H, m), 1.57−1.2 (2 H, m), 0.94 (9 H, s), 0.14, 0.11 (6 H, 2 s); ^{13}C NMR δ: 155 (C), 144.9 (C), 110.6 (CH), 92 (CH_2), 73.1 (CH), 37.6 (CH_2), 31 (CH_2), 30.3 (CH_3), 25.9 (CH_3), 23.6 (CH_2), 18.3 (C), −5.1 (CH_3), −4.7 (CH_3); LRMS [*m*/*z* (%)]: 378.3 (M^+, 1.6), 363.25 (M^+ − Me, 2), 320.9 (M^+ − *t*-Bu, 40), 263.20 (M^+ − TBS, 10); HRMS calcd for $C_{15}H_{27}OISi$: 378.0876; found: 378.0882.

3-Deoxy-1α-[(*t*-butyldimethylsilyl)oxy]-6-methylvitamin D_3 (17). *t*-Butyllithium (0.22 mL, 0.28 mmol, 1.3 M in pentane) was slowly added to a solution of bromide **9** (45 mg, 0.13 mmol) in Et_2O (1 mL) at −78 °C. The mixture was stirred for 15 min, and a solution of $ZnBr_2$ (32.4 mg, 0.14 mmol) in Et_2O (1 mL) was added. After stirring at −10 °C for 1 h, the reaction mixture was cooled at −78 °C, and a solution of iodide **16** (33 mg, 0.09 mmol) and $Pd(Ph_3P)_4$ (approximately 4 mg) in THF (1 mL) was added. The resulting solution was allowed to reach rt and stirred for 2 h. The reaction was quenched with H_2O (3 mL). The mixture was extracted with hexanes. The combined organic layers were dried, filtered, and concentrated in vacuo. Flash chromaography (hexanes) gave **17** [38 mg, 94%, $R_f = 0.5$ (hexanes), colorless oil]. ^{1}H NMR [CD_2Cl_2, 500 MHz] δ: 5.61 (1 H, s), 5.12 (1 H, br s), 4.69 (1 H, br s), 3.96 (1 H, m), 2.53 (1H, br d, $J = 5.4$), 2.48 (1H, br d, $J = 3.2$), 1.96 (1 H, m), 1.79 (3 H, s), 0.88−0.82 (18 H, m), 0.51 (3H, s), 0.06, 0.05 (6 H, 2 s); ^{13}C NMR [CD_2Cl_2, 500 MHz] δ: 151.9 (C), 139.0 (C), 137.0 (C), 127.0 (C), 124.4 (CH), 110.2 (CH_2), 74.1, 56.9, 56.5, 46.0, 40.9, 39.9, 37.8, 36.5, 30.9, 30.2, 28.5, 28.0, 26.1, 24.3, 24.2, 23.9, 23.1, 22.8, 19.9, 19.0, 18.8, 12.1, −4.7, −4.9; LRMS [*m*/*z* (%)]: 512 (M^+, 5), 455.2 (M^+ − *t*-Bu, 15), 366.25 (12), 326.2 (18); HRMS calcd for $C_{34}H_{60}OSi$: 512.4416; found: 512.4419; UV (Et_2O, nm): λ_{min} 220; λ_{max} 242.

3-Deoxy-1α-[(*t*-butyldimethylsilyl)oxy]-6-methylprevitamin D_3 (18a). A solution of **17** in CH_2Cl_2 was heated at reflux for two days in the dark. After removal of the solvent under reduced pressure, ^{1}H NMR analysis showed the previtamin **18a** to be the major component. ^{1}H NMR [CD_2Cl_2, 500 MHz] δ: 5.48 (2 H, br s), 3.97 (1 H, br s), 1.73 (3 H, s), 1.24 (3 H, s), 0.91−0.81 (18 H, m), 0.66 (3 H, s), 0.09, 008 (6 H, 2 s); ^{13}C NMR δ: [CD_2Cl_2, 125.76 MHz] δ: 139.2, 136.1, 125.0, 124.6, 70.9, 55.0, 51.4, 42.5, 39.9, 36.7, 36.6, 33.4, 30.1, 29.2, 28.7, 28.4, 26.0, 25.3, 24.2, 24.1, 23.1, 22.9, 22.7, 19.0, 18.3, 11.3, 11.2, −4.1, −4.6; UV (Et_2O, nm): λ_{min} 224; λ_{max} 248.

3-Deoxy-1α-hydroxy-6-methylprevitamin D_3 (18b). Tetrabutylammonium fluoride (0.06 mL, 0.06 mmol, 1 M in THF) was added to a solution of **19a** (10 mg, 0.019 mmol) in THF (1 mL). The mixture was stirred for 12 h at rt, diluted with H_2O (6 mL), and extracted with Et_2O. The combined organic phases were dried, filtered, and concentrated in vacuo. Flash chromatography gave **19b** [5 mg, 65%, R_f 0.5 (20% EtOAc/hexanes)]. ^{1}H NMR δ: 5.57 (1 H, br s), 5.41 (1 H, br s), 3.87 (1H, m), 2.11 (2H, m), 1.80 (3 H, s), 1.75 (3 H, s), 0.93 (3 H, d, $J = 6.1$), 0.86 (6 H, d, $J = 6.0$), 0.66 (3 H, s).

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Supporting Information Available: Copies of the ^{1}H and ^{13}C NMR spectra (18 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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