Supporting Information

New 2-Alkylidene 1α,25-Dihydroxy-19-norvitamin D_3 Analogues of High Intestinal Activity: Synthesis and Biological Evaluation of 2-(3'-Alkoxypropylidene)- and 2-(3'-Hydroxypropylidene) Derivatives

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Contents:

Purity criteria for the synthesized compounds

Table 2. Combustion Analyses of Crystalline Compounds

Compd.	C		H		Br	
no.	calc.	found	calc.	found	calc.	found
9	54.14	53.94	8.39	8.36		
10	51.29	51.09	7.95	7.90		
11	54.86	54.88	7.37	7.37		
A	62.03	61.87	5.88	5.77	17.94	17.90
B	62.90	62.99	7.04	6.90	15.50	15.40

All final vitamin D analogs synthesized by us gave single sharp peaks on HPLC and they were judged at least 99% pure. Two HPLC systems (straight- and reversed-phase) were employed as indicated in the Table 3. The purity and identity of the synthesized vitamins were additionally confirmed by inspection of their 500 MHz ^{1}H NMR and high-resolution mass spectra

Table 3. Purity Criteria for Target Vitamin D Compounds

Compound	Compd. no.	HPLC Retention Volumes	
		Straight-phase[a] (**h**exane/2-**p**ropanol)	Reversed-phase[b] (**m**ethanol/**w**ater)
2-[3'-OMOM-propylidene]-19-nor-1α,25-$(OH)_2D_3$	**5a**	h/p (75:25) 26 mL	m/w (80:20) 35 mL
2-[3'-OH-propylidene]-19-nor-1α,25-$(OH)_2D_3$ (*E*-isomer)	**6a**	h/p (80:20) 37.5 mL	m/w (80:20) 23 mL
2-[3'-OH-propylidene]-19-nor-1α,25-$(OH)_2D_3$ (*Z*-isomer)	**7a**	h/p (80:20) 37 mL	m/w (80:20) 29 mL
2-[3'-OH-propylidene]-19-nor-(20*S*)-1α,25-$(OH)_2D_3$ (*E*-isomer)	**6b**	h/p (80:20) 36.5 mL	m/w (80:20) 18 mL
2-[3'-OH-propylidene]-19-nor-(20*S*)-1α,25-$(OH)_2D_3$ (*Z*-isomer)	**7b**	h/p (80:20) 36 mL	m/w (80:20) 28 mL

[a]Zorbax-Sil 10 mm x 25 cm column. [b]Zorbax-ODS 6.2 mm x 25 cm column.

Spectral data of the synthesized compounds

(1*R*,3*R*,4*S*,5*R*)-3-[(*tert*-butyldimethylsilyl)oxy]-1,4-dihydroxy-6-oxa-bicyclo[3.2.1]octan-7-one (9): m.p. 90-94 ^{o}C (from hexane); $[\alpha]^{24}_{D}$ -44^{o} (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.095 (6H, s, 2 x $SiCH_3$), 0.901 (9H, s, Si-*t*-Bu), ca. 2.0 (2H, br m, 2α- and 2β-H), 2.29 (1H, ddd, J = 11.6, 6.0, 2.6 Hz, 8β-H), 2.63 (1H, d, J = 11.6 Hz, 8α-H), 3.89 (1H, ddd, J = 10.4, 7.0, 4.5 Hz, 3β-H), 3.98 (1H, t, J = 4.6 Hz, 4β-H), 4.88 (1H, dd, J = 6.0, 4.8 Hz, 5α-H); ^{13}C NMR (125 MHz) δ -5.0 (Si-CH_3), -4.7 (Si-CH_3), 17.9 [$\underline{C}(CH_3)_3$], 25.6 [$C(\underline{C}H_3)_3$], 36.4 (C_8), 40.2 (C_2), 65.8 (C_4), 67.0 (C_3), 71.9 (C_1), 76.3 (C_5), 177.9 (C=O), MS (EI) m/z (relative intensity) 288(M^+, 1), 231 (41), 213 (21), 185 (85), 75 (100); HRMS (ESI), exact mass calcd for $C_{13}H_{24}O_5SiNa$ (M^+ + Na) 311.1291, measured 311.1287; Anal. ($C_{13}H_{24}O_5Si$) C, H.

(1*R*,3*R*,5*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-1-hydroxy-6-oxa-bicyclo[3.2.1]octane-4,7-dione (10): mp 92-95 ^{o}C (from hexane); $[\alpha]^{24}_{D}$ -87^{o} (*c* 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.040 and 0.133 (3H and 3H, each s, 2 x $SiCH_3$), 0.895 (9H, s, Si-*t*-Bu), 2.15 (1H, dd, J = 12.4, 10,4 Hz, 2α-H), 2.42 (1H, d, J = 12.5 Hz, 8α-H), 2.54 (1H, ddd, J = 12.4, 9.0, 3.9 Hz, 2β-H), 2.86 (1H, ddd, J = 12.5, 6.7, 3.9 Hz, 8β-H), 4.54 (1H, dd, J = 10.4, 9.0 Hz, 3β-H), 4.73 (1H, d, J = 6.7 Hz, 5α-H); ^{13}C NMR (125 MHz) δ -5.6 (Si-CH_3), -4.8 (Si-CH_3), 18.2 [$\underline{C}(CH_3)_3$], 25.6 [$C(\underline{C}H_3)_3$], 42.3 (C_8), 43.0 (C_2), 70.3 (C_3), 71.8 (C_1), 78.7 (C_5), 177.1 (C=O), 202.4 (C_4); MS (EI) m/z (relative intensity) no M^+, 271 (M^+ - CH_3, 4), 229 (92), 201 (28), 157 (100); HRMS (ESI) exact mass calcd for $C_9H_{13}O_5Si$ (M^+ - *t*-Bu) 229.0532, measured 229.0539; Anal. ($C_{13}H_{22}O_5Si$) C, H.

(1*R*,3*R*,5*R*)-1-Acetoxy-3-[(*tert*-butyldimethylsilyl)oxy]-6-oxa-bicyclo[3.2.1]octane-4,7-dione (11): mp 134-7 ^{o}C (from hexane/ethyl acetate); $[\alpha]^{24}_{D}$ -78^{o} (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.046 and 0.141 (3H and 3H, each s, 2 x $SiCH_3$), 0.901 (9H, s, Si-*t*-Bu), 2.17 (3H, s, CH_3CO), 2.28 (1H, dd, J = 12.2, 10.4 Hz, 2α-H), 2.32 (1H, d, J = 12.1 Hz, 8α-H), 2.65 (1H, ddd, J = 12.2, 8.8, 3.9 Hz, 2β-H), 3.56 (1H, ddd ,J = 12.1, 6.9, 3.9 Hz, 8β-H), 4.58 (1H, dd, J = 10.4, 8.8 Hz, 3β-H), 4.80 (1H, d, J = 6.9 Hz, 5α-H); ^{13}C NMR (125 MHz) δ -5.8 (Si-CH_3), -4.9 (Si-CH_3), 18.2 [$\underline{C}(CH_3)_3$], 20.9 ($\underline{C}H_3$-C=O), 25.6 [$C(\underline{C}H_3)_3$], 38.3 (C_8), 40.3 (C_2), 70.4 (C_3), 75.3 (C_1), 78.4 (C_5), 169.1 (CH_3-$\underline{C}$=O), 171.5 (C=O), 201.8 (C_4); MS (EI) m/z (relative intensity) 328 (M^+, 6), 271 (100), 256 (38), 229 (54), 211 (53); HRMS (ESI) exact mass calcd for $C_{11}H_{15}O_6Si$ (M^+ - *t*-Bu) 271.0638, measured 271.0646; Anal. ($C_{15}H_{24}O_6Si$) C, H.

1-Bromo-3-(methoxymethoxy)propane: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (2H, m, CH_2-C$\underline{H}_2$-CH_2), 3.37 (3H, s, O-CH_3), 3.53 (2H, br t, J = 6.5 Hz, Br-CH_2), 3.67 (2H, br t, J = 5.8 Hz, CH_2-C$\underline{H}_2$-O), 4.63 (2H, s, O-CH_2-O).

[3-(Methoxymethoxy)propyl]triphenylphosphonium bromide (A): mp 165-168 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.96 (2H, m, CH_2-C$\underline{H}_2$-CH_2), 3.31 (3H, s, O-CH_3), 3.85 (2H, br t, J = 5.6 Hz, CH_2-C$\underline{H}_2$-O), 4.00 (2H, m, P-CH_2), 4.60 (2H, s, O-CH_2-O), 7.70, 7.79 and 7.86 (6H, 3H and 6H, each m, Ar-H); Anal. ($C_{23}H_{26}O_2PBr$) C, H, Br.

[3-[(*tert*-Butyldimethylsilyl)oxy]propyl]triphenylphosphonium bromide (B): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.039 (6H, s, 2 x $SiCH_3$), 0. 857 (9H, s, Si-*t*-Bu), 1.93 (2H, m, CH_2-$C\underline{H}_2$-CH_2), 3.86 – 3.94 (4H, br m, CH_2-$C\underline{H}_2$-O and P-CH_2), 7.70, 7.79 and 7.85 (6H, 3H and 6H, each m, Ar-H); Anal. ($C_{27}H_{36}OSiPBr$) C, H, Br.

[(1*R*,3*R*,5*R*)-1-Acetoxy-3-[(*tert*-butyldimethylsilyl)oxy]-6-oxa-4-[3'-(methoxymethoxy)propylidene]bicyclo[3.2.1]octan-7-one (12 and 13).

12 (major *E*-isomer): $[\alpha]^{24}_D$ -63^o (*c* 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.074 (6H, s, 2 x $SiCH_3$), 0.914 (9H, s, Si-*t*-Bu), 2.13 (3H, s, OCH_3), 2.00 (1H, br t, J = 11.2, Hz, 2α-H), 2.10 (1H, d, J = 10.8 Hz, 8α-H), 2.34 (1H, ddd, J = 11.7, 7.0, 2.9 Hz, 2β-H), 2.38 and 2.43 (1H and 1H, each m, =C-CH_2), 3.31 (1H, ddd, J = 10.8, 6.5, 2.9 Hz, 8β-H), 3.35 (3H, s, O-CH_3), 3.54 and 3.60 (1H and 1H, each m, CH_2-$C\underline{H}_2$-O), 4.41 (1H, t, J = 8.2 Hz, 3β-H), 4.60 (2H, s, O-CH_2-O), 5.52 (1H, d, J = 6.5 Hz, 5α-H), 5.71 (1H, br t, J = 7.1 Hz, =CH); ^{13}C NMR (125 MHz) δ -5.1 (Si-CH_3), -4.9 (Si-CH_3), 18.1 [$\underline{C}(CH_3)_3$], 21.1 $\underline{C}H_3$-C=O), 25.7 [$C(\underline{C}H_3)_3$], 27.5 (CH_2-$C\underline{H}_2$-C=), 40.5 (C_8), 41.5 (C_2), 55.2 (O-CH_3), 66.7 (O-$\underline{C}H_2$-CH_2), 66.8 (C_3), 77.1 (C_1), 73.9 (C_5), 96.3 (O-CH_2-O), 121.9 (=$\underline{C}$-CH_2), 136.8 (C_4), 169.1 (CH_3-$\underline{C}$=O), 172.9 (C=O); MS (EI) m/z (relative intensity), no M^+, 383 (M^+ - OCH_3, 3), 357 (10), 325 (44), 297 (12), 267 (15), 265 (40), 237 (89), 75 (100); HRMS (ESI) exact mass calcd for $C_{20}H_{34}O_7SiNa$ (M^+ + Na) 437.1972, measured 437.1975.

13 (minor *Z*-isomer): $[\alpha]^{24}_D$ –67.5^o (*c* 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.108 and 0.125 (3H and 3H, each s, 2 x $SiCH_3$), 0.912 (9H, s, Si-*t*-Bu), 2.13 (3H, s, OCH_3), 2.15 (1H, dd, J = 12.6, 8.3 Hz, 2α-H), 2.31 (1H, d, J = 10.8 Hz, 8α-H), 2.33 (1H, 2β-H overlapped with 8α-H),

2.67 and 2.73 (1H and 1H, each m, =C-CH_2), 3.25 (1H, ddd, J = 10.8, 6.3, 2.8 Hz, 8β-H), 3.36 (3H, s, O-CH_3), 3.55 (2H, m, CH_2-C$\underline{H}_2$-O), 4.61 (2H, s, O-CH_2-O), 4.71 (1H, br t, J ~ 7 Hz, 3β-H), 4.94 (1H, d, J = 6.3 Hz, 5α-H), 5.64 (1H, dt, J = 1.7, 7.1 Hz, =CH); ^{13}C NMR (125 MHz) δ -4.6 (Si-CH_3), -4.5 (Si-CH_3), 17.9 [$\underline{C}(CH_3)_3$], 21.1 ($\underline{C}H_3$-C=O), 25.7 [C($\underline{C}H_3)_3$], 27.8 (CH_2-C$\underline{H}_2$-C=), 38.9 (C_8), 41.2 (C_2), 55.3 (O-CH_3), 67.1 (O-$\underline{C}H_2$-CH_2), 67.2 (C_3), 77.1 (C_1), 81.8 (C_5), 96.4 (O-CH_2-O), 128.9 (=$\underline{C}$-CH_2), 134.8 (C_4), 169.1 (CH_3-$\underline{C}$=O), 173.0 (C=O); MS (EI) m/z (relative intensity), no M^+, 383 (M^+ - OCH_3, 2), 357 (2), 325 (22), 297 (17), 267 (35),265 (14), 237 (96), 75 (100); HRMS (ESI) exact mass calcd for $C_{20}H_{34}O_7SiNa$ (M^+ + Na) 437.1972, measured 437.1974.

[(1*R*,3*R*,5*R*)-1-Acetoxy-3-[(*tert*-butyldimethylsilyl)oxy]-6-oxa-4-[3'-((*tert*-butyldimethylsilyl)oxy)propylidene]bicyclo[3.2.1]octan-7-one (14 and 15).

14 (major *E*-isomer): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.049 and 0.073 (6H and 6H, each s, 4 x $SiCH_3$), 0. 889 and 0.914 (9H and 9H, each s, 2 x Si-*t*-Bu), 2.01 (1H, br t, J = 11.0 Hz, 2α-H), 2.07 (1H, d, J = 10.5 Hz, 8α-H), 2.13 (3H, s, OAc), 2.26-2.36 (3H, m, 2β-H overlapped with =C-CH_2), 3.29 (1H, ddd, J = 10.5, 6.4, 2.8 Hz, 8β-H), 3.65 (2 H, m, CH_2-C$\underline{H}_2$-O), 4.40 (1H, ~ t, J = 8.5 Hz, 3β-H), 5.50 (1H, d, J = 6.4 Hz, 5α-H), 5.71 (1H, t, J = 7.3 Hz, =CH), MS (EI) m/z (relative intensity) no M^+, 469 (M^+ - Me, 1), 427 (64), 367 (13), 337 (26), 73 (100); HRMS (ESI) exact mass calcd for $C_{24}H_{44}O_6Si_2Na$ (M^+ + Na) 507.2574, measured 507.2575.

15 (minor *Z*-isomer): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.042 (6H, s, 2 x $SiCH_3$), 0.098 and 0.117 (3H and 3H, each s, 2 x $SiCH_3$), 0.885 and 0.907 (9H and 9H, each s, 2 x Si-*t*-Bu), 2.13 (3H, s, OAc), 2.14 (1H, m, 2α-H), 2.31 (1H, 2β-H overlapped with 8α-H), 2.32 (1H, d, J = 11.0 Hz, 8α-

H), 2.51 and 2.64 (1H and 1H, each m, =C-CH_2), 3.24 (1H, m, 8β-H), 3.62 (2H, m, CH_2-C$\underline{H}_2$-O), 4.69 (1H, ~ t, J = 7.2 Hz, 3β-H), 4.93 (1H, d, J = 6.3 Hz, 5α-H), 5.63 (1H, t, J = 7.0 Hz, =CH), MS (EI) m/z (relative intensity) no M^+, 469 (M^+ - Me, 1), 427 (32), 367 (13), 337 (40), 73 (100); HRMS (ESI) exact mass calcd for $C_{24}H_{44}O_6Si_2Na$ (M^+ + Na) 507.2574, measured 507.2560.

[(1'*R*,3'*R*,5'*R*)-3'-[(*tert*-Butyldimethylsilyl)oxy]-1',5'-dihydroxy-4'-[3''-(methoxymethoxy)propylidene]cyclohexyl]methanol (*E*-isomer 16): $[\alpha]^{24}_D$ -59° (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.087 and 0.110 (3H and 3H, each s, 2 x $SiCH_3$), 0.895 (9H, s, Si-*t*-Bu), 1.66 (1H, dd, J = 13.0, 9.1 Hz, 6'β-H), 1.69 (1H, dd, J = 13.8, 3.1 Hz, 2'β-H), 1.84 (1H, s, O$\underline{H}$), 1.96 (1H, ddd, J = 13.8, 5.0, 1.7 Hz, 2'α-H), 2.04 (1H, ddd, J = 13.0, 4.6, 1.7 Hz, 6'α-H), 2.54 (1H, s, O$\underline{H}$), 2.63 (2H, m, =C-CH_2), 3.34 (3H, s, O-CH_3), 3.39 and 3.50 (1H and 1H, after D_2O: each d, J = 11.0 Hz, C$\underline{H}_2$-OH), 3.50 (1H, s, O$\underline{H}$), 3.58 (2H, m, CH_2-C$\underline{H}_2$-O), 4.19 (1H, s, O$\underline{H}$), 4.47 (1H, m, w/2 = 10 Hz, 3'β-H), 4.63 (2H, s, -O-CH_2-O), 4.89 (1H, m; after D_2O: dd, J =9.1, 4.6 Hz, 5'α-H), 5.51 (1H, t, J = 8.3 Hz, =CH); ^{13}C NMR (125 MHz) δ −5.2 (Si-CH_3), -4.7 (Si-CH_3), 18.0 [$\underline{C}(CH_3)_3$], 25.7 [C($\underline{C}H_3)_3$], 27.2 (CH_2-C$\underline{H}_2$-C=), 41.3 (C_2), 44.1 (C_6), 55.4 (O-CH_3), 66.4 (C_5), 66.7 (O-$\underline{C}H_2$-CH_2), 70.3 (CH_2-OH), 73.7 (C_1), 75.9 (C_3), 96.4 (O-CH_2-O), 122.0 (=$\underline{C}$-CH_2), 144.2 (C_4); MS (EI) m/z (relative intensity), no M^+, 358 (M^+ - H_2O, 2), 327 (3), 297 (3), 239 (17), 75 (100); HRMS (ESI) exact mass calcd for $C_{18}H_{36}O_6SiNa$ (M^+ + Na) 399.2179, measured 399.2198.

[(1'*R*,3'*R*,5'*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-1',5-dihydroxy-4'-[3''-[((*tert*-butyldimethylsilyl)oxy)propylidene]cyclohexyl]methanol (17 and 18).

17 (major *E*-isomer): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.077, 0.082, 0.084 and 0.110 (4 x 3H, each s, 4 x $SiCH_3$), 0.887 and 0.902 (9H and 9H, 2 x s, 2 x Si-*t*-Bu), 1.58 (1H, dd, J = 12.8, 10.2 Hz, 6'β-H), 1.62 (1H, dd, J = 14.0, 2.8 Hz, 2'β-H), 2.03 (1H, ddd, J = 14.0, 3.9, 1.9 Hz, 2'α-H), 2.11 (1H, ddd, J = 12.8, 4.5, 1.9 Hz, 6'α-H), 2.46 and 2.66 (1H and 1H, each m, =C-CH_2), 3.35 and 3.47 (1H and 1H, after D_2O: 2 x d, J = 10.8 Hz, 1-H_2), 3.68 (2H, m, CH_2-C$\underline{H}_2$-O), 4.46 (1H, ~ t, J = 3.3 Hz, 3'β-H), 4.88 (1H, after D_2O: dd, J =10.2, 4.5 Hz, 5'α-H), 5.45 (1H, t, J = 8.6 Hz, =CH); ^{13}C NMR (125 MHz) δ -5.6 (Si-CH_3), -5.38 (Si-CH_3), -5.36 (Si-CH_3), -4.5 (Si-CH_3), 17.9 [$\underline{C}(CH_3)_3$], 18.4 [$\underline{C}(CH_3)_3$], 25.7 [C($\underline{C}H_3)_3$], 26.0 [C($\underline{C}H_3)_3$], 29.2 (CH_2-C$\underline{H}_2$-C=), 40.4 ($C_{2'}$), 44.1 ($C_{6'}$), 62.2 (O-$\underline{C}H_2$-CH_2), 66.2 ($C_{5'}$), 70.3 (C_1), 73.8 ($C_{1'}$), 74.1 ($C_{3'}$), 121.9 (=$\underline{C}$-CH_2), 145.0 ($C_{4'}$), HRMS (ESI) exact mass calcd for $C_{22}H_{46}O_5Si_2Na$ (M^+ + Na) 469.2824, measured 469.2781.

(3*R*,5*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-5-hydroxy-4-[3'-(methoxymethoxy)propylidene]cyclohexanone (*E*-isomer 19): $[\alpha]^{24}_D$ +41° (*c* 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.048 and 0.076 (3H and 3H, each s, 2 x $SiCH_3$), 0.863 (9H, s, Si-*t*-Bu), 2.34 (1H, m, one of =C-CH_2), 2.50 (1H, dd, J = 16.0, 6.0 Hz, 2α-H), 2.62 (1H, m, dd, J = 16.1, 3.2 Hz, 6α-H), 2.65 (1H, m, =C-CH_2), 2.70 (1H, dd, J = 16.0, 3.4 Hz, 2β-H), 2.75 (1H, dd, J =16.1, 3.4 Hz, 6β-H), 3.33 (3H, s, O-CH_3), 3.53 and 3.74 (1H and 1H, each m, CH_2-C$\underline{H}_2$-O), 4.62 (3H, br m, 3β-H and O-CH_2-O), 4.95 (1H, t, J ~ 3.3 Hz, 5α-H), 5.73 (1H, dd, J = 10.2, 6.3 Hz, =CH); ^{13}C NMR (125 MHz) δ -4.9 (Si-CH_3), -4.7 (Si-CH_3), 18.0 [$\underline{C}(CH_3)_3$], 25.6 [C($\underline{C}H_3)_3$],

28.0 (CH_2-C<u>H</u>$_2$-C=), 45.3 (C_2), 48.3 (C_6), 55.4 (O-CH_3), 63.1 (C_5), 65.7 (O-<u>C</u>H_2-CH_2), 70.3 (C_3), 96.3 (O-CH_2-O), 126.7 (=<u>C</u>-CH_2), 142.5 (C_4), 208.7 (C_1); MS m/z (relative intensity), no M^+, 313 (M^+ - OCH_3, 3), 287 (15), 269 (7), 255 (21), 237 (11), 227 (68), 225 (91), 213 (17), 195 (57), 75 (100); HRMS (ESI) exact mass calcd for $C_{13}H_{21}O_5Si$ (M^+ - *t*-Bu) 287.1315, measured 287.1312.

[(3*R*,5*R*)-3-[(*tert*-Butyldimethylsilyl)oxy]-5-hydroxy-4-[3'-[((*tert*-butyldimethylsilyl)oxy)propylidene]]cyclohexanone (20 and 21).

20 (major *E*-isomer): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.042, 0.065 and 0.074 (3H, 6H and 3H, each s, 4 x $SiCH_3$), 0.849 and 0.880 (9H and 9H, each s, 2 x Si-*t*-Bu), 2.28 (1H, m, one of =C-CH_2), 2.50 (1H, dd, J = 16.2, 5.4 Hz, 2α-H), 2.55-2.70 (3H, m, 2β-H overlapped with one of 6-H and =C-CH_2), 2.77 (1H, dd, J =16.2, 2.5 Hz, one of 6-H), 3.62 (1H, dt, J = 2.6, 10.2 Hz, one of CH_2-C<u>H</u>$_2$-O), 3.85 (1H, m, one of CH_2-C<u>H</u>$_2$-O), 4.60 (1H, m, 3β-H), 4.90 (1H, narr m, 5α-H), 5.66 (1H, dd, J = 10.5, 6.0 Hz, =CH); ^{13}C NMR (125 MHz) δ -5.6 (Si-CH_3), -5.4 (Si-CH_3), -4.9 (Si-CH_3), -4.6 (Si-CH_3), 18.0 [<u>C</u>$(CH_3)_3$], 18.5 [<u>C</u>$(CH_3)_3$], 25.7 [C(<u>C</u>$H_3)_3$], 26.0 [C(<u>C</u>$H_3)_3$], 30.7 (CH_2-C<u>H</u>$_2$-C=), 45.1 (C_2), 47.9(C_6), 63.0 (C_5), 61.8 (O-<u>C</u>H_2-CH_2), 70.8 (C_3), 127.5 (=<u>C</u>-CH_2), 142.9 (C_4), 208.9 (C_1); MS m/z (relative intensity) no M^+, 399 (M^+ - Me, 2), 357 (69), 339 (12), 327 (41), 299 (9), 265 (10), 225 (81), 73 (100); HRMS (ESI) exact mass calcd for $C_{21}H_{42}O_4Si_2Na$ (M^+ + Na) 437.2519, measured 437.2537.

[(3*R*,5*R*)-3,5-Bis[(*tert*-Butyldimethylsilyl)oxy]-4-[3'-(methoxymethoxy)propylidene]cyclohexanone (22): $[\alpha]^{24}_{D}$ -26° (*c* 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.019 and 0.065 (3H and 9H, each s, 4 x $SiCH_3$), 0.838 and 0.912 (9H and 9H, each s, 2 x Si-*t*-Bu), 2.32 (1H, dd, J = 14.1, 10.4 Hz, 2α-H), 2.45 (3H, br m, =C-CH_2 and 6α-H), 2.53 (1H, ddd, J = 14.4, 3.2, 2.1 Hz, 6β-H), 2.75 (1H, ddd, J = 14.1, 5.6, 2.1 Hz, 2β-H), 3.36 (3H, s, O-CH_3), 3.58 (2H, m, CH_2-C$\underline{H}_2$-O), 4.62 (2H, s, O-CH_2-O), 4.75 (1H, ddd, J = 10.4, 5.6, 1.4 Hz, 3β-H), 5.01 (1H, t, J ~ 3.2 Hz, 5α-H), 5.70 (1H, dt, J = 1.7, 7.8 Hz, =CH); ^{13}C NMR (125 MHz) δ −5.08 (Si-CH_3), -5.06 (Si-CH_3), −5.05 (Si-CH_3), −5.00 (Si-CH_3), 17.9 [$\underline{C}(CH_3)_3$], 25.5 [C($\underline{C}H_3)_3$], 27.7 (CH_2-C$\underline{H}_2$-C=), 50.2 (C_6), 52.4 (C_2), 55.2 (O-CH_3), 65.8 (C_3), 67.1 (O-$\underline{C}H_2$-CH_2), 67.8 (C_5), 96.4 (O-CH_2-O), 118.5 (=$\underline{C}$-CH_2), 141.5 (C_4), 207.5 (C_1); MS (EI) m/z (relative intensity) 443 (M^+ + H, 2), 427 (M^+ - CH_3, 5), 401 (55), 371 (15), 339 (20), 75 (100); exact mass calcd for $C_{12}H_{43}O_4Si_2$ (M^+ - CH_3) 427.2700, measured 427.2701.

[(3*R*,5*R*)-3,5-Bis[(*tert*-Butyldimethylsilyl)oxy]-4-[3'-[((*tert*-butyldimethylsilyl)oxy)propylidene]cyclohexanone (23): $[\alpha]^{24}_{D}$ −17° (*c* 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.008 (3H, s, $SiCH_3$), 0.061 (15H, s , 5 x $SiCH_3$), 0.833, 0.900 and 0.910 (3 x 9H, each s, 3 x Si-*t*-Bu), 2.32 (1H, dd, J = 14.2, 10.4 Hz, 2α-H), 2.32-2.43 (2H, br m, =C-CH_2), 2.43 (1H, dd, J = 14.4, 2.8 Hz, 6α-H), 2.52 (1H, ddd, J =14.4, 3.4, 2.2 Hz, 6β-H), 2.75 (1H, ddd, J = 14.2, 5.6, 2.2 Hz, 2β-H), 3.65 and 3.71 (each 1H, each m, CH_2-C$\underline{H}_2$-O), 4.76 (1H, ddd, J = 10.4, 5.6, 1.7 Hz, 3β-H), 5.01 (1H, ~ t, J =3.2 Hz, 5α-H), 5.70 (1H, dt, J = 1.7, 7.6 Hz, =CH); ^{13}C NMR (125 MHz) δ −5.27 (Si-CH_3), −5.25 (Si-CH_3), −5.01 (Si-CH_3), −5.00 (Si-CH_3), -4.95 (Si-CH_3), −4.89 (Si-CH_3), 17.9 [$\underline{C}(CH_3)_3$], 18.3 [$\underline{C}(CH_3)_3$], 18.4 [C($\underline{C}H_3)_3$], 25.6

[C($\underline{C}$H$_3$)$_3$], 25.8 [C($\underline{C}$H$_3$)$_3$], 26.0 [C($\underline{C}$H$_3$)$_3$], 29.7 (CH$_2$-C$\underline{H}_2$-C=), 50.4 (C_6), 52.5 (C_2), 62.8 (O-$\underline{C}$H$_2$-CH$_2$), 65.9 (C_3), 67.9 (C_5), 119.1 (=$\underline{C}$-CH$_2$), 141.1 (C_4), 207.5 (C_1); MS (EI) m/z (relative intensity) no M^+, 513 (M^+ - Me, 2), 471 (74), 381 (5), 339 (63), 73 (100); exact mass calcd for $C_{27}H_{56}O_4Si_3$ (M^+ - C_4H_9) 471.2782, measured 471.2796.

[(3'*R*,5'*R*)-3',5'-Bis[(*tert*-butyldimethylsilyl)oxy]-4'-[3''-(methoxymethoxy)propylidene]cyclohexylidene]acetic Acid Methyl Esters (24 and 25).

24 (major *E*-isomer): $[\alpha]^{24}_D$ -76^o (*c* 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.006, 0.056, 0.078, 0.107 (each 3H, each s, 4 x Si$\underline{C}$H$_3$), 0.832 and 0.923 (9H and 9H, each s, 2 x Si-*t*-Bu), 1.87 (1H, t, J = 11.8 Hz, 6'α-H), 2.28 (1H, br d, J = 13.2 Hz, 2'α-H), 2.34 (1H, br d, J = 13.2 Hz, 2'β -H), 2.42 (2H, q, J ~ 7 Hz, =C-CH$_2$), 3.36 (3H, s, CH$_2$-O-C$\underline{H}_3$), 3.55 (2H, m, CH$_2$-C$\underline{H}_2$-O), 3.70 (3H, s, CO-O-CH$_3$), 4.14 (1H, dd, J = 12.8, 3.8 Hz, 6'β-H), 4.45 (1H, br m, 5'β-H), 4.62 (2H, s, O-CH$_2$-O), 4.88 (1H, narr m, 3'α-H), 5.55 (1H, br t, J = 7.5 Hz, =C$\underline{H}$-CH$_2$), 5.65 (1H, br s, =CH-CO); MS (EI) m/z (relative intensity) no M^+, 499 (M^+ - CH_3, 2), 482 (11), 469 (31), 457 (65), 425 (63), 351 (70), 293 (76), 89 (100); HRMS (ESI) exact mass calcd for $C_{26}H_{50}O_6Si_2Na$ 537.3044, measured 537.3018.

25 (minor *Z*-isomer): $[\alpha]^{24}_D$ +41^o (*c* 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.008, 0.048, 0.057 and 0.063 (each 3H, each s, 4 x Si$\underline{C}$H$_3$), 0.804 and 0.915 (9H and 9H, each s, 2 x Si-*t*-Bu), 1.95 (1H, br d, J = 13.8 Hz, 6'β-H), 2.17 (1H, t, J ~ 11.6 Hz, 2'β -H), 2.42 (2H, m, =C-CH$_2$), 2.55 (1H, ddd, J ~ 12.4, ~5.0, ~ 1.2 Hz, 2'α-H), 3.36 (3H, s, CH$_2$-O-C$\underline{H}_3$), 3.55 (2H, m, CH$_2$-C$\underline{H}_2$-O), 3.67 (3H, s, CO-O-CH$_3$), 3.96 (1H, br d, J = 13.8 Hz, 6'α-H), 4.51 (1H, br m, 3'α-H), 4.62 (2H, s, O-CH$_2$-O), 4.89 (1H, narr m, 5'β-H), 5.50 (1H, br t, J = 7.5 Hz, =C$\underline{H}$-CH$_2$), 5.80

(1H, br s, =CH-CO); MS m/z (relative intensity) no M^+, 499 (M^+ - CH_3, 4), 482 (14), 469 (34), 457 (82), 425 (69), 351 (58), 293 (59), 89 (100); HRMS (ESI) exact mass calcd for $C_{26}H_{50}O_6Si_2Na$ 537.3044, measured 537.3053.

[(3'*R*,5'*R*)-3',5'-Bis[(*tert*-butyldimethylsilyl)oxy]-4'-[3''-[((*tert*-butyldimethylsilyl)oxy)propylidene]cyclohexylidene]acetic Acid Methyl Esters (26 and 27).

26 (major *E*-isomer): ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.014, 0.054, 0.059, 0.070, 0.080 and 0.109 (each 3H, each s, 6 x $SiCH_3$), 0.830, 0.845 and 0.926 (each 9H, each s, 3 x Si-*t*-Bu), 1.87 (1H, ~ t, J = 12 Hz, 6'α-H), 2.26 (1H, br d, J = 13.2 Hz, 2'α-H), 2.33 (1H, br d, J = 13.2 Hz, 2'β -H), 2.3 –2.4 (2H, m, =C-CH_2), 3.6 –3.7 (2H, m, CH_2-C$\underline{H_2}$-O), 3.71 (3H, s, $COOCH_3$), 4.15 (1H, ddd, J = 12.7, 4.9, 1.5 Hz, 6'β-H), 4.46 (1H, dd, J = 10.7, 4.9 Hz, 5'β-H), 4.88 (1H, ~ t, J = 3 Hz, 3'α-H), 5.54 (1H, dt, J = 1.5, 7.3 Hz, =CH), 5.65 (1H, br s, 2-H); **27** (minor *Z*-isomer, selected signals): δ 5.50 (1H, dt, J = 1.5, 7.3 Hz, =CH), 5.80 (1H, br s, 2-H); MS (EI) m/z (relative intensity) no M^+, 569 (M^+ - CH_3, 3), 527 (53), 452 (12), 395 (50), 320 (43), 196 (85), 73 (100); HRMS (ESI) exact mass calcd for $C_{26}H_{51}O_5Si_3$ (M^+ - *t*-Bu) 527.3044, measured 527.3048.

2-[(3'*R*,5'*R*)-3',5'-Bis[(*tert*-butyldimethylsilyl)oxy]-4'-[3''-(methoxymethoxy)propylidene]cyclohexylidene]ethanols (28 and 29).

28 (major *E*-isomer): $[\alpha]^{24}_D$ -29° (*c* 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.007, 0.057, and 0.067 (3H, 6H and 3H, each s, 4 x $SiCH_3$), 0.839 and 0.916 (9H and 9H, each s, 2 x Si-*t*-Bu), 1.81 (1H, t, J = 11.7 Hz, 6'α-H), 2.17 (1H, d, J = 13.4 Hz, 2'α-H), 2.26 (1H, br d, J = 13.4 Hz, 2'β-H), 2.41 (2H, q, J = 7 Hz, =C-C$\underline{H_2}$-CH_2), 2.86 (1H, dd, J = 12.5, 3.8 Hz, 6'β-H), 3.36 (3H, s,

O-CH_3), 3.54 (2H, m, CH_2-C<u>H</u>$_2$-O), 4.38 (1H, dd, J = 10.6, 3.8 Hz, 5'β-H), 4.17 (2H, t, J ~ 6 Hz; after D_2O: d, J = 6.9 Hz, C<u>H</u>$_2$-OH), 4.62 (2H, s, O-CH_2-O), 4.81 (1H, narr m, 3'α-H), 5.48 (2H, m, 2 x =CH-); MS (EI) m/z (relative intensity) 486 (M^+, 3), 468 (30), 454 (17), 441 (32), 429 (24), 423 (34), 89 (100); HRMS (ESI) exact mass calcd for $C_{25}H_{50}O_5Si_2Na$ 509.3095, measured 509.3111.

29 (minor *Z*-isomer): $[\alpha]^{24}_D$ -12° (*c* 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.011, 0.054, 0.069 (3H, 3H and 6H, each s, 4 x $SiCH_3$), 0.850 and 0.917 (9H and 9H, each s, 2 x Si-*t*-Bu), 1.88 (1H, br d, J = 13.4 Hz, 6'β-H), 2.03 (1H, t, J = 11.4 Hz, 2'β-H), 2.42 (2H, m, =C-CH_2), 2.51 (1H, ddd, J = 12.0, 4.8, 1.2 Hz, 2'α-H), 2.75 (1H, br d, J = 13.4 Hz, 6'α-H), 3.36 (3H, s, O-CH_3), 3.55 (2H, m, CH_2-C<u>H</u>$_2$-O), 4.02 and 4.15 (1H and 1H, each m; after D_2O: each dd, J =11.8, 7.2 Hz, C<u>H</u>$_2$-OH), 4.40 (1H, br m, 3'α-H), 4.62 (2H, s, O-CH_2-O), 4.90 (1H, narr m, 5'β-H), 5.53 (1H, br t, J = 7.4 Hz, =C<u>H</u>-CH_2), 5.71 (1H, t, J =7.2 Hz, =C<u>H</u>-CH_2-OH); MS (EI) m/z (relative intensity) 486 (M^+, 5), 468 (27), 454 (11), 441 (22), 429 (30), 423 (29), 89 (100); HRMS (ESI) exact mass calc. for $C_{25}H_{50}O_5Si_2Na$ 509.3095, measured 509.3108.

2-[(3'*R*,5'*R*)-3',5'-Bis[(*tert*-butyldimethylsilyl)oxy]-4'-[3''-[((*tert*-butyldimethylsilyl)oxy)propylidene]cyclohexylidene]ethanol (30 and 31).

30 (major *E*-isomer): $[\alpha]^{24}_D$ –33° (*c* 0.5, $CHCl_3$);^{1}H NMR (500 MHz, $CDCl_3$) δ -0.016, 0.055, 0.059, and 0.068 (3H, 6H, 6H and 3H, each s, 6 x $SiCH_3$), 0.831, 0.888 and 0.911 (each 9H, each s, 3 x Si-*t*-Bu), 1.80 (1H, t, J = 11.8 Hz, 6'α-H), 2.16 (1H, br d, J = 13.2 Hz, 2'α-H), 2.26 (1H, br d, J = 13.2 Hz, 2'β-H), 2.34 (2H, m, =C-C<u>H</u>$_2$-CH_2), 2.86 (1H, ddd, J = 12.4, 4.4, 1.5 Hz, 6'β-H), 3.62 (2H, m, CH_2-C<u>H</u>$_2$-O), 4.19 (2H, t, J ~ 6 Hz; after D_2O: d, J = 7.0 Hz, 1-H), 4.37 (1H, after

D_2O: dm, J = 10.4 Hz, 5'β-H), 4.80 (1H, ~ t, J = 3 Hz, 3'α-H), 5.47 (2H, m, 2 x =C<u>H</u>); MS (EI) m/z (relative intensity) no M^+, 538 (M^+ - H_2O, 9), 499 (12), 471 (7), 424 (39), 407 (11), 349 (23), 73 (100), HRMS (ESI) exact mass calcd for $C_{29}H_{60}O_4Si_3Na$ (M^+ + Na) 579.3697, measured 579.3704.

31 (minor *Z*-isomer): $[\alpha]^{24}_D$ -9° (*c* 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.029, 0.055, 0.060, 0.064 and 0.069 (3H, 6H, 3H, 3H and 3H, each s, 6 x $SiCH_3$), 0.849, 0.898 and 0.918 (each 9H, each s, 3 x Si-*t*-Bu), 1.87 (1H, br d, J = 13.8 Hz, 6'β-H), 2.03 (1H, br t, J = 11.5 Hz, 6'β-H), 2.34 (2H, m, =C-CH_2), 2.51 (1H, ddd, J = 12.0, 5.0, 1.6 Hz, 2'α-H), 2.76 (1H, br d, J = 13.8 Hz, 6'α-H), 3.36 (3H, s, O-CH_3), 3.64 (2H, m, CH_2-C<u>H</u>$_2$-O), 4.02 and 4.13 (1H and 1H, each m; after D_2O: each dd, J =11.8, 7.2 Hz, C<u>H</u>$_2$-OH), 4.39 (1H, br m, 5'α-H), 4.89 (1H, narr m, 3'β-H), 5.52 (1H, dt, J = 1.3, 7.5 Hz, =C<u>H</u>-CH_2), 5.71 (1H, t, J =7.2 Hz, =C<u>H</u>-CH_2-OH); MS (EI) m/z (relative intensity) no M^+, 538 (M^+ - H_2O, 4), 499 (6), 471 (4), 424 (12), 407 (6), 349 (11), 73 (100), HRMS (ESI) exact mass calcd for $C_{29}H_{58}O_3Si_3$ (M^+ - H_2O) 538.3694, measured 538.3689.

[2-[(3'*R*,5'*R*)-3',5'-Bis[(*tert*-butyldimethylsilyl)oxy]-4'-[3''-(methoxymethoxy)propylidene]cyclohexylidene]ethyl]diphenylphosphine Oxide (*E*-isomer 32): $[\alpha]^{24}_D$ -25° (*c* 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.031, -0.013, 0.017, and 0.024 (each 3H, each s, 4 x $SiCH_3$), 0.795 and 0.899 (9H and 9H, each s, 2 x Si-*t*-Bu), 1.47 (1H, br t, J ~ 11 Hz, 6'α-H), 2.06 (1H, br m, 2'α-H), 2.23 (1H, d, J = 13.5 Hz, 2'β-H), 2.37 (2H, q, J = 7.0, =C-C<u>H</u>$_2$-CH_2), 2.62 (1H, dd, J = 12.8, 4.5 Hz, 6'β-H), 3.34 (3H, s, O-CH_3), 3.51 (2H, m, CH_2-C<u>H</u>$_2$-O), 4.33 (1H, dd, J = 10.6, 4.5 Hz, 5'β-H), 3.15 (2H, dd, J = 15.2, 7.6 Hz, CH_2-PO), 4.60

(2H, s, O-CH_2-O), 4.74 (1H, narr m, 3'α-H), 5.28 (1H, m, =C<u>H</u>-CH_2-PO), 5.44 (1H, t, J ~ 7 Hz, =C<u>H</u>-CH_2-CH_2), 7.45, 7.52 and 7.73 (4H, 2H and 4H, each m, Ar-H); MS (EI) m/z (relative intensity) no M^+, 613 (100), 538 (9), 481 (31), 449 (22); HRMS (ESI) exact mass calcd for $C_{37}H_{59}O_5Si_2PNa$ 693.3536, measured 693.3506.

[2-[(3'*R*,5'*R*)-3',5'-Bis[(*tert*-butyldimethylsilyl)oxy]-4'-[3''-[((*tert*-butyldimethylsilyl)oxy)propylidene]cyclohexylidene]ethyl]diphenylphosphine Oxides (33 and 34).

33 (major *E*-isomer): ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.044, -0.022, 0.011, 0.020, 0.030, and 0.035 (each 3H, each s, 6 x $SiCH_3$), 0.787, 0.878 and 0.894 (each 9H, each s, 3 x Si-*t*-Bu), 1.47 (1H, br t, J ~ 11 Hz, 6'α-H), 2.04 (1H, m, 2'α-H), 2.22 (1H, d, J = 13.7 Hz, 2'β-H), 2.28 (2H, m, =C-C<u>H</u>$_2$-CH_2), 2.62 (1H, dd, J = 12.8, 4.2 Hz, 6'β-H), 3.58 (2H, m, CH_2-C<u>H</u>$_2$-O), 4.32 (1H, dm, J ~ 10 Hz, 5'β-H), 3.17 (2H, dd, J = 15.2, 7.6 Hz, CH_2-PO), 4.73 (1H, br s, 3'α-H), 5.27 (1H, m, =C<u>H</u>-CH_2-CH_2), 5.43 (1H, br t, J ~ 7 Hz, =C<u>H</u>-CH_2-PO), 7.46, 7.51 and 7.72 (4H, 2H and 4H, each m, Ar-H); HRMS (ESI) exact mass calcd for $C_{41}H_{69}O_4Si_3PNa$ (M^+ + Na) 763.4139, measured 763.4157.

1α-[(*tert*-Butyldimethylsilyl)oxy]-2-[3'-(methoxymethoxy)propylidene]-25-[(triethylsilyl)oxy]-19-norvitamin D_3 *tert*-Butyldimethylsilyl Ether (36a): UV (in hexane) λ_{max} 244.0, 252.5, 262.5 nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.015**,** 0.056, 0.061, and 0.069 (each 3H, each s, 4 x $SiCH_3$), 0.556 (3H, s, 18-H_3), 0.565 (6H, q, J = 7.9 Hz, 3 x $SiCH_2$), 0.821 and 0.921 (9H and 9H, each s, 2 x Si-*t*-Bu), 0.930 (3H, d, J ~ 7 Hz, 21-H_3), 0.947 (9H, t, J = 7.9

Hz, 3 x $SiCH_2C\underline{H}_3$), 1.191 (6H, s, 26- and 27-H_3), 1.79 (1H, t, J = 12.2 Hz, 10α-H), 1.90 (1H, m), 2.00 (2H, m), 2.20 (1H, br d, J = 13.2 Hz, 4β-H), 2.29 (1H, br d, J = 13.2 Hz, 4α-H), 2.41 (2H, q, J ~ 7 Hz, =CH-$C\underline{H}_2$), 2.79 (1H, br d, J = 12.6 Hz, 9β-H), 3.04 (1H, dd, J = 12.4, 4.5 Hz, 10β-H), 3.36 (3H, s, O-CH_3), 3.54 (2H, m, CH_2-$C\underline{H}_2$-O), 4.35 (1H, m, w/2 = 21 Hz, 1β-H),4.62 (2H, s, O-CH_2-O), 4.81 (1H, t, J ~ 2.7 Hz, 3α-H), 5.47 (1H, dt, J = 1.5, 7.6 Hz, $\underline{H}C$=C-CH_2), 5.87 and 6.12 (1H and 1H, each d, J = 11.0 Hz, 7- and 6-H).

1α-[(*tert*-Butyldimethylsilyl)oxy]-2-[3'-[((*tert*-butyldimethylsilyl)oxy)propylidene]-25-[(triethylsilyl)oxy]-19-norvitamin D_3 *tert*-Butyldimethylsilyl Ether (37a): UV (in EtOH) λ_{max} 244.0, 252.5, 262.5 nm;^{1}H NMR (500 MHz, $CDCl_3$) δ -0.023**,** 0.052, 0.056, 0.061, 0.063, and 0.070 (each 3H, each s, 6 x $SiCH_3$), 0.555 (3H, s, 18-H_3), 0.565 (6H, q, J = 7.9 Hz, 3 x $SiCH_2$), 0.819, 0.897, and 0.923 (9H and 9H, each s, 3 x Si-*t*-Bu), 0.878 (3H, d, J = 7.1 Hz, 21-H_3), 0.947 (9H, t, J = 7.9 Hz, 3 x $SiCH_2C\underline{H}_3$), 1.190 and 1.191 (3H and 3H, each s, 26- and 27-H_3), 1.79 (1H, t, J = 11.6 Hz, 10α-H), 1.90 (1H, m), 2.00 (2H, m), 2.19 (1H, br d, J ~14 Hz, 4β-H), 2.27 (1H, br d, J ~ 14 Hz, 4α-H), 2.33 (2H, m, =CH-$C\underline{H}_2$), 2.79 (1H, br d, J ~13 Hz, 9β-H), 3.05 (1H, dd, J = 12.0, 4.0 Hz, 10β-H), 3.62 (2H, m, CH_2-$C\underline{H}_2$-O), 4.34 (1H, m, w/2 = 20 Hz, 1β-H), 4.81 (1H, t, J ~ 2.8 Hz, 3α-H), 5.47 (1H, dt, J ~1.5, ~7.5 Hz, $\underline{H}C$=C-CH_2), 5.88 and 6.12 (1H and 1H, each d, J = 11.0 Hz, 7- and 6-H); HRMS (ESI) exact mass calcd for $C_{53}H_{104}O_4Si_4Na$ (M^+ + Na) 939.6909, measured 939.6900.

(20*S*)-1α-[(*tert*-Butyldimethylsilyl)oxy]-2-[3'-[((*tert*-butyldimethylsilyl)oxy)propylidene]-25-[(triethylsilyl)oxy]-19-norvitamin D_3 *tert*-Butyldimethylsilyl Ether (37b): UV (in EtOH) λ_{max} 243.5, 252.5, 262.5 nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.024, 0.057, 0.059, and 0.069 (3H, 3H, 6H, and 6H, each s, 6 x $SiCH_3$), 0.550 (3H, s, 18-H_3), 0.560 (6H, q, J = 7.5 Hz, 3 x $SiCH_2$), 0.818, 0.895, and 0.923 (each 9H, each s, 3 x Si-*t*-Bu), 0.867 (3H, d, J = 7.0 Hz, 21-H_3), 0.943 (9H, t, J = 7.5 Hz, 3 x $SiCH_2C\underline{H}_3$), 1.191 (6H, s, 26- and 27-H_3), 1.79 (1H, t, J ~12 Hz, 10α-H), 1.90 (1H, m), 2.00 (2H, m), 2.19 (1H, br d, J ~13 Hz, 4β-H), 2.27 (1H, br d, J ~13 Hz, 4α-H), 2.33 (2H, m, =CH-C$\underline{H}_2$), 2.79 (1H, br d, J ~11.5 Hz, 9β-H), 3.05 (1H, dm, J ~12 Hz, 10β-H), 3.62 (2H, m, CH_2-C$\underline{H}_2$-O), 4.34 (1H, m, w/2 = 20 Hz, 1β-H), 4.80 (1H, br s, 3α-H), 5.47 (1H, t, J = 7.0 Hz, $\underline{H}$C=C-CH_2), 5.88 and 6.11 (1H and 1H, each d, J = 11.2 Hz, 7- and 6-H); HRMS (ESI) exact mass calcd for $C_{53}H_{104}O_4Si_4Na$ (M^+ + Na) 939.6909, measured 939.6907.

1α,25-Dihydroxy-2-[3'-(methoxymethoxy)propylidene]-19-norvitamin D_3 (5a): UV (in EtOH) λ_{max} 243.5, 252.0, 262.0 nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.549 (3H, s, 18-H_3), 0.940 (3H, d, J = 6.4 Hz, 21-H_3), 1.220 (6H, s, 26- and 27-H_3), 2.38 (1H, m, one of =CH-C$\underline{H}_2$), 2.47 (2H, narr m, 4α- and 4β-H), 2.59 (1H, m, one of =CH-C$\underline{H}_2$), 2.82 (1H, br d, J = 12.8 Hz, 9β-H), 3.14 (1H, dd, J = 13.1, 4.9 Hz, 10β-H), 3.34 (3H, s, O-CH_3), 3.55 and 3.63 (1H and 1H, each m, CH_2-C$\underline{H}_2$-O), 4.44 (1H, m, w/2 = 20 Hz, 1β-H), 4.62 (2H, s, O-CH_2-O), 4.84 (1H, m, w/2 = 10 Hz, 3α-H), 5.68 (1H, t, J = 7.4 Hz, $\underline{H}$C=C-CH_2), 5.88 and 6.31 (1H and 1H, each d, J = 11.2 Hz, 7- and 6-H); HRMS (ESI) exact mass calcd for $C_{31}H_{52}O_5Na$ 527.3712, measured 527.3702.

1α,25-Dihydroxy-2-[3'-hydroxypropylidene]-19-norvitamin D_3 (*E*-isomer 6a): UV (in EtOH) λ_{max} 243.0, 251.0, 261.5 nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.549 (3H, s, 18-H_3), 0.940 (3H, d, J = 6.3 Hz, 21-H_3), 1.22 (6H, s, 26- and 27-H_3), 2.33 and 2.55 (1H and 1H, each m, =CH-C$\underline{H}_2$), 2.47 (2H, narr m, 4α- and 4β-H), 2.82 (1H, br d, J ~13 Hz, 9β-H), 3.16 (1H, dd, J = 13.0, 4.8 Hz, 10β-H), 3.66 and 3.76 (1H and 1H, each m, CH_2-C$\underline{H}_2$-O), 4.45 (1H, m, w/2 = 20 Hz, 1β-H), 4.85 (1H, narr m, 3α-H), 5.66 (1H, t, J = 7.3 Hz, $\underline{H}$C=C-CH_2), 5.88 and 6.31 (1H and 1H, each d, J = 11.2 Hz, 7- and 6-H); HRMS (ESI) exact mass calcd for $C_{29}H_{48}O_4Na$ (M^+ + Na) 483.3450, measured 483.3461.

(20*S*)-1α,25-Dihydroxy-2-[3'-hydroxypropylidene]-19-norvitamin D_3 (*E*-isomer 6b): UV (in EtOH) λ_{max} 243.0, 251.5, 261.0 nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.548 (3H, s, 18-H_3), 0.858 (3H, d, J = 6.4 Hz, 21-H_3), 1.21 (6H, s, 26- and 27-H_3), 2.35 and 2.54 (1H and 1H, each m, =CH-C$\underline{H}_2$), 2.47 (2H, narr m, 4α- and 4β-H), 2.82 (1H, br d, J = 12.7 Hz, 9β-H), 3.16 (1H, dd, J = 13.1, 4.9 Hz, 10β-H), 3.65 and 3.76 (1H and 1H, each m, CH_2-C$\underline{H}_2$-O), 4.45 (1H, m, w/2 = 25 Hz, 1β-H), 4.85 (1H, narr m, 3α-H), 5.66 (1H, t, J = 7.4 Hz, $\underline{H}$C=C-CH_2), 5.88 and 6.31 (1H and 1H, each d, J = 11.4 Hz, 7- and 6-H); HRMS (ESI) exact mass calcd for $C_{29}H_{48}O_4Na$ (M^+ + Na) 483.3450, measured 483.3427.

[(1*R*,3a*S*,7a*R*)-7a-Methyl-1-[(*R*)-6-[(triethylsilyl)oxy]-6-methylheptan-2-yl]-octahydro-inden-(4*E*)-ylidene]acetic acid ethyl ester: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.562 (6H, q, J = 7.9 Hz, 3 x $SiCH_2$), 0.581 (3H, s, 7a-H_3), ca. 0.94 (3H, overlapped, C*H*$_3$-CH), 0.944 (9H, t, J = 7.9 Hz, 3 x $SiCH_2CH_3$), 1.187 [6H, s, $C(CH_3)_2$], 1.284 (3H, t, J = 7.1 Hz, CH_3CH_2O),

3.84 (1H, m, 5β-H), 4.15 (2H, m, CH_3CH_2O), 5.45 (1H, br s, =CH); MS (EI) m/z (relative intensity) 464 (M^+, 2), 435 ($M^+ - C_2H_5$, 100), 406 (19), 173 (98); HRMS (ESI) exact mass calcd for $C_{26}H_{47}O_3Si$ ($M^+ - C_2H_5$) 435.3294, measured 435.3309.

[(1*R*,3a*S*,7a*R*)-7a-Methyl-1-[(*S*)-6-[(triethylsilyl)oxy]-6-methylheptan-2-yl]-octahydro-inden-(4*E*)-ylidene]acetic acid ethyl ester: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.561 (6H, q, J = 7.9 Hz, 3 x $SiCH_2$), 0.576 (3H, s, 7a-H_3), 0.847 (3H, d, J = 6.2 Hz, CH_3-CH), 0.943 (9H, t, J = 7.9 Hz, 3 x $SiCH_2CH_3$), 1.187 [6H, s, $C(CH_3)_2$], 1.285 (3H, t, J = 7.1 Hz, CH_3CH_2O), 3.86 (1H, m, 5β-H), 4.15 (2H, m, CH_3CH_2O), 5.46 (1H, br s, =CH); MS (EI) m/z (relative intensity) 464 (M^+, 1), 435 ($M^+ - C_2H_5$, 100), 406 (17), 173 (93); HRMS (ESI) exact mass calcd for $C_{26}H_{47}O_3Si$ ($M^+ - C_2H_5$) 435.3294, measured 435.3303.

2-[(1*R*,3a*S*,7a*R*)-7a-Methyl-[(*R*)-6-[(triethylsilyl)oxy]-6-methylheptan-2-yl]-octahydro-inden-(4*E*)-ylidene]ethanol (38a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.563 (6H, q, J = 7.9 Hz, 3 x $SiCH_2$), 0.554 (3H, s, 7a-H_3), 0.928 (3H, d, J = 7 Hz, CH_3-CH), 0.945 (9H, t, J = 7.9 Hz, 3 x $SiCH_2CH_3$), 1.188 [6H, s, $C(CH_3)_2$], 2.63 (1H, dd, J = 12.0, 4.5 Hz, 5β-H), 4.20 (2H, m; after D_2O d, J = 7.0 Hz, CH_2OH), 5.22 (1H, t, J = 7.0 Hz, =CH); MS (EI) m/z (relative intensity) no M^+, 407 ($M^+ - CH_3$, 5), 375 (6), 273 (33), 217 (53), 173 (100); exact mass calcd for $C_{25}H_{47}O_2Si$ ($M^+ - CH_3$) 407.3345, measured 407.3353.

2-[(1*R*,3a*S*,7a*R*)-7a-Methyl-[(*S*)-6-[(triethylsilyl)oxy]-6-methylheptan-2-yl]-octahydro-inden-(4*E*)-ylidene]ethanol (38b): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.561 (6H, q, J = 7.9 Hz, 3 x $SiCH_2$), 0.550 (3H, s, 7a-H_3), 0.844 (3H, d, J = 6.5 Hz, C*H*$_3$-CH), 0.943 (9H, t, J = 7.9 Hz, 3 x $SiCH_2CH_3$), 1.187 [6H, s, $C(CH_3)_2$], 2.63 (1H, m, 5β-H), 4.21 (2H, m; after D_2O d, J = 6.9 Hz, C*H*$_2$OH), 5.22 (1H, t, J = 7.0 Hz, =CH); MS (EI) m/z (relative intensity) no M^+, 407 (M^+ - CH_3, 7), 375 (3), 273 (28), 217 (51), 173 (100); exact mass calcd for $C_{25}H_{47}O_2Si$ (M^+ - CH_3) 407.3345, measured 407.3349.

(1*R*,3a*S*,7a*R*)-4-[2-(Benzothiazole-2-sulfonyl)-(4*E*)-ethylidene]-7a-methyl-1-[(*R*)-6-[(triethylsilyl)oxy]-6-methylheptan-2-yl]-octahydro-indene (39a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.262 (3H, s, 7a-H_3), 0.552 (6H, q, J = 7.9 Hz, 3 x $SiCH_2$), 0.852 (3H, d, J = 6.2 Hz, C*H*$_3$-CH), 0.935 (9H, t, J = 7.9 Hz, 3 x $SiCH_2CH_3$), 1.173 [6H, s, $C(CH_3)_2$], 2.55 (1H, br d, J ~ 13 Hz, 5β-H), 4.21 (1H, dd, J = 14.2, 6.9 Hz, one of CH_2S), 4.43 (1H, dd, J = 14.2, 8.9 Hz, one of CH_2S), 5.02 (1H, t, J = 7.8 Hz, =CH), 7.61 (2H, m, Ar-H), 8.00 and 8.22 (1H and 1H, each d, J = 8.0 Hz, Ar-H); MS (EI) m/z (relative intensity) no M^+, 588 (M^+ - CH_3, 2), 457 (11), 435 (4), 387 (16), 103 (100); exact mass calcd for $C_{33}H_{53}S_2NO_3SiNa$ (M^+ + Na) 626.3134, measured 626.3122.

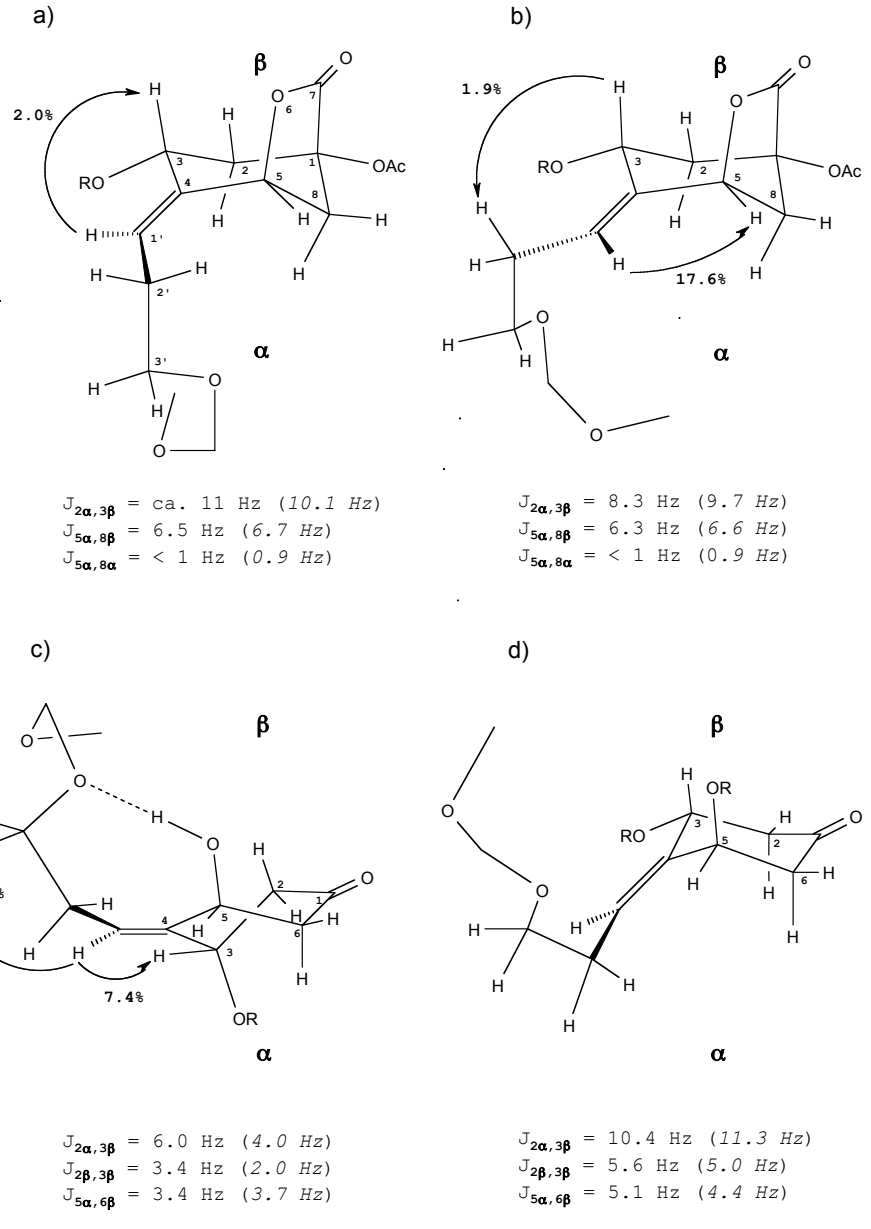
(1*R*,3a*S*,7a*R*)-4-[2-(Benzothiazole-2-sulfonyl)-(4*E*)-ethylidene]-7a-methyl-1-[(*S*)-6-[(triethylsilyl)oxy]-6-methylheptan-2-yl]-octahydro-indene (39b): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.268 (3H, s, 7a-H_3), 0.549 (6H, q, J = 7.9 Hz, 3 x $SiCH_2$), 0.798 (3H, d, J = 6.4 Hz, C*H*$_3$-CH), 0.931 (9H, t, J = 7.9 Hz, 3 x $SiCH_2CH_3$), 1.167 [6H, s, $C(CH_3)_2$], 2.55 (1H, br d, J ~

13 Hz, 5β-H), 4.21 (1H, dd, J = 14.2, 6.8 Hz, one of CH_2S), 4.43 (1H, dd, J = 14.2, 8.8 Hz, one of CH_2S), 5.01 (1H, t, J = 7.8 Hz, =CH), 7.61 (2H, m, Ar-H), 8.00 and 8.22 (1H and 1H, each d, J = 8.0 Hz, Ar-H); MS (EI) m/z (relative intensity) no M^+, 588 (M^+ - CH_3, 1), 457 (7), 435 (6), 387 (13), 103 (100); exact mass calcd for $C_{33}H_{54}S_2NO_3SiNa$ (M^+ + Na) 626.3134, measured 626.3112.

1α,25-Dihydroxy-2-[3'-hydroxypropylidene]-19-norvitamin D_3 (*Z*-isomer 7a): UV (in EtOH) λ_{max} 243.0, 251.5, 262.0 nm; ^1H NMR (500 MHz, $CDCl_3$) δ 0.553 (3H, s, 18-H_3), 0.939 (3H, d, J = 6.6 Hz, 21-H_3), 1.22 (6H, s, 26- and 27-H_3), 2.19 (1H, t, J = 11.0 Hz, 4β-H), 2.25 (1H, br d, J = 14.6 Hz, 10β-H), 2.40 and 2.56 (1H and 1H, each m, =CH-C$\underline{H}_2$), 2.74 (1H, dd, J = 13.0, 4.8 Hz, 4α-H), 2.81 (1H, br d, J = 12.5 Hz, 9β-H), 2.93 (1H, dd, J = 14.6, 3.8 Hz, 10α-H), 3.67 and 3.76 (1H and 1H, each m, CH_2-C$\underline{H}_2$-O), 4.48 (1H, m, w/2 =19 Hz, 3α-H), 4.89 (1H, narr m, 1β-H), 5.65 (1H, t, J = 8.1 Hz, $\underline{H}$C=C-CH_2), 5.85 and 6.40 (1H and 1H, each d, J = 11.0 Hz, 7- and 6-H). HRMS (ESI) exact mass calcd for $C_{29}H_{48}O_4Na$ (M^+ + Na) 483.3450, measured 483.3441.

(20*S*)-1α,25-Dihydroxy-2-[3'-hydroxypropylidene]-19-norvitamin D_3 (*Z*-isomer 7b): UV (in EtOH) λ_{max} 243.0, 251.5, 262.0 nm; ^1H NMR (500 MHz, $CDCl_3$) δ 0.550 (3H, s, 18-H_3), 0.854 (3H, d, J = 6.6 Hz, 21-H_3), 1.21 (6H, s, 26- and 27-H_3), 2.19 (1H, t, J ~12 Hz, 4β-H), 2.24 (1H, br d, J = 14.6 Hz, 10β-H), 2.40 and 2.56 (1H and 1H, each m, =CH-C$\underline{H}_2$), 2.74 (1H, dd, J = 13.2, 4.4 Hz, 4α-H), 2.82 (1H, br d, J = 12.4 Hz, 9β-H), 2.92 (1H, dd, J = 14.6, 3.7 Hz, 10α-H), 3.61 and 3.72 (1H and 1H, each m, CH_2-C$\underline{H}_2$-O), 4.47 (1H, m, w/2 = 18 Hz, 3α-H), 4.88 (1H,

narr m, 1β-H), 5.65 (1H, t, J ~ 7.5 Hz, HC=C-CH_2), 5.85 and 6.40 (1H and 1H, each d, J = 11.0 Hz, 7- and 6-H); HRMS (ESI) exact mass calcd for $C_{29}H_{48}O_4Na$ (M^+ + Na) 483.3450, measured 483.3448.



a) $J_{2\alpha,3\beta}$ = ca. 11 Hz (*10.1 Hz*)
$J_{5\alpha,8\beta}$ = 6.5 Hz (*6.7 Hz*)
$J_{5\alpha,8\alpha}$ = < 1 Hz (*0.9 Hz*)

b) $J_{2\alpha,3\beta}$ = 8.3 Hz (*9.7 Hz*)
$J_{5\alpha,8\beta}$ = 6.3 Hz (*6.6 Hz*)
$J_{5\alpha,8\alpha}$ = < 1 Hz (*0.9 Hz*)

c) $J_{2\alpha,3\beta}$ = 6.0 Hz (*4.0 Hz*)
$J_{2\beta,3\beta}$ = 3.4 Hz (*2.0 Hz*)
$J_{5\alpha,6\beta}$ = 3.4 Hz (*3.7 Hz*)

d) $J_{2\alpha,3\beta}$ = 10.4 Hz (*11.3 Hz*)
$J_{2\beta,3\beta}$ = 5.6 Hz (*5.0 Hz*)
$J_{5\alpha,6\beta}$ = 5.1 Hz (*4.4 Hz*)

R = TBDMS

Figure 8. Preferred, energy-minimized (HyperChem and ChemPlus) conformations of the synthesized compounds: **12** (a), **13** (b),. **19** (c), and **22** (d). Hydrogen atoms from the methoxymethyl units are omitted for clarity. The most informative NOEs and ^{1}H-^{1}H coupling constants are given. Values of the calculated (PC MODEL) couplings are given in parentheses.

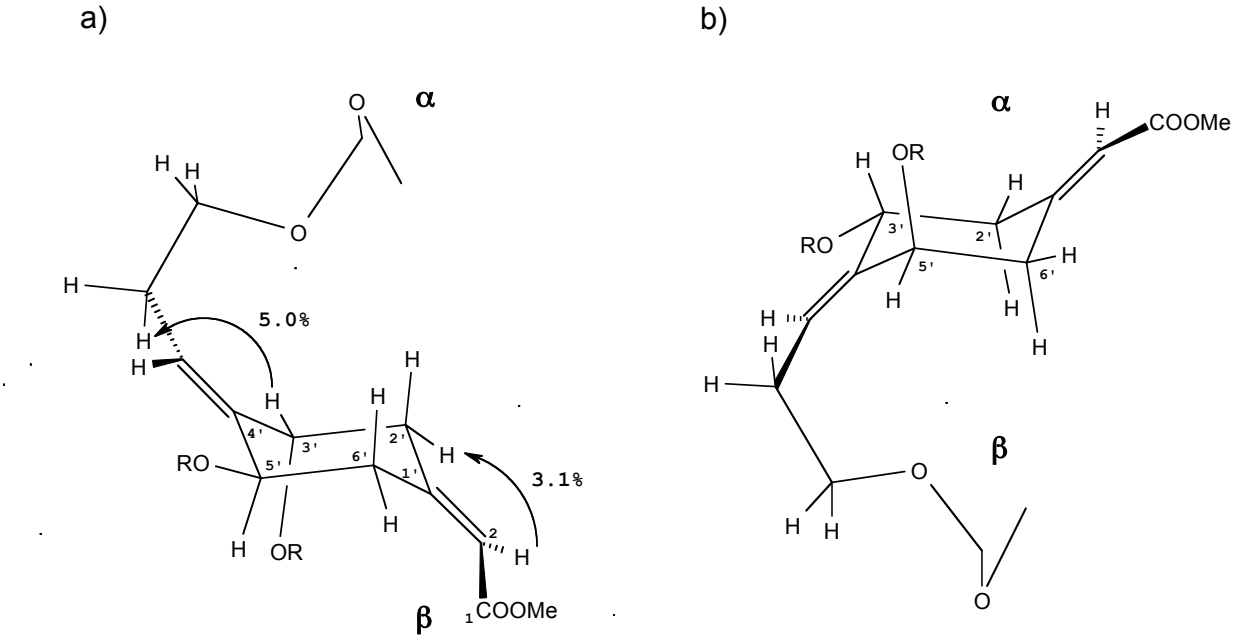


Figure 9. Preferred, energy-minimized (HyperChem and ChemPlus) conformations of the synthesized compounds: **24** (a) and **25** (b). Hydrogen atoms from the methoxymethyl units are omitted for clarity. The most informative NOEs and ^{1}H-^{1}H coupling constants are given.

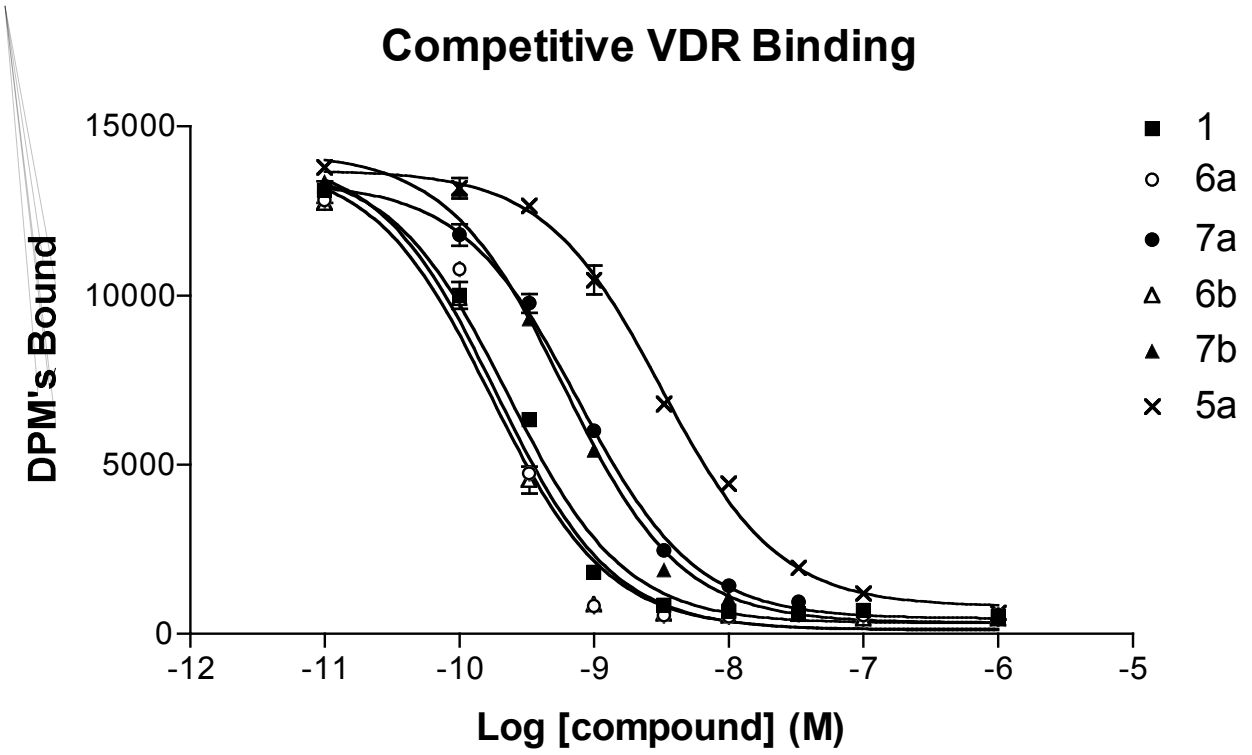


Figure 10. Competitive binding of 1α,25-$(OH)_2D_3$ (**1**) and the synthesized vitamin D analogs **5a**, **6a**,**b** and **7a**,**b** to the full-length recombinant rat vitamin D receptor. The experiments were carried out in duplicate on two-three different occasions.

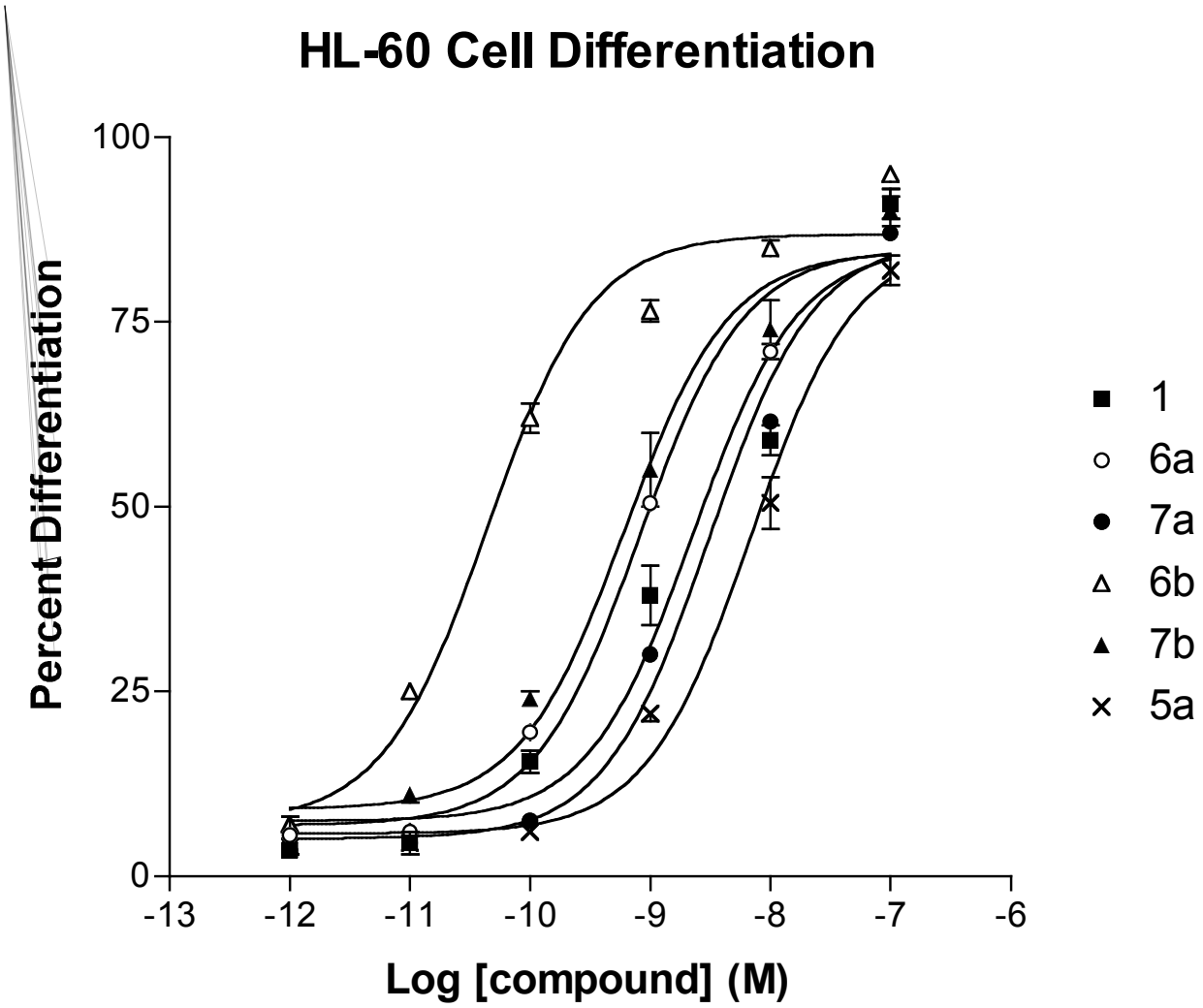


Figure 11. Induction of differentiation of HL-60 promyelocytes to monocytes by 1α,25-$(OH)_2D_3$ (**1**) and the synthesized vitamin D analogs **5a**, **6a**,**b** and **7a**,**b**. Each analog was tested two-three times.

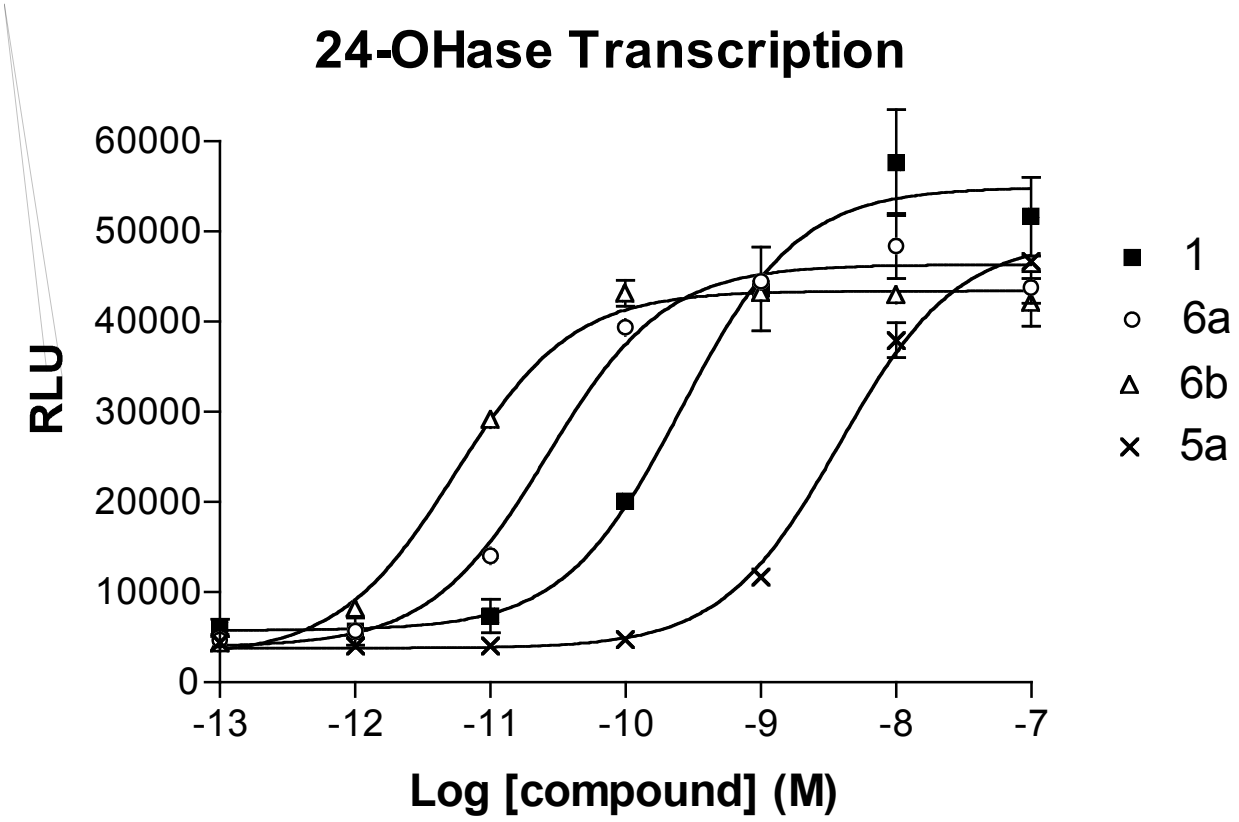


Figure 12. Transcriptional assay of 1α,25-$(OH)_2D_3$ (**1**) and the synthesized vitamin D analogs **5a**, **6a** and **6b** in rat osteosarcoma cells stably transfected with a 24-hydroxylase genereporter plasmid. Each analog was tested for transcriptional activity two different times.