Synthesis of 5-methyl-5-methoxymethyloxy-2-hexanone (8) from γ-valerolactone.

2-Methylhexane-2,5-diol. A solution of methyl iodide (34 mL, 0.55 mol) in ether (150 mL) was added dropwise to the mixture of magnesium (13 g) and ether (50 mL). The mixture was stirred at room temperature for 20 min. To this solution was added γ-valerolactone (25 g, 0.25 mol) in THF (80 mL) at 0 °C and the mixture was stirred at that temperature for 2.5 h. The reaction mixture was quenched with aqueous HCl and extracted with ether and then with AcOEt. Combined organic layer was washed with aqueous Na₂S₂O₃ and water, dried and evaporated. The residue was chromatographed on silica gel (180 g) with AcOEt to yield 2-methylhexane-2,5-diol (15.7 g, 48%).

\(^1\)H-NMR δ 1.21 (d, 3 H, J=6.2 Hz, H-6), 1.225 and 1.230 (s, each 3 H, (CH₃)₂C), 1.54-1.64 (m, 4 H, H-3 and -4), 3.81 (m, 1 H, H-5). IR (neat) 3347, 2969, 1466, 1375, 1302, 1267, 1219, 1159, 1121, 1063 cm⁻¹.

5-Hydroxy-5-methyl-2-hexanone. To a solution of oxalyl chloride (3.1 mL, 36 mmol) in CH₂Cl₂ (16 mL) was added a solution of DMSO (5.6 mL, 79 mmol) in CH₂Cl₂ (4 mL) at -78 °C, and the mixture was stirred at that temperature for 15 min. To this solution was added a solution of 2-methylhexane-2,5-diol (4.1 g, 31 mmol) in CH₂Cl₂ (20 mL), and the mixture was stirred for 15 min. Triethylamine (23 mL, 0.16 mol) was added to the reaction mixture at -78°C and then the mixture was allowed to warm to room temperature. The reaction mixture was diluted with CH₂Cl₂, washed with water, dried and evaporated. The residue was chromatographed on silica gel (60 g) with 20% AcOEt-benzene to yield 5-hydroxy-5-methyl-2-hexanone (1.78 g, 44%).

\(^1\)H-NMR δ 1.22 (s, 6 H, (CH₃)₂C ), 1.77 (t, 2 H, J=7. 4 Hz, H-4), 2.18 (s, 3 H, H-1), 2.59 (t, 2 H, J=7.4 Hz, H-3). \(^{13}\)C-NMR δ 29.3, 30.0, 36.6, 38.7, 70.1, 209.7. IR
(neat) 3409, 2969, 1742 cm⁻¹.

5-Methyl-5-methoxymethyloxy-2-hexanone (8). To a solution of 5-hydroxy-5-methyl-2-hexanone (5.47 g, 42 mmol) and N,N-diisopropylethylamine (22 mL, 127 mmol) in dry CH₂Cl₂ (30 mL) was added chloromethyl methyl ether (9.5 mL, 125 mmol) at 0 °C. The mixture was stirred at room temperature for 5 h. The mixture was poured into water and extracted with CH₂Cl₂. The extracts were washed with water, dried and evaporated. The residue was chromatographed on silica gel (160 g) with 10% AcOEt-hexane to yield MOM ether 8 (5.31 g, 73%) and to recover the starting alcohol (0.72 g, 13%). 8. \(^1\)H-NMR δ 1.22 (s, 6 H, (CH₃)₂C), 1.79 (t, 2 H, J=7.7 Hz, H-4), 2.17 (s, 3 H, H-1), 2.53 (t, 2 H, J=7.7 Hz, H-3), 3.35 (s, 3 H, CH₃O), 4.67 (s, 2 H, OCH₂O). \(^1^3\)C-NMR δ 26.2, 29.9, 35.3, 38.4, 55.1, 75.2, 90.9, 208.9. IR (neat) 2977, 1716 cm⁻¹.
Competitive Binding to Bovine Thymus VDR
Transcriptional Activity
Differentiation of HL-60 Cells
Bone Calcium Mobilization