The Synthesis of 19-Nor-1α, 25-dihydroxy-22-oxo-vitamin D_3

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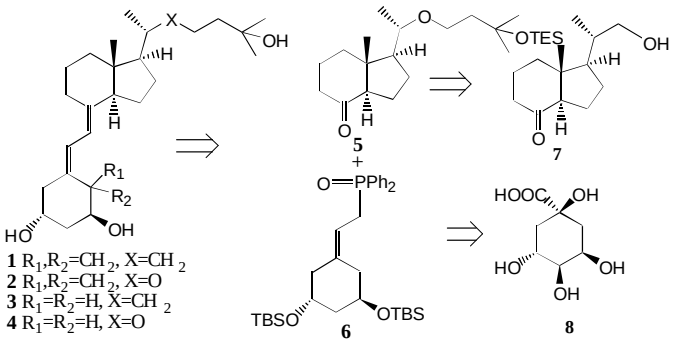
Abstract: 19-Nor-1α, 25-dihydroxy-22-oxo-vitamin D_3 **4** was synthesized by the coupling of known compound **5** and the A-ring phosphine oxide **6** followed by deprotection of the hydroxy functions.

Keywords: 19-Nor-1α, 25-dihydroxy-22-oxo-vitamin D_3, device, synthesis.

Since the last decade, there has been a growing interest in the development of analogues of 1α, 25- dihydroxyvitamin D_3 **1** with low calcemic effect but increased cell differentiating ability[1]. Among side chain and the A-ring modifications of **1**, the 1α, 25- dihydroxy-22-oxo-vitamin D_3 **2**[2] and 19-nor-1α, 25- dihydroxyvitamin D_3 **3**[3] have shown much lower calcemic effect and stronger cell differentiating ability than **1**. In this paper, we reported synthesis of 19-nor-1α, 25-dihydroxy-22-oxo-vitamin D_3 **4** which was devised by the structural characters of **2** and **3**. The retrosynthetic pathway was outlined in **scheme 1**.

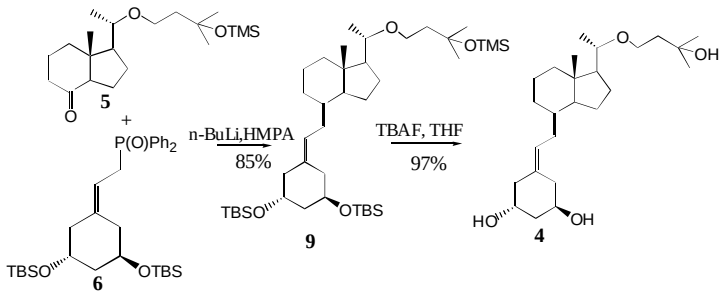
Scheme1 Retrosynthetic pathway



The known intermediate **5** and A-ring phosphine oxide **6** were obtained respectively by Fall's method[4] and DeLuca's method[5]. Coupling of the compound **5** and the A-ring phosphine oxide **6** yielded an intermediate **9**, which was deprotected to

afford the title compound **4** as outlined in **Scheme 2**[6].

Scheme 2



In summary, we have provided a concise route to prepare the compound **4**. Biological evaluation of **4** is in progress.

Acknowledgment

Financial support from the National Natural Science foundation of China (No: 29972013) is gratefully acknowledged.

References and notes

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6. All new compounds were characterized by elemental analysis, IR and ^{1}H-NMR spectral data. Selected analytical data (^{1}H-NMR in $CDCl_3$ at 400MHz) **4**: δ , 6.29 (1H,d, J=11.3Hz), 5.82 (1H, d, J=11.3Hz), 4.11 (1H,m), 4.03 (1H,m), 3.83 (1H,dt, J=5.6,9.3Hz), 3.78 (1H, s, br) 3.49 (1H, dt J=5.6,9.3Hz), 3.42 (1H, m), 2.79 (1H, dd, J=4.3, 12.5Hz), 2.71 (1H, dd, J=3.6, 13.3Hz), 2.48 (1H,dd,J=3.2,13.3Hz), 2.22 (2H, m), 1.95 (4H,m), 1.82 (1H,m), 1.80 (1H,m) 1.30-1.75 (10H,m), 1.22 (3H,s), 1.21 (3H,s), 1.18 (3H,d, J=6.2Hz), 0.90 (1H, m), 0.52 (3H,s)ppm; $[\alpha]_D^{20}$ +76.6 (*c* 2.61, $CHCl_3$).

Received June 8, 2000