Supporting Information for

Stabilizing vitamin D_3 by conformationally selective co-crystallization

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EXPERIMENTAL SECTION

Materials. Vitamin D_3 (1), cholesterol (a) and cholestanol (b) were obtained from J&K Chemical Ltd, with greater than 99% purity. All analytical grade solvents were purchased from Sinopharm Chemical Reagent Co., Ltd and used without further purification.

Preparation of 1a. A mixture of (**1**) (38.4 mg, 0.1 mmol) and (**a**) (38.6 mg, 0.1 mmol) was dissolved in 3 mL of EtOAc in a sealed flask, and stirred at room temperature for 2 h. The resulting solution was filtrated and evaporated slowly at 5 °C. After about 2 days, colorless colunmar-shaped crystals of 1a were isolated by filtration, and dried under vacuum (62.5 mg, 81.2% yield). Anal. (%) Calcd for $C_{54}H_{90}O_2$: C, 84.09; H, 11.76. Found: C, 84.02; H, 11.73.

Preparation of 1b. A mixture of (**1**) (38.4 mg, 0.1 mmol) and (**b**) (38.8 mg, 0.1 mmol) was dissolved in 3 mL of EtOAc in a sealed flask, and stirred at room temperature for 2 h. The resulting solution was filtrated and evaporated slowly at 5 °C. After about 2 days, colorless colunmar-shaped crystals of 1b were isolated by filtration, and dried under vacuum (65.8 mg, 85.2% yield). Anal. (%) Calcd for $C_{54}H_{92}O_2$: C, 83.87; H, 11.99. Found: C, 83.92; H, 12.02.

Differential scanning calorimetry (DSC). Differential scanning calorimetry (DSC) was conducted in Tzero aluminium pans using a TA Instruments Q2000 unit under nitrogen gas flow of 20 mL/min purge. Samples weighting 3–5 mg were heated in standard aluminium pans at scan rates from 10 °C/min. Two-point calibration using indium and tin was carried out to check the temperature axis and heat flow of the equipment.

Thermogravimetric analysis (TGA). Thermogravimetric analysis was carried out in Netzsch TG 209 F3 equipment, using dry air with a nitrogen gas flow of 20 mL/min and a scan rate of 10 °C/min.

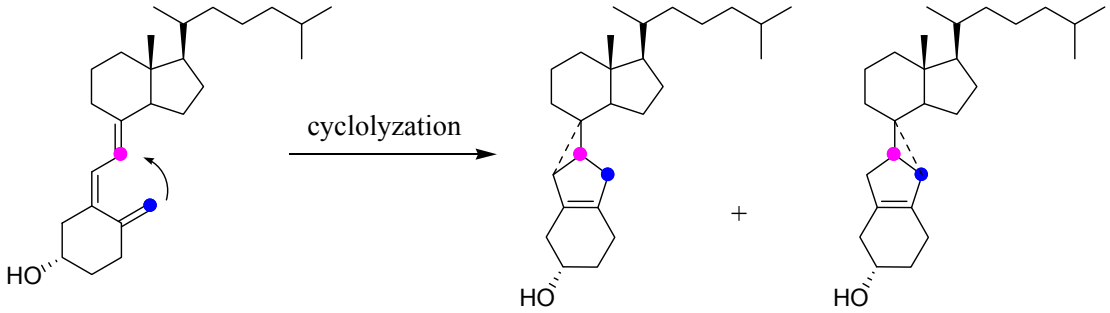
Powder X-ray diffraction (PXRD). PXRD patterns were obtained using a Bruker D8 Advance X-ray diffractometer (Cu Kα radiation). The voltage and current applied were 40 kV and 40 mA respectively. Samples were measured in reflection mode in the 2θ range 3–40° with a scan speed of 1.2 °/min (step size 0.025°, step time 1.0 s) using a LynxEye detector. Data were imaged and integrated with RINT Rapid, and the peaks are analysed with Jade 6.0 software from Rigaku. Calibration of the instrument was performed using Corindon (Bruker AXS Korundprobe) standard.

Single crystal X-ray diffraction. Single crystal X-ray diffractions of 1a (0.25 × 0.12 × 0.12 mm^3) and 1b (0.20 × 0.10 × 0.10 mm^3) were performed on a Bruker Apex II CCD diffractometer using Mo Kα radiation (λ = 0.71073 Å) at 100 K. The structures were solved by direct methods and refined with full-matrix least-squares difference Fourier analysis using SHELX-97 software. All non-hydrogen

atoms were refined with anisotropic displacement parameters, and all hydrogen atoms were placed in calculated positions and refined with a riding model. Data were corrected for the effects of absorption using SADABS.

Dynamic vapor sorption (DVS). Dynamic vapor sorption experiments were performed on a DVS instrument from Surface Measurement Systems, Ltd. Samples were studied over a humidity range of 0 to 95% RH at 25 °C. Each humidity step was made if less than 0.02% weight change occurred over 10 min, with a maximum holding time of 3 h.

Scheme S1 Main impurities produced under heat or irradiation conditions



vitamin D_3 suprasterol I suprasterol II

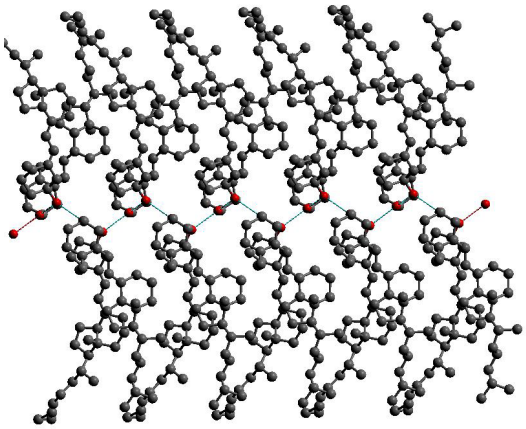
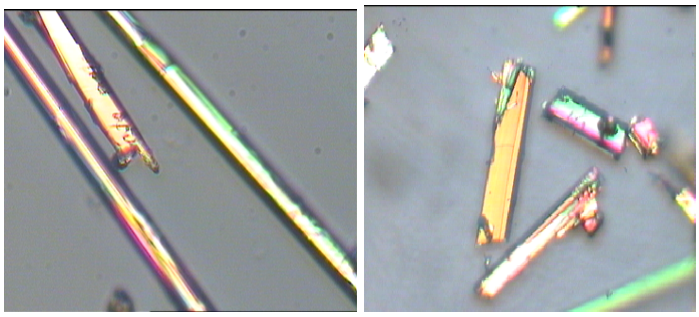


Figure S1 Packing of **1** along C_2 screw axis (from CCDC CHOCAL)

Table S1 Crystallographic Data for **1a** and **1b**.

	1a	**1b**
Formula	$C_{54}H_{90}O_2$	$C_{54}H_{92}O_2$
Formula weight	771.26	773.28
Crystal system	monoclinic	monoclinic
Space group	C_2	C_2
Temperature (K)	100(2)	100(2)
a (Å)	33.5853(15)	33.2196(10)
b (Å)	6.6602(3)	6.8885(3)
c (Å)	21.7816(10)	21.6120(7)
α (°)	90	90
β (°)	99.059(2)	98.464(2)
γ (°)	90	90
Cell volume ($Å^3$)	4811.4(4)	4891.7(3)
Calc. density (g/cm^3)	1.062	1.049
Z	4	4
λ (Mo-Kα)	0.71073	0.71073
Flack parameter	-1.3(14)	-0.1(15)
S	1.035	0.986
R_1	0.053	0.064
R_{int}	0.029	0.048
wR_2	0.125	0.102



1a **1b**

Figure S2 Optical micrographs of co-crystals **1a** and **1b**

Table S2 Distance between C_7 and C_{19} for **1**, **1a**, and **1b**

	α	β	**1a**	**1b**
C_7-C_{19} (Å)	3.145	3.212	3.242	3.241

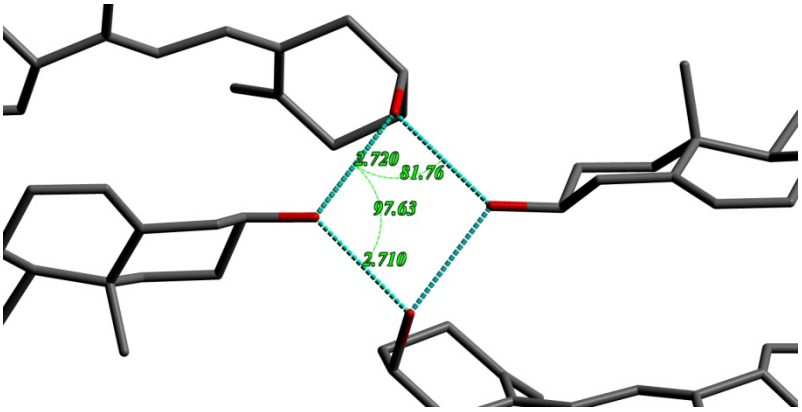


Figure S3 Square-shaped assembling of Co-crystal **1a**

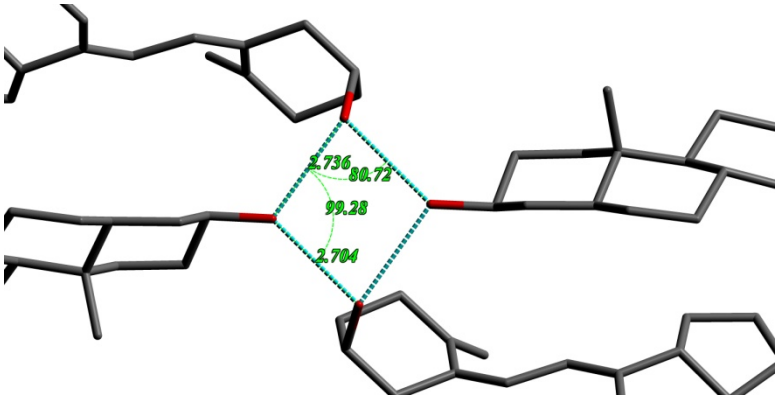


Figure S4 Square-shaped assembling of Co-crystal **1b**

Table S3 Hydrogen bonding distances and angles for **1**, **1a**, and **1b**

	D-H···A	H···A (Å)	D···A (Å)	D-H···A (°)	Symop for A
1	O_1-H_1···O_2	1.748	2.707	180	
	O_2-H_2···O_1	1.766	2.726	180	
1a	O_1-H_1···O_2	1.931(2)	2.710(2)	159(1)	
	O_2-H_2···O_1	1.950(2)	2.720(3)	156(1)	(1-x, y, 1-z)
1b	O_2-H_2···O_1	1.950(29)	2.736(3)	165(3)	
	O_1-H_1···O_2	1.913(27)	2.704(3)	165(3)	(1-x, y, 1-z)

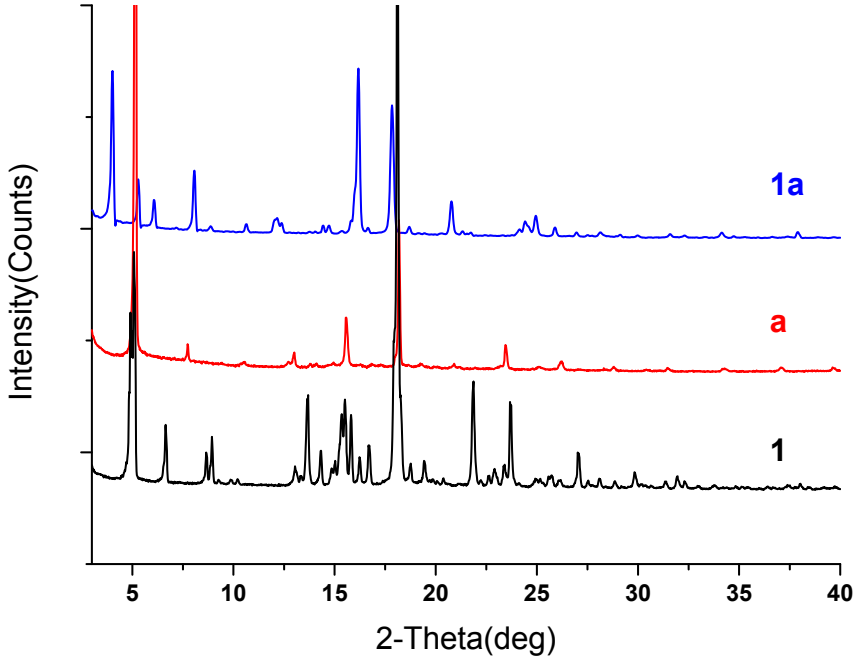


Figure S5 Comparison of XRPD patterns of **1**, **a** and **1a**

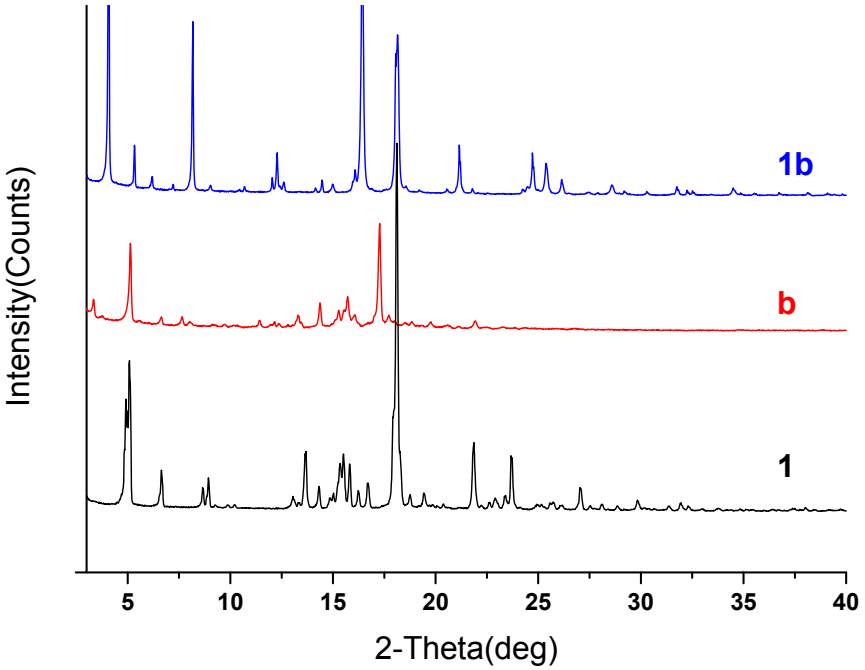


Figure S6 Comparison of XRPD patterns of **1**, **b** and **1b**

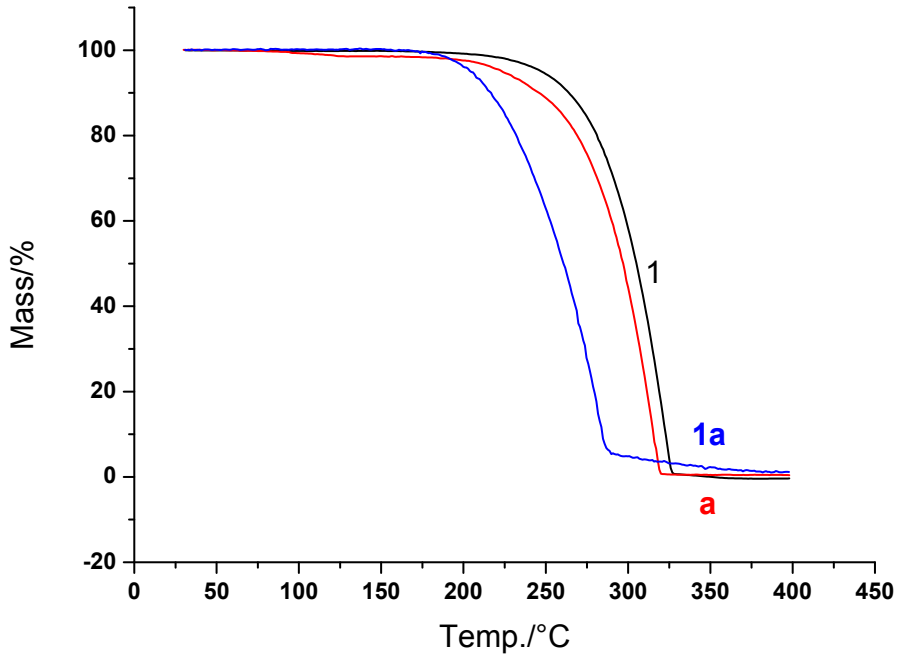


Figure S7 Comparison of TGA diagrams of **1**, **a** and **1a**

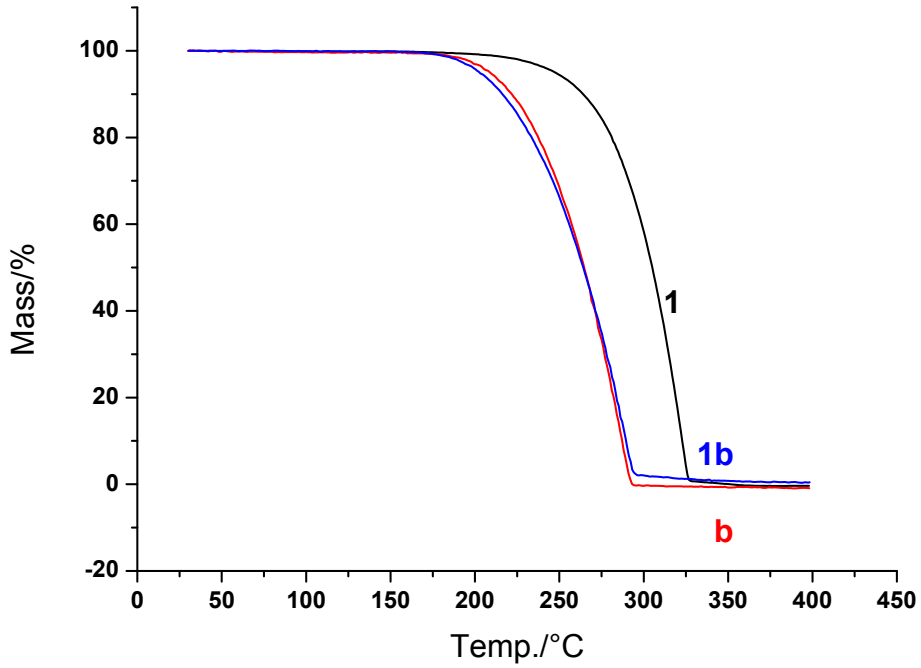


Figure S8 Comparison of TGA diagrams of **1**, **b** and **1b**

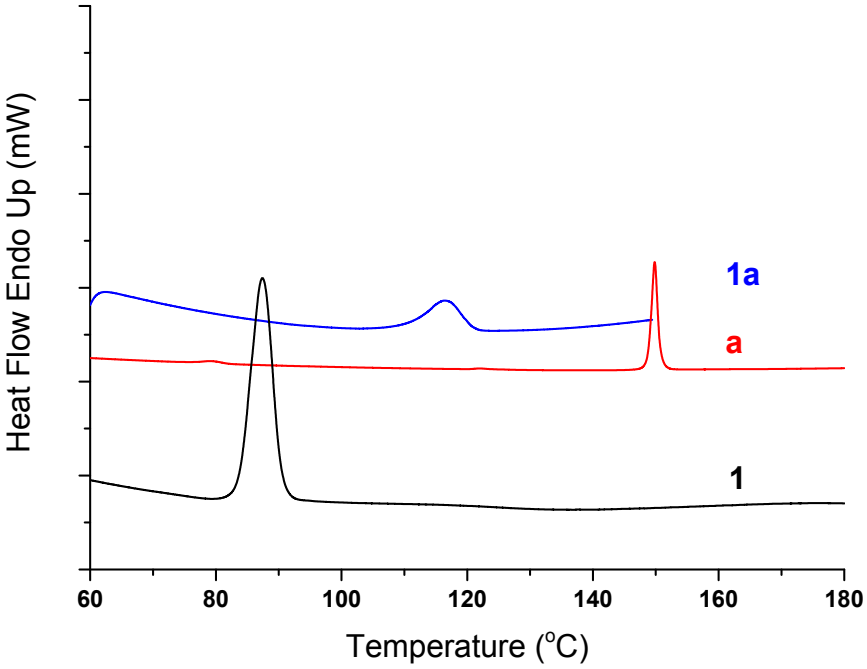


Figure S9 Comparison of DSC diagrams of **1**, **a** and **1a**

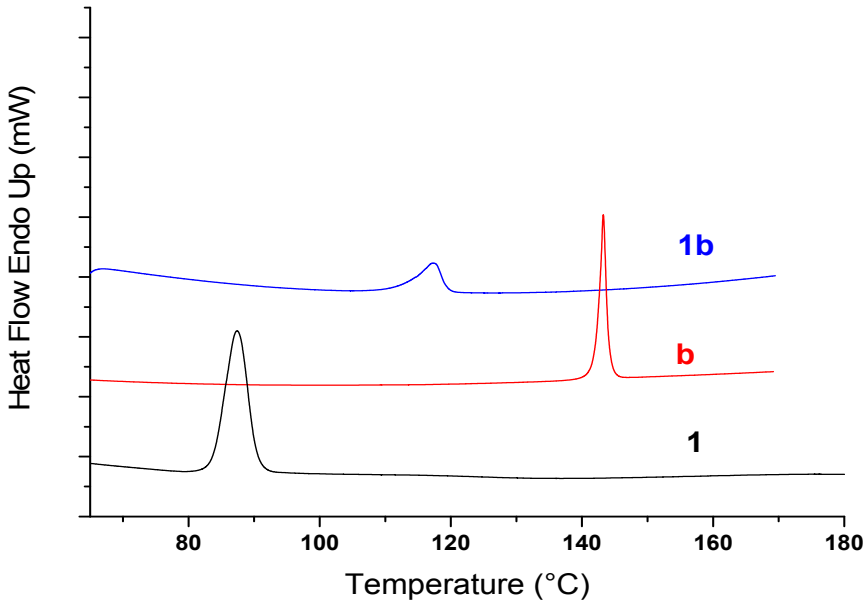


Figure S10 Comparison of DSC diagrams of **1**, **b** and **1b**

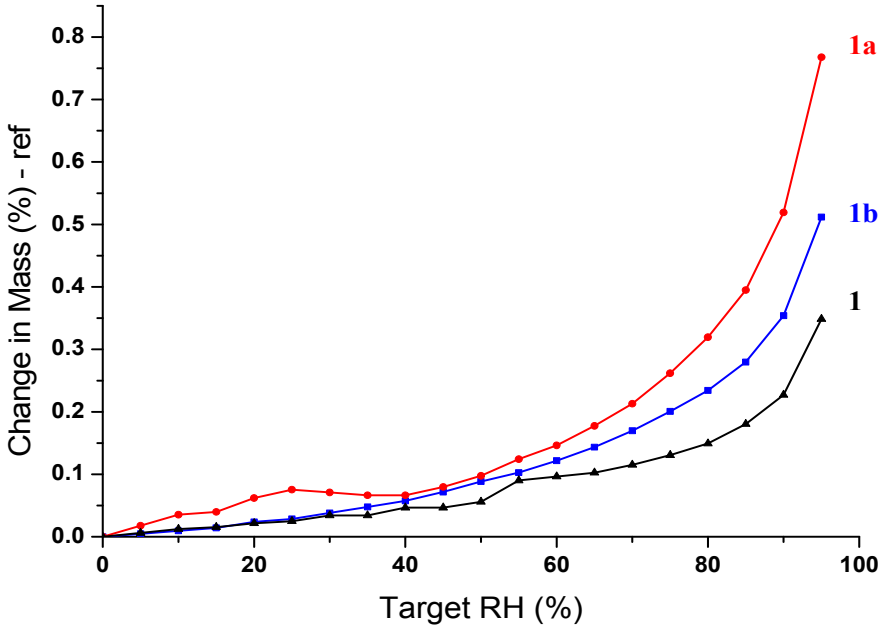


Figure S11 Dynamic water vapor sorption isotherms of **1**, **1a** and **1b**