The Unusual Self-Organising Behaviour of a Glycosteroidal Bolaphile

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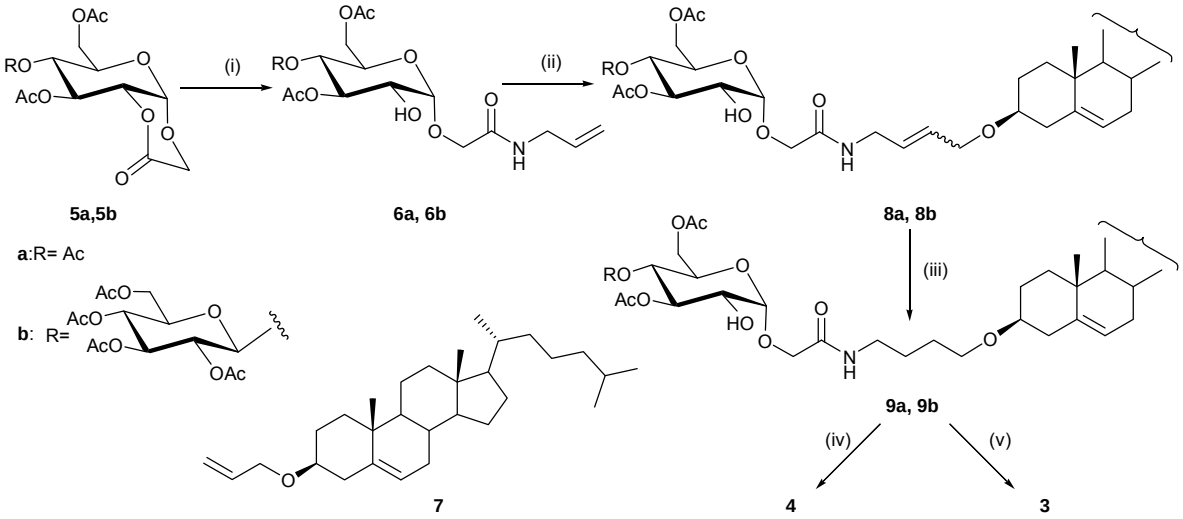
Contents

Synthesis

The detailed synthesis of compounds **3** and **4** including complete characterization of the synthetic intermediates will be published in a due course. As showed on the following scheme, the simple addition of allylamine to easy accessible acetylated carboxymethylglycoside lactones (CMGLs) containing a glucose (**5a**) or a cellobiose (**5b**) skeletons furnished in high yields the corresponding olefins **6a** and **6b**, respectively. Interestingly, these two compounds possessed a single unprotected hydroxyl function readily available for further modification. The use of olefin cross-metathesis with the readily accessible allyl cholesteryl ether **7** provided the corresponding adducts **8a** and **8b**. Selective hydrogenation of the hexocyclic double bond gave access to compounds **9a** and **9b,** containing saturated butyl linkers. A two step procedure applied on compound **9a** and **9b**, including a first reaction of the free hydroxyl group with dodecyl isocyantate followed by deprotection afforded compounds **4** and **3**, respectively.



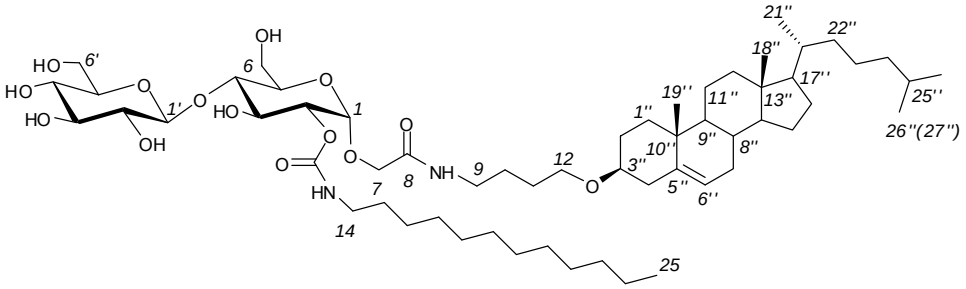
Reagents and conditions: (i) **a**: see ref 4 and references therein, **b**: allylamine, CH_2Cl_2, 24h, RT, 96%; (ii) **a**: **7**, 5% Grubbs-Hoveyda II, CH_2Cl_2, 24h, RT, 72%, **b**: same conditions, 63%; (iii) **a**: H_2, Pd/C, THF, 1h, RT, 82%, **b**: same conditions, 95%; (iv) **3:** dodecyl isocyanate, Et_3N, CH_2Cl_2, 3 days, RT, followed by MeOH/NEt_3/H_2O (8/1/1, v/v), 3h, 40°C, 63%, **4:** same conditions, 65%.

General Experimental Details

Starting compounds and reagents were obtained from Aldrich. Chromatography solvents were purchased from SDS and Carlo Erba. Reactions were monitored by TLC using glass silica gel plates (Merck 60 F_{254}). The plates were developed using vaporisation with a solution of 10% H_2SO_4 in EtOH (v/v). Flash-chromatography separations were performed using Merck Gerudan silica gel Si 60 (40-63μm). NMR spectra were recorded on Bruker AC spectrometers at 75.47 MHz (or 125.77 MHz) for ^{13}C NMR and 300.13 MHz (or 500.13 MHz) for ^{1}H NMR. Chemical shifts (δ) are given in parts per million (ppm) and were measured relative to the signal of tetramethylsilane (δ = 0). Mass spectra were recorded by the Centre de Spectrométrie de Masse of the Université Claude Bernard (Villeurbanne) using electrospray (ESI) technique. Microanalyses were performed by the Service Central d'Analyse of CNRS (Vernaison). Optical rotations were measured at 20 °C with a Perkin Elmer 241 polarimeter at 589 nm (sodium D line) and concentrations (c) are reported in g/100 mL.

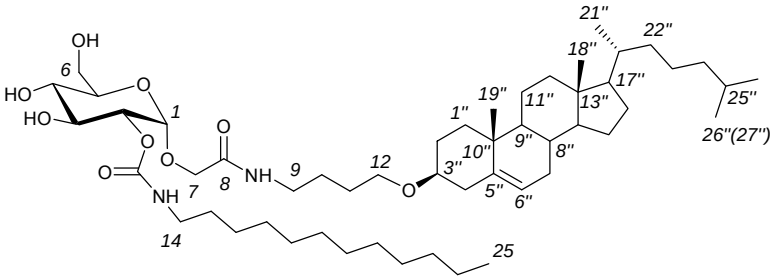
Characterisation Data for New Compounds

Compound **3**



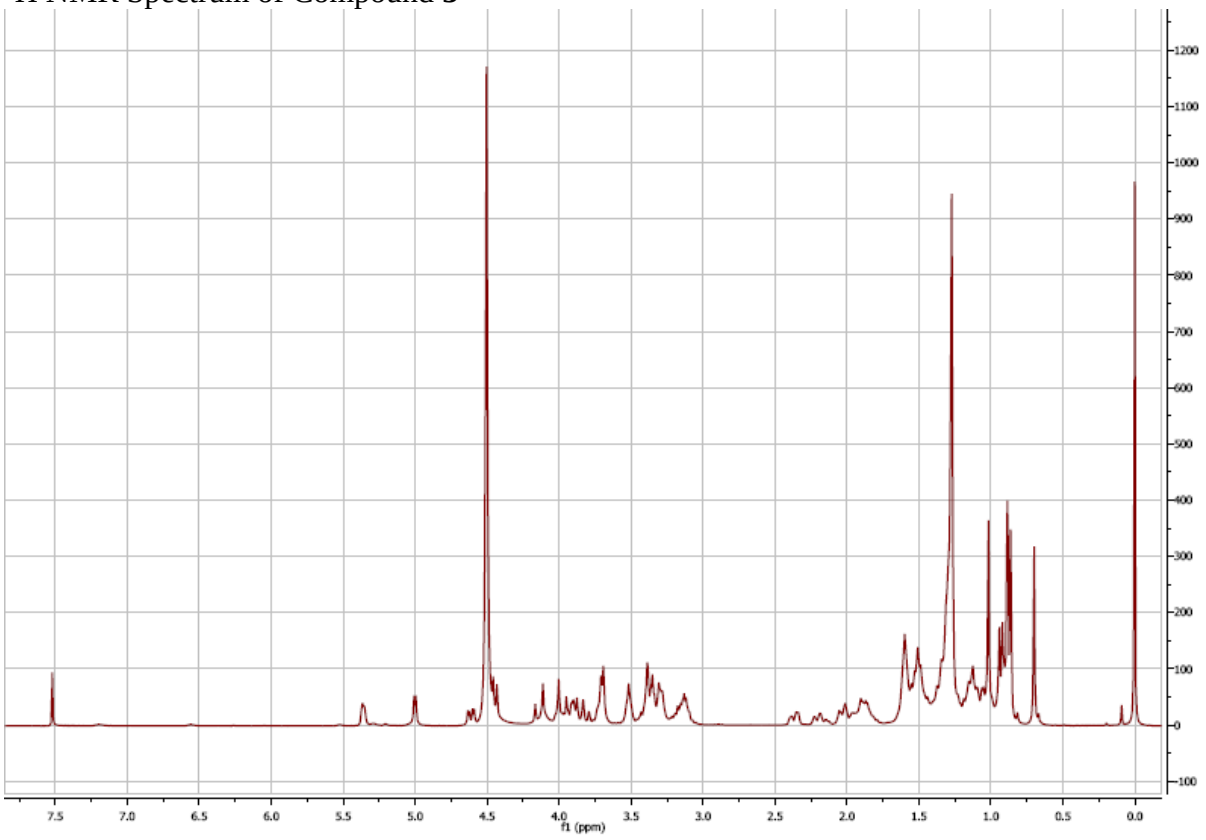
$[\alpha]_D^{20}$ = + 32 (c = 1.3, $CHCl_3$/MeOH, 7:3). ^{1}H NMR (300 MHz, $CDCl_3$/MeOD 7:3) δ 7.15 (1H, t, *J* = 5.5 Hz, NH), 6.48 (1H, t, *J* = 5.7 Hz, NH), 5.36 (1H, m, H6"), 5.00 (1H, d, $J_{1,2}$ = 3.57 Hz, H1), 4.61 (1H, dd, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ =10.1 Hz, H2), 4.45 (1H, d, $J_{1',2'}$ = 7.7 Hz, H1'), 4.16-3.78 (6H, m, H7a, H3, H7b, H6a, H6'a, H6b), 3.74-3.68 (3H, m, H6'b, H4, H5), 3.50 (2H, m, $CH_2$12), 3.42 (3H, m, H3', H5', H4'), 3.31-3.29 (3H, m, $CH_2$9, H2'), 3.21-3.09 (3H, m, $CH_2$14, H3"), 2.37 (1H, m, H4"a), 2.20 (1H, m, H4"b), 2.04-0.85 (65H, m, cholesterol, $CH_2$10, $CH_2$11, $CH_2$15 to $CH_2$24, $CH_3$25), 0.69 (3H, s, $CH_3$19") ppm. ^{13}C NMR (125 MHz, $CDCl_3$/MeOD 7:3) δ 170.2, 156.8, 140.9, 122.2, 103.5, 97.6, 79.7, 79.4, 77.0, 76.7, 73.6, 73.5, 71.5, 70.2, 70.1, 67.9, 66.9, 61.5, 60.8, 57.1, 56.5, 50.6, 42.6, 41.4, 40.1, 39.8, 39.4, 39.2, 37.5, 37.2, 36.5, 36.1, 32.3, 32.3, 30.1, 30.0, 30.0, 30.0, 30.0, 30.0, 29.7, 29.7, 28.7, 28.5, 28.3, 27.6, 27.2, 26.6, 24.6, 24.1, 23.0, 22.9, 22.7, 21.4, 19.6, 18.9, 14.2, 12.0 ppm. HRMS (ESI+) calcd for $C_{56}H_{102}O_{14}N_2Na$ ($[M+Na]^+$): 1073.7229, found: 1073.7235. Elemental analysis calcd (%) for $C_{58}H_{102}O_{14}N_2 \cdot 1.5H_2O$: C 64.31, H 9.63, N 2.50, found: C 64.19, H 9.68, N 2.64.

Compound **4**

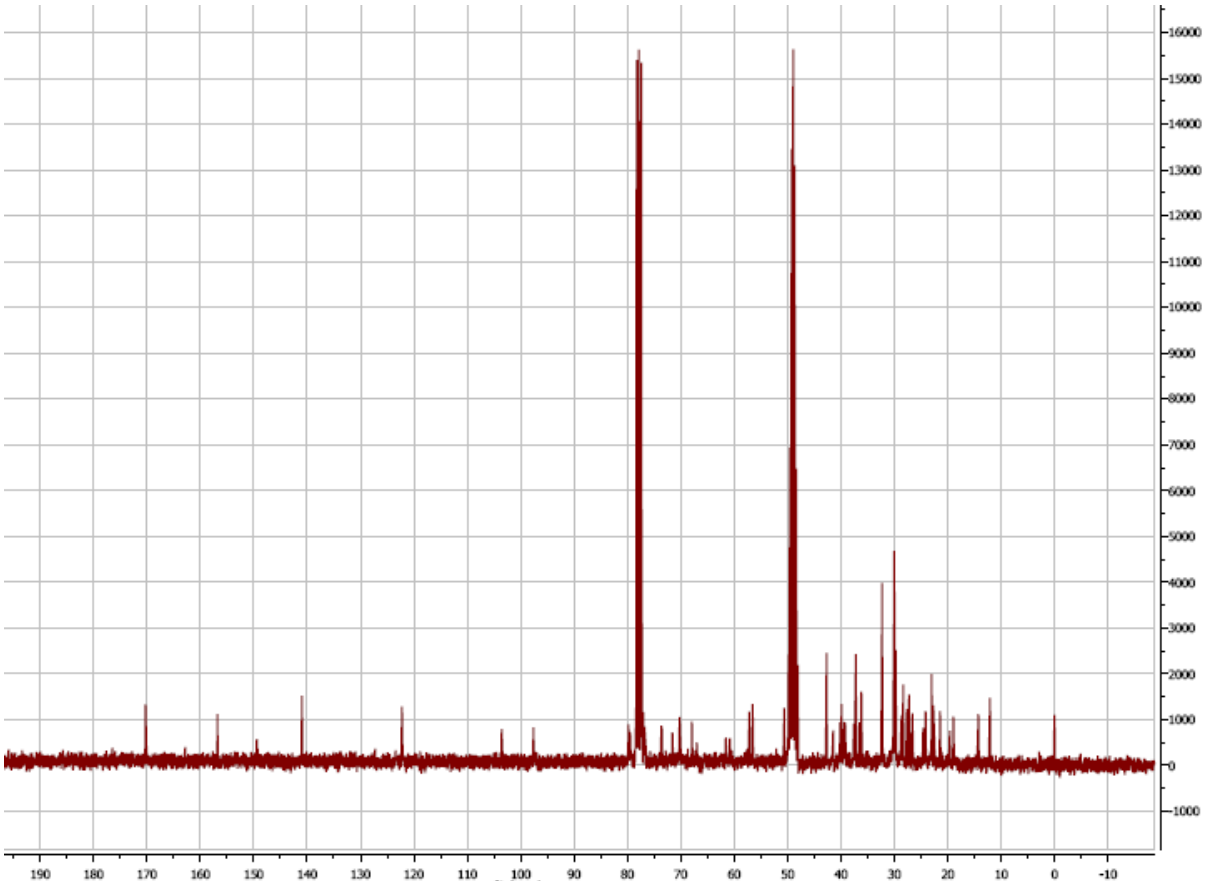


$[\alpha]_D^{20}$ = + 41 (c = 0.8, $CHCl_3$/MeOH, 8:2). ^{1}H NMR (300 MHz, $CDCl_3$/MeOD, 8:2) δ 5.28 (1H, m, H6"), 4.91 (1H, d, $J_{1,2}$ = 3.6 Hz, H1), 4.45 (1H, dd, $J_{2,3}$ = 10.1 Hz, H2), 4.06 (1H, d, $J_{7a,7b}$ = 15.6 Hz, H7a), 3.88 (1H, d, H7b), 3.76-3.68 (3H, m, H6a, H6b, H3), 3.52-3.37 (4H, m, H5, H4, $CH_2$12), 3.20 (2H, m, $CH_2$9), 3.08-2.98 (3H, m, H3", $CH_2$14), 2.26 (1H, m, H4"a), 2.09 (1H, m, H4"b), 1.96-0.77 (65H, m, cholesterol, $CH_2$10, $CH_2$11, $CH_2$15 to $CH_2$24, $CH_3$25), 0.60 (3H, s, $CH_3$19") ppm. ^{13}C NMR (75 MHz, $CDCl_3$/MeOD, 8:2) δ 169.8, 156.5, 140.6, 121.8, 97.3, 79.4, 73.4, 72.4, 71.2, 70.1, 67.5, 66.5, 61.2, 56.7, 56.1, 50.2, 42.3, 41.0, 39.7, 39.5, 39.0, 38.8, 37.2, 36.8, 36.2, 35.7, 31.9, 31.8, 29.7, 29.7, 29.7, 29.7, 29.6, 29.6, 29.3 29.3, 28.3, 28.2, 27.9, 27.2, 26.8, 26.2, 24.2, 23.7, 22.7, 22.6, 22.4, 21.0, 19.2, 18.6, 13.9, 11.7 ppm. LRMS (ESI+) 912 ($[M+Na]^+$). Elemental analysis calcd (%) for $C_{52}H_{92}O_9N_2 \cdot 0.5\ H_2O$: C 69.53, H 10.44, N = 3.12, found: C 69.57, H 10.44, N 3.12.

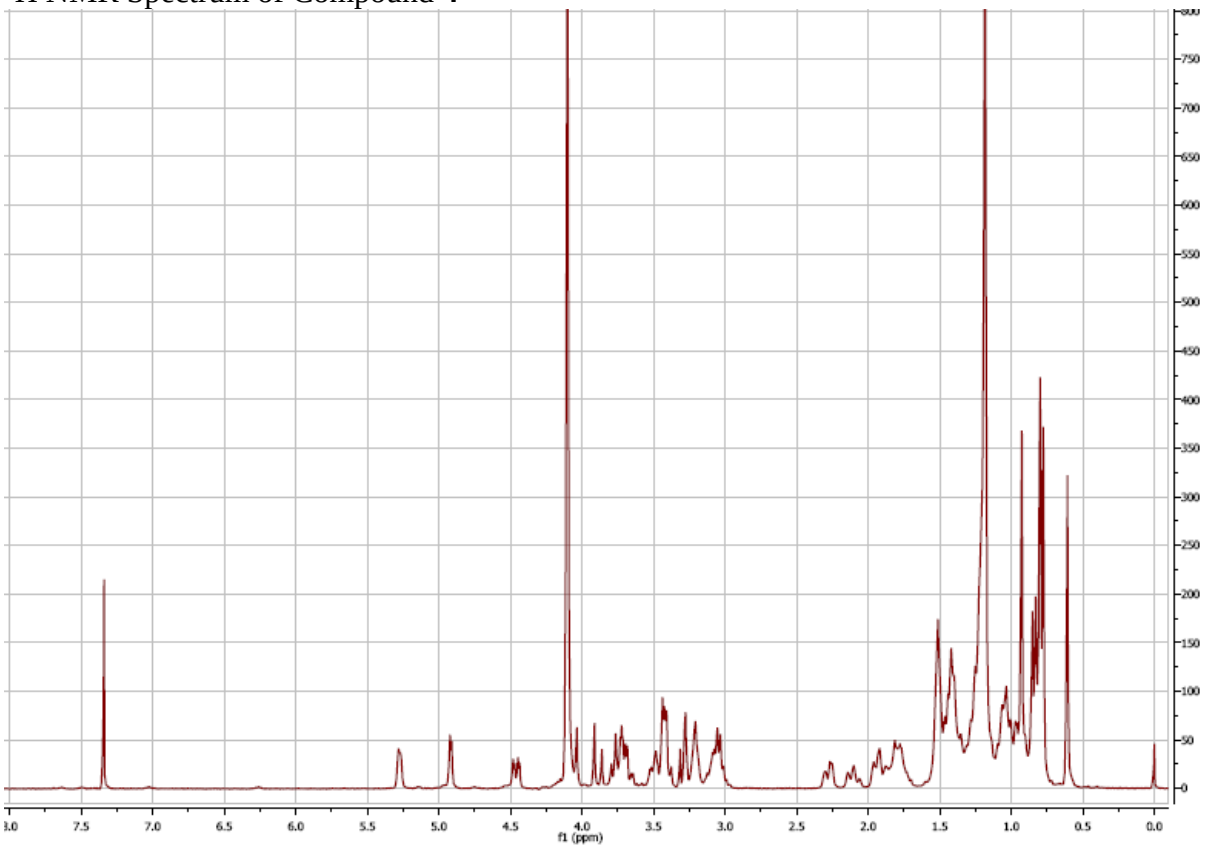
^{1}H NMR Spectrum of Compound **3**



^{13}C NMR Spectrum of Compound **3**



^{1}H NMR Spectrum of Compound **4**



^{13}C NMR Spectrum of Compound **4**