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## New Journal of Chemistry

### **Supporting Information for**

# Low molecular weight supramolecular dehydroepiandrosterone-based gelators: Synthesis and molecular modeling study

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### Spectroscopic, analytical, and calculation data

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### S1. Reagents and analytics.

All commercially available reagents and solvents were purchased from Sigma Aldrich and used without further purification. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a Varian MR-400 spectrometer 400 MHz and Varian MR-400 spectrometer 100 MHz, respectively, with TMS as an internal reference and CDCl<sub>3</sub> as a solvent. Elemental analyses were carried out on an EA 3000 Eurovector elemental analyzer. Melting points were determined on a Kofler hot bench. The progress of reactions as well as purity of the obtained compounds were monitored by TCL on Alugram® Xtra SIL G/UV<sub>254</sub> plates with DCM as an eluent. FAB-mass-spectrometric analyses were performed in the liquid matrix of the *meta*-nitrobenzyl alcohol using a magnetic sector mass spectrometer VG 70-70EQ equipped with primary FAB ion source for generating a bombarding beam of argon atoms. The region of molecular ion is represented by ion-radical M<sup>+</sup> and protonated molecular ion [MH]<sup>+</sup>. SEM images were obtained on a JSM-6390LV instrument.

### S2. Synthetic procedures and characterization data

**Dehydroepiandrosterone chloracetate (4, Scheme 2)**. To a stirred solution of dehydroepiandrosterone (5.00 g, 17.36 mmol) in 40 mL of dry  $CH_2Cl_2$  chloroacetyl chloride (1.53 mL, 19.09 mmol) and pyridine (0.5 mL) were added under a nitrogen atmosphere. The mixture was allowed to stir for 10 h at room temperature. After completion of the reaction, the solvent was evaporated and the crude was refluxed in 40 mL of methanol. White powder was filtered and washed

with methanol twice, yield (5,83 g, 92 %), white powder, m.p.  $145 - 147^{\circ}$ C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  5.43 (s, 1H C<sup>6</sup>H). 4.76 – 4.59 (m, 1H C<sup>3</sup>H), 4.04 (s, 2H, COCH<sub>2</sub>), 1.05 (s, 3H, CH<sub>3</sub>), 0.89 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  220.89 (s), 166.70 (s), 139.45 (s), 122.34 (s), 75.87 (s), 51.68 (s), 50.11 (s), 47.50 (s), 41.16 (s), 37.83 (s), 36.82 (s), 36.69 (s), 35.82 (s), 31.44 (s), 31.39 (s), 30.76 (s), 27.51 (s), 21.87 (s), 20.32 (s), 19.31 (s), 13.54 (s). MS, (FAB): 364.9 (+FAB). Found, %: C, 69.17; H, 8.00; C<sub>21</sub>H<sub>29</sub>ClO<sub>3</sub>. Calculated, %: C, 69.12; H, 8.01.





**Dehydroepiandrosterone azido-acetate (5, Scheme 2).** To a stirred solution of compound **4** (3.00 g, 8.22 mmol) in CH<sub>3</sub>CN (40 mL), NaN<sub>3</sub> was added (0.80 g, 12.33 mmol) and the reaction mixture was refluxed for 5 h. After completion of the reaction, the solution was filtered from inorganic precipitate, evaporated off and the target product was recrystallized from methanol, yield (2,71 g, 89 %), white powder, m.p. 125 – 127°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  5.42 (s, 1H C<sup>6</sup>H). 4.77

- 4.59 (m, 1H C<sup>3</sup>H), 3.84 (s, 2H, COCH<sub>2</sub>), 1.05 (s, 3H, CH<sub>3</sub>), 0.88 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  220.85 (s), 167.68 (s), 139.42 (s), 122.36 (s), 75.59 (s), 51.68 (s), 50.50 (s), 50.10 (s), 47.48 (s), 37.94 (s), 36.82 (s), 36.69 (s), 35.80 (s), 31.44 (s), 31.39 (s), 30.76 (s), 27.62 (s), 21.86 (s), 20.32 (s), 19.30 (s), 13.53 (s). MS, (FAB): 371.4 (+FAB). Found, %: C, 67.79; H, 7.71; N, 11.33. C<sub>21</sub>H<sub>29</sub>N<sub>3</sub>O<sub>3</sub>. Calculated, %: C, 67.90; H, 7.87; N, 11.31.





Benzene-1,2-bis-((2-(4-methyloxy)-1H-1,2,3-triazole-1-yl)acetate-3dehydroepiandrosterone) (6a, Scheme 2).

To a stirred solution of compound **2a** (1.00 g, 2.69 mmol) and compound **5** (0.25 g, 1.34 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (20 mL), water solution of sodium ascorbate (0.10 g, 0.5 mmol) and water solution of CuSO<sub>4</sub>\*5H<sub>2</sub>O (0.08 g, 0.32 mmol) was added and left for 24 h under r.t. After completion of the reaction, the solvent was evaporated off and the product was purified by column chromatography. Eluent

CH<sub>2</sub>Cl<sub>2</sub>-EtOAc in ratio 9:1, yield (1,14 g, 91 %); white powder, m.p. 168 – 170°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.79 (s, 2H, CH<sub>triazole</sub>), 7.05 (dd, 2H, J = 5.8, 3.7 Hz, Ar), 6.94 (dd, 2H, J = 5.9, 3.6 Hz, Ar), 5.42 (s, 2H C<sup>6</sup>H), 5.28 (s, 4H, 2OCH<sub>2</sub>), 5.13 (s, 4H, 2COCH<sub>2</sub>), 4.70 (dd, 2H, J = 11.1, 5.7 Hz, C<sup>3</sup>H), 1.04 (s, 6H, 2CH<sub>3</sub>), 0.89 (s, 6H, 2CH<sub>3</sub>). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  220.80 (s), 165.69 (s), 148.52 (s), 144.75 (s), 139.26 (s), 124.46 (s), 122.52 (s), 122.28 (s), 115.63 (s), 76.19 (s), 63.58 (s), 51.70 (s), 51.03 (s), 50.10 (s), 47.49 (s), 37.84 (s), 36.77 (s), 36.67 (s), 35.80 (s), 31.43 (s), 31.39 (s), 30.76 (s), 27.54 (s), 21.86 (s), 20.33 (s), 19.31 (s), 13.54 (s). MS, (FAB): 929.2 (+FAB). Found, %: C, 69.59; H, 7.16; N, 9.03. C<sub>54</sub>H<sub>68</sub>N<sub>6</sub>O<sub>8</sub>. Calculated, %: C, 69.80; H, 7.38; N, 9.04.





Benzene-1,3-bis-((2-(4-methyloxy)-1H-1,2,3-triazole-1-yl)acetate-3-

**dehydroepiandrosterone**) (**6b**, **Scheme 2**). Yield (1,11 g, 89 %); white powder, m.p. 152 – 154°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.76 (s, 2H, CH<sub>triazole</sub>) 7.15 (s, 1H, Ar), 6.67 – 6.48 (m, 3H, Ar), 5.38 (s, 2H C<sup>6</sup>H), 5.15 (d, 8H, 2OCH<sub>2</sub>, 2COCH<sub>2</sub>), 4.68 (s, 2H, C<sup>3</sup>H), 1.02 (s, 6H, 2CH<sub>3</sub>), 0.86 (s, 6H, 2CH<sub>3</sub>). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  220.90 (s), 165.59 (s), 159.39 (s), 139.22 (s), 130.09 (s), 124.17 (s), 122.54 (s), 107.70 (s), 102.18 (s), 76.28 (s), 62.00 (s), 51.67 (s), 51.09 (s), 50.07 (s), 47.49 (s), 37.82 (s), 36.75 (s), 36.66 (s), 35.81 (s), 31.42 (s), 31.38 (s), 30.75 (s), 27.53 (s), 21.85 (s), 20.31 (s), 19.30 (s), 13.54 (s). MS, (FAB): 929.2 (+FAB). Found, %: C, 69.67; H, 7.22; N, 8.75.  $C_{54}H_{68}N_6O_8$ . Calculated, %: C, 69.80; H, 7.38; N, 9.04.





Benzene-1,4-bis-((2-(4-methyloxy)-1H-1,2,3-triazole-1-yl)acetate-3dehydroepiandrosterone) (6c). Yield (1,13 g, 90 %); white powder, m.p. 205 – 207°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.70 (s, 2H, CH<sub>triazole</sub>) 6.85 (s, 4H, Ar) 5.36 (s, 2H C<sup>6</sup>H) 5.10 (d, 8H, 2OCH<sub>2</sub>, 2COCH<sub>2</sub>) 4.65 (s, 2H, C<sup>3</sup>H), 0.99 (s, 6H, 2CH<sub>3</sub>), 0.82 (s, 6H, 2CH<sub>3</sub>); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>):  $\delta$  220.85 (s), 165.59 (s), 152.76 (s), 144.79 (s), 139.22 (s), 124.04 (s), 122.54 (s), 115.89 (s), 76.26 (s), 62.61 (s), 51.67 (s), 51.07 (s), 50.07 (s), 47.48 (s), 37.83 (s), 36.75 (s), 36.66 (s), 35.80 (s),

31.41 (s), 31.38 (s), 30.75 (s), 27.53 (s), 21.85 (s), 20.31 (s), 19.29 (s), 13.54 (s). MS, (FAB): 929.2 (+FAB). Found, %: C, 69.83; H, 7.36; N, 8.89. C<sub>54</sub>H<sub>68</sub>N<sub>6</sub>O<sub>8</sub>. Calculated, %: C, 69.80; H, 7.38; N, 9.04.





### S3. Gelation test and determination of gel-sol transition temperature (Tg)

The respective amounts (0.03 mmol) of compounds **6a-c** were dissolved in 2 mL of desired organic solvents (Table 1) forming a homogeneous solution, heated slightly and then allowed to cool slowly to room temperature to form a gel. All the gels were tested by an inversion of the vial method.

The gel-to-sol transition temperature (Tg) was measured by the dropping ball method. In this test, a small glass ball was carefully placed on the top of the gel to be tested, which was present in a test tube. The tube was slowly heated in a thermalized oil bath until the ball fell to the bottom of the test tube. The temperature at which the ball reaches the bottom of the test tube is taken as Tg of the system.

Tg for gels obtained from compound <b>6a-c</b>			
<b>6a</b> (in methanol)	<b>6b</b> (in cyclohexanol)	<b>6c</b> (in cyclohexanol)	
49-50 °C	33-34 °C	69-70°C	

### S3. SEM images of xerogels of compounds 6a-c

Scanning electron microscopy (SEM) was used to get visual insights into the aggregation mode and the microscopic morphology of the 6a-c gels. SEM results show the different microstructures of the xerogels obtained by drying gelators **6a-c** from the appropriate solvents. An unstable gel obtained with compound **6a** in the MeOH/CH<sub>2</sub>Cl<sub>2</sub> mix turns after solvent drying into an amorphous powder of heterogeneous structure. The architecture of this xerogel is represented by 10 nm wide fibers. The xerogel 6b has flake-like morphology with a finer structure. The most stable gel formed by compound **6c** in cyclohexanol turns after solvent drying into a xerogel representing a dense film without clear morphological features except surface roughness and traces of destruction.



**6**c

#### ortho 3.0 <sub>T</sub> In ethanol 3.0 · In water In cyclohexanol - ortho ortho meta - meta meta para para para 2.5 2.5 Distance (nm) Distance (nm) 2.0 2.0 1.5 1.5

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0

5

10

Distance (nm)







# S6. Average intramolecular tail-tail distance (M8) over the production trajectory

### **S7.** Tail-tail distance radial distribution functions (M1)



### **S8.** Benzene-benzene distance radial distribution function (M8)



### **S9.** Triazole-triazole intramolecular distance radial distribution function (M8)





### **S10.** Triazole-triazole intermolecular distance radial distribution function (M8)



### S11. Tail-tail intramolecular distance radial distribution functions (M8)



### S12. Tail-tail intermolecular distance radial distribution functions (M8)

S13. Tail-tail distance-angle-energy scatterplot for M1







# S14. Tail-tail distance-angle scatterplot for every molecule in the M8 cell





