Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Release of bioactive volatiles from supramolecular hydrogels: influence of reversible acylhydrazone formation on gel stability and volatile compound evaporation‡

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Electronic Supplementary Information (ESI)

General

Commercially available reagents and solvents were used without further purification and reactions were carried out in standard glassware under N_2. Demineralised water was obtained from a Millipore Synergy 185 water purifier. ^{1}H- and ^{13}C-NMR Spectra were recorded at 25°C on a Bruker 400 MHz DPX or 500 MHz Avance spectrometer, δ in ppm downfield from Me_4Si as internal standard, J in Hz. Standard pulse sequences and parameters were used for one-dimensional ^{1}H- and ^{13}C-spectra and two-dimensional, gradient selected COSY, NOESY, ^{1}H-,^{13}C-HSQC, and ^{1}H-,^{13}C-HMBC spectra, respectively. LC-MS (ESI) measurements were performed on an Agilent 1100 LC-MS system equipped with a Waters Nova-Pak C18 60 Å 4 m (2.1 x 150 mm i.d.) or a Macherey-Nagel Nucleosil C2 (2.0 x 250 mm i.d.) column, eluted at 0.5 mL min^{-1} with a gradient of H_2O and acetonitrile (both containing 0.1% of formic acid) and coupled to a G1946D mass spectrometer. The ionisation source of the mass spectrometer was used with the following parameters: drying gas flow 12 L min^{-1}, nebuliser pressure 40 psig, drying gas temperature 350°C, capillary voltage 4000 V (pos.), for direct infusion (200 µL min^{-1}) the drying gas flow was set at 10 L min^{-1} and the nebuliser pressure at 20 psig, fragment ions *m/z* (rel. int. in % of the base peak). Dynamic headspace measurements were carried out with a Perkin Elmer TurboMatrix ATD desorber coupled to a Carlo Erba MFC 500 gas chromatograph equipped with a J&W Scientific DB1 capillary column (30 m, i.d. 0.45 mm, film 0.42 µm) and a FID detector. The volatiles were analysed using a two-step temperature gradient starting from 70°C to 130°C at 3°C min^{-1} and then going to 260°C at 25°C min^{-1}. The injection temperature was at 240°C, the detector temperature at 260°C.

Synthesis of (3a*S*,4*S*,6*R*,6a*R*)-6-(2-amino-6-oxo-1,6-dihydro-9H-purin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-D][1,3]dioxole-4-carboxylic acid (4)[20]

Acetone and water (1:1, 114 mL) were added to a mixture of 2-amino-9-[(3a*R*,4*R*,6*R*,6a*R*)-6-(hydroxymethyl)-2,2-dimethyltetrahydrofuro[3,4-*D*][1,3]dioxol-4-yl]-1,9-dihydro-6H-purin-6-one (7.47 g, 23.1 mmol), [bis(acetoxy)iodo]benzene (BAIB, 16.38 g, 50.9 mmol, 2.2 eq.), 2,2,6,6-tetramethyl-1-piperidinyloxyl radical (TEMPO, 0.72 g, 4.6 mmol, 0.2 eq.) and sodium hydrogencarbonate (3.89 g, 46.3 mmol, 2 eq.). The reaction was stirred at r.t. for 6 h, filtered and the residue washed with ether and acetone. Drying under vacuum gave 4.84 g (62%) of a white solid. Concentration of the filtrate and re-filtration gave another 2.26 g (29%) of the compound containing an unknown impurity. IR (neat): $\tilde{\nu}_{max}$ 3332m (br.), 3224w, 3100w, 2988w, 2935w, 2846w, 2778w, 2737w, 1681m, 1639m, 1582s, 1534m, 1486w, 1459w, 1400m, 1378m, 1174w, 1156w, 1089m, 1058m, 995w, 973w, 936w, 862s, 842w, 816m, 780m, 760m, 741m, 728w, 708w, 682m, 642s, 616w, 608w cm^{-1}. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.42 (br. s, 1 H), 8.31 (s, 1 H), 6.88 (br. s, 2 H), 5.95 (d, J = 2.6, 1 H), 5.10-5.04 (m, 1 H), 5.01-4.94 (m, 1 H), 4.32 (d, J = 2.0, 1 H), 1.50 (s, 3 H), 1.30 ppm (s, 3 H). ^{13}C-NMR (100.6 MHz, DMSO-d_6): δ 172.25 (s), 157.04 (s), 153.92 (s), 150.80 (s), 136.51 (d), 116.10 (s), 112.19 (s), 89.33 (d), 87.15 (d), 84.61 (d), 83.93 (d), 26.89 (q), 25.00 ppm (q). MS (ESI): *m/z* 675 ([2M+1]$^+$, 4), 340 (3), 339 (17), 338 ([M+1]$^+$, 100).

Synthesis of methyl (2*S*,3*S*,4*R*,5*R*)-5-(2-amino-6-oxo-1,6-dihydro-9H-purin-9-yl)-3,4-dihydroxytetrahydro-2-furancarboxylate (5)[21]

A suspension of **4** (4.84 g, 14.3 mmol) in methanol (190 mL) was cooled to 5°C before thionyl chloride (6.77 mL = 11.1 g, 93.3 mmol, 6.5 eq.) was added dropwise during 10 min. The transparent reaction mixture was left warming to r.t. and stirred for 1 d. The precipitate formed during the reaction was filtered and washed with methanol. Concentration of the filtrate and re-filtration gave a total of 4.10 g (92%) of a white solid. IR (neat): $\tilde{\nu}_{max}$ 3455w, 3401m, 3299w, 3169m (br.), 3120m, 3047w, 3003w, 2975w, 2955w, 2924w, 2852w, 2817w, 2775w, 2724w, 2674w, 2610w, 2544w, 1823w, 1713s, 1643s, 1601m, 1586s, 1554w, 1536w, 1461m, 1447w, 1438w, 1413w, 1399w, 1381m, 1360m, 1335m, 1316m, 1294w, 1274w, 1249m, 1217m, 1209m, 1170w, 1151m, 1125m, 1103m, 1077s, 1047m, 1027m, 969w, 950w, 918m, 885m, 863m, 819m, 788m, 772m, 760m, 730m, 683m, 667m, 645m, 619m cm^{-1}. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.64 (br. s, 1 H), 8.90 (s, 1 H), 7.27 (br. s, 2 H), 5.95 (d, J = 5.1, 1 H), 4.55-4.50 (m, 2 H), 4.37 (t, J = 3.8, 1 H), 3.74 ppm (s, 3 H). ^{13}C-NMR (100.6 MHz, DMSO-d_6): δ 170.85 (s), 155.22 (s), 154.08 (s), 150.20 (s), 135.00 (d), 110.23 (s), 87.81 (d), 82.29 (d), 73.68 (d),

72.95 (d), 52.34 ppm (q). ^{13}C-NMR (125.8 MHz, DMSO-d_6, after addition of 40 µL of 1 M NaOD): δ 171.04 (s), 156.93 (s), 153.88 (s), 151.94 (s), 135.40 (d), 116.41 (s), 86.15 (d), 82.31 (d), 73.58 (d), 73.14 (d), 52.49 ppm (q). MS (ESI): *m/z* 623 ($[2M+1]^+$, 4), 314 (3), 313 (15), 312 (100).

Synthesis of (2*S*,3*S*,4*R*,5*R*)-5-(2-amino-6-oxo-1,6-dihydro-9H-purin-9-yl)-3,4-dihydroxytetrahydro-2-furancarbohydrazide (1)[10]

A suspension of **5** (3.75 g, 12.1 mmol) and hydrazine hydrate (51% in water, 1.47 mL = 1.51 g, 24.0 mmol) in ethanol (120 mL) was heated under reflux overnight. After cooling to r.t., the reaction mixture was filtered to give 3.62 g of a white solid still containing *ca*. 30 mol-% of the starting methyl ester. The product was re-suspended in ethanol (120 mL), hydrazine hydrate (1.42 mL = 1.46 g, 23.1 mmol) was added, and the mixture heated at reflux for another 3 d. After cooling to r.t., the reaction mixture was filtered to give 3.23 g (86%) of a white solid. M.p.: 217.1-218.7°C. UV/Vis (ethanol): λ (ε) 321 (sh, 710), 285 (sh, 3000), 274 (sh, 4400), 255 (6100), 249 (sh, 5900), 203 nm (7700). IR (neat): $\tilde{\nu}_{max}$ 3487w, 3449w, 3314w, 3243w, 3169w (br.), 3109w, 2989w (br.), 2932w, 2870w, 2743w, 1761w, 1709s, 1633s, 1609m, 1585s, 1557m, 1542m, 1495m, 1445w, 1423w, 1410w, 1380m, 1359m, 1340m, 1312m, 1297w, 1280w, 1248m, 1228m, 1206w, 1163m, 1128m, 1081m, 1054s, 1024m, 1001m, 962m, 926m, 884m, 843m, 826m, 781m, 751m, 686s, 674m, 653m, 607m cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.01 (br. s, 1 H), 10.62 (br. s, 1 H), 7.96 (s, 1 H), 6.65 (s, 2 H), 5.79 (d, *J* = 7.7, 1 H), 5.74 (m, 1 H), 5.59 (m, 1 H), 4.46 (m, 1 H), 4.34 (d, *J* = 1.0, 1 H), 4.11 (br. d, *J* = 3.8, 1 H), 4.0-2.8 ppm (br. m, 2 H). ^{1}H-NMR (400 MHz, D_6O + NaOD): δ 8.15 (s, 1 H), 5.70 (d, *J* = 6.6, 1 H), 4.69 (dd, *J* = 5.5, 0.7, 1 H), 4.29-4.25 (m, 1 H), 4.25-4.21 ppm (m 1 H). ^{13}C-NMR (125.8 MHz, DMSO-d_6): δ 168.63 (s), 156.58 (s), 153.45 (s), 149.88 (s), 137.08 (d), 117.25 (d), 87.46 (d), 84.01 (d), 73.00 (d), 72.15 ppm (d). ^{13}C-NMR (100.6 MHz, D_2O + NaOD): δ 188.62 (s), 167.51 (s), 154.76 (s), 151.89 (s), 139.41 (d), 120.44 (s), 90.78 (d), 88.79 (d), 78.49 (d), 76.27 ppm (d). MS (ESI): *m/z* 312 ($[M+1]^+$, 8), 299 (12), 298 (100). Please note that in D_2O/NaOD the compound decomposes to form **23**.

Synthesis of (2S,3*S*,4*R*,5*R*)-5-(2-amino-6-oxo-1,6-dihydro-9H-purin-9-yl)-3,4-dihydroxytetrahydro-2-furancarboxylic acid (23)[25]

A solution of **4** (0.60 g, 1.8 mmol) in a 1:1 mixture of formic acid and water (40 mL) was heated at 80°C for 1.5 h. After cooling to r.t., the mixture was concentrated, taken up in water and re-concentrated until the smell of formic acid disappeared (5-6 cycles) to give 0.51 g (96%) of a white solid, still containing some formic acid. IR (neat): $\tilde{\nu}_{max}$ 3429w, 3404w, 3118m (br.), 2776w, 2696w, 2165w, 1884w (br.), 1739m, 1686m, 1658m, 1591s, 1543m, 1477m, 1373m (br.), 1319m (br.), 1242w, 1213w, 1200w, 1173m, 1127m, 1115m, 1084m, 1053s, 942m, 880m, 848w, 810m, 778m, 766w, 728w, 686m, 671w, 659w, 629m, 604m cm^{-1}. ^{1}H-NMR (400 MHz, D_2O): δ 8.27 (s, 1 H), 5.99 (d, *J* = 6.6, 1 H), 4.65 (dd, *J* = 6.6, 2.0, 1 H), 4.55-4.47 ppm (m, 2 H). ^{1}H-NMR (400 MHz, D_2O + NaOD): δ 8.13 (s, 1 H), 5.79 (d, *J* = 7.2, 1 H), 4.60 (dd, *J* = 7.2, 2.3, 1 H), 4.40 (d, *J* = 2.0, 1 H), 4.29 ppm (dd, *J* = 4.8, 2.0, 1 H). ^{13}C-NMR (100.6 MHz, D_2O): δ 179.27 (s), 172.63 (s), 161.71 (s), 156.90 (s), 140.79 (d), 118.78 (s), 89.47 (d), 87.60 (d), 77.05 (d), 76.69 ppm (d). ^{13}C-NMR (100.6 MHz, D_2O + NaOD): δ 180.50 (s), 171.13 (s), 164.15 (s), 155.15 (s), 139.16 (d), 120.35 (s), 89.97 (d), 87.81 (d), 78.64 (d), 78.19 ppm (d). HRMS (ESI): *m/z* calc. for $C_{10}H_{12}N_5O_6^+$: 298.0782 ($[M+H]^+$), found: 298.0759 ($[M+H]^+$).

Dynamic heqadspace analysis

Table S1 (numerical data for Figure 8). Average headspace concentrations (in ng/L air) and standard deviation (in brackets) measured for the release of a mixture of two volatile carbonyl compounds from hydrogels prepared with hydrogelator **1** (average values of three measurements).

	Headspace concentration [ng L^{-1}] of					
(*R*)-Citronellal (**14**) in the presence of	1 d	2 d	4 d	7 d	9 d	15 d
Furfural (**15**)	33.9 (17.8)	31.2 (20.6)	30.3 (21.9)	22.4 (16.3)	18.8 (14.9)	11.0 (3.8)
Benzaldehyde (**16**)	25.0 (8.5)	29.6 (14.7)	27.6 (17.5)	20.9 (14.0)	15.6 (11.9)	8.0 (6.2)
4-Methylacetophenone (**17**)	44.8 (12.1)	31.8 (19.0)	31.5 (20.0)	21.5 (15.6)	16.7 (12.5)	8.4 (6.3)
Furfural (**15**) in the presence of						
(*R*)-Citronellal (**14**)	18.4 (19.1)	14.5 (10.0)	10.8 (8.8)	8.6 (0.1)	8.2 (2.8)	6.6 (0.2)
Benzaldehyde (**16**)	25.4 (31.0)	4.8 (1.1)	7.0 (3.9)	6.1 (1.7)	4.4 (0.7)	4.3 (2.0)
4-Methylacetophenone (**17**)	73.1 (63.5)	38.5 (44.5)	20.6 (22.8)	14.1 (10.3)	10.4 (6.7)	5.8 (3.6)
Benzaldehyde (**16**) in the presence of						
(*R*)-Citronellal (**14**)	10.8 (0.2)	12.4 (3.8)	10.7 (2.1)	11.3 (3.3)	11.1 (2.8)	9.3 (0.4)
Furfural (**15**)	12.9 (2.2)	11.2 (1.2)	11.4 (3.1)	15.2 (1.1)	13.0 (1.8)	11.1 (2.4)
4-Methylacetophenone (**17**)	10.7 (1.7)	10.2 (2.4)	11.5 (2.2)	12.7 (4.4)	11.7 (3.4)	11.0 (2.4)
4-Methylacetophenone (**17**) in the presence of						
(*R*)-Citronellal (**14**)	336.1 (86.4)	255.6 (27.3)	301.0 (151.0)	194.3 (89.4)	149.3 (50.8)	82.4 (25.3)
Furfural (**15**)	226.9 (157.2)	259.5 (21.6)	216.9 (8.9)	147.0 (5.3)	117.8 (12.8)	62.0 (17.5)
Benzaldehyde (**16**)	221.1 (68.0)	176.5 (12.4)	173.1 (15.6)	131.9 (20.7)	110.2 (14.0)	69.2 (11.5)