# Testing the limits of synthon engineering: Salts of salicylic and sulfosalicylic acid with nucleobases and derivatives

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## Experimental Section

### SYNTHETIC PROCEDURES

The compounds were dissolved in minimal amount of solvents (typically 3-4 mL) and each crystallization process yielded crystals within a week upon slow evaporation at room temperature.

Benzimidazolium salicylate (1:1), **1**. Salicylic acid (22.8 mg, 0.17 mmol) and benzimidazole (19.5 mg, 0.17 mmol) were dissolved in methanol. Light pink, small block shaped crystals were obtained, mp. 124-128 °C.

Adeninium salicylate monohydrate (1:1:1), **2**. Salicylic acid (66.1 mg, 0.48 mmol) and adenine (64.5 mg, 0.48 mmol) were dissolved in a 30:70 methanol/water mixture. Colourless needle shaped crystals were obtained, mp. 194-199 °C.

Cytosinium salicylate (1:1), **3**. Salicylic acid (82.9 mg, 0.60 mmol) and cytosine (66.7 mg, 0.60 mmol) were dissolved in a mixture of dioxane/water (30:70). Colourless block shaped crystals were obtained, mp. 230-238 °C.

Di-benzimidazolium sulfosalicylate monohydrate (2:1:1), **4**. 5-Sulfosalicylic acid (61.1 mg, 0.28 mmol) and benzimidazole (32.5 mg, 0.28 mmol) were dissolved in a mixture of 30:70 acetonitrile/water. Pink crystals were obtained, mp. 246-248°C.

Adeninium sulfosalicylate monohydrate (1:1:1), **5**. 5-Sulfosalicylic acid (77.1 mg, 0.35 mmol) and adenine (47.7 mg, 0.35 mmol) were dissolved in a methanol/water solution (30:70). Colourless plate-like crystals were obtained, mp. 166-168°C.

Cytosinium sulfosalicylate cytosine monohydrate (1:1:1:1), **6**. 5-Sulfosalicylic acid (111.9 mg, 0.51 mmol) and cytosine (56.9 mg, 0.51 mmol) were dissolved in an ethanol/water solution (30:70). Colourless block shaped crystals were obtained, mp. 223-227°C.

Fluorocytosinium sulfosalicylate fluorocytosine (1:1:1), **7**. 5-Sulfosalicylic acid (100.5 mg, 0.460 mmol) and fluorocytosine (59.4 mg, 0.460 mmol) were dissolved in methanol/water solution (30:70). The mixture yielded colourless block shaped crystals, mp. 254-259°C.

## CRYSTALLOGRAPHY

Data sets were collected on a Bruker DUO APEX II diffractometer [1] with graphite-monochromated $MoK_{\alpha 1}$ radiation (λ = 0.71073 Å) at 173 K. The temperature was controlled using an Oxford Cryostream 700. Data reduction and cell refinement were performed using SAINT-Plus. [2] The space groups were determined from systematic absences by XPREP[3] and further justified by the refinement results. The structures were solved with the aid of X-Seed[4] by direct methods using SHELXS-97 and SHELXL-97. [5] Non-hydrogen atoms were refined anisotropically. The hydrogen atoms bound to carbon atoms were placed at idealized positions and refined as riding atoms. Hydrogen atoms involved in hydrogen bonding were located in the difference electron density map and refined independently. Diagrams and publication material were generated using PLATON[6] and X-Seed. Crystallization of **2** yielded crystals which, judging from their diffraction, were inter-grown. Attempts were made with the program CELL_NOW[7] to index individual domains. This program assigned 80% of the reflections (maximum deviation from integer values set to 0.1) to the main domain. Twin integration was not successful and instead the data obtained from the main domain were treated in a default manner, i.e. indexing and data reduction as if the data were from a single crystal. Supplementary crystallographic data for structures **1-7** are in CCDC 1451655-1451661 for **1-7**, respectively.

[1] Bruker, APEX2, Version 1.0-27, Bruker AXS Inc, Madison, Wisconsin, USA, 2005.
[2] Bruker, SAINT-Plus (including XPREP), Version 7.12, Bruker AXS Inc, Madison, Wisconsin, USA, 2004.
[3] Bruker, XPREP, Version 6.14, Bruker AXS Inc, Madison, Wisconsin, USA, 2003.
[4] L. J. Barbour, *J. Supramol. Chem.*, **2001**, *1*, 189–191.
[5] G. M. Sheldrick, SHELXS-97 and SHELXL-97 Programs for Crystal Structure Determination and Refinement, University of Göttingen, 1997.
[6] A. L. Spek, PLATON, A Multipurpose Crystallographic Tool, Utrecht University, Utrecht, The Netherlands, 2008.
[7] G. M. Sheldrick, CELL_NOW Version 2008-2, Index Twins and Other Problem Crystals, University of Göttingen, 2008.

**Table 1S Crystallographic Data**

| | **1** | **2** | **3** | **4** | **5** | **6** | **7** |
|---|---|---|---|---|---|---|---|
| Chemical formula | $C_{14}H_{12}N_2O_3$ | $C_{12}H_{13}N_5O_4$ | $C_{11}H_{11}N_3O_4$ | $C_{21}H_{20}N_4O_7S_1$ | $C_{12}H_{13}N_5O_7S_1$ | $C_{15}H_{18}N_6O_9S_1$ | $C_{15}H_{14}N_6O_8S_1F_2$ |
| Molecular weight | 256.26 | 291.27 | 249.23 | 472.47 | 371.33 | 458.41 | 476.38 |
| Crystal system<br>Space group | Monoclinic<br>$P2_1/c$ | Monoclinic<br>$P2_1/c$ | Monoclinic<br>$P2_1/n$ | Monoclinic<br>$P2_1/c$ | Triclinic<br>$P\bar{1}$ | Triclinic<br>$P\bar{1}$ | Triclinic<br>$P\bar{1}$ |
| Temperature / K | 173(2) | 173(2) | 173(2) | 173(2) | 173(2) | 173(2) | 173(2) |
| Wavelength / Å | 0.71073 | 0.71073 | 0.71073 | 0.71073 | 0.71073 | 0.71073 | 0.71073 |
| a/Å | 7.3538 (4) | 6.9999 (14) | 9.6386(19) | 9.909 (2) | 6.7311(13) | 7.2974(15) | 6.9579 (14) |
| b/Å | 6.7000 (4) | 16.700 (3) | 8.5322 (2) | 9.817 (2) | 10.314(2) | 8.4044(17) | 9.6421 (19) |
| c/Å | 24.9855 (15) | 11.685 (2) | 13.910(3) | 22.872 (3) | 10.743(2) | 15.470(3) | 14.749 (3) |
| α (°) | 90 | 90 | 90 | 90 | 85.32(3) | 77.82(3) | 101.51(3) |
| β (°) | 95.147 (2) | 101.81 (3) | 109.93(3) | 102.12 (3) | 85.11(3) | 83.19(3) | 101.98(3) |
| γ (°) | 90 | 90 | 90 | 90 | 86.41(3) | 88.82(3) | 98.62(3) |
| Volume/Å$^3$ | 1226.08 (12) | 1337.0 (5) | 1075.4 (4) | 2175.4 (8) | 739.5(3) | 920.8 (3) | 929.3(3) |
| Z | 4 | 4 | 4 | 4 | 2 | 2 | 2 |
| $D_{calc}$ / Mg m$^{-3}$ | 1.3883 | 1.447 | 1.539 | 1.443 | 1.668 | 1.653 | 1.702 |
| $\mu$ (mm$^{-1}$) | 0.100 | 0.112 | 0.120 | 0.201 | 0.271 | 0.245 | 0.257 |
| $F$(000) | 536 | 608 | 520 | 984 | 384 | 476 | 488 |
| Colour | Light pink | Colourless | Colourless | Pink | Colourless | Colourless | Colourless |
| Habit | Blocks | Needles | Blocks | Blocks | Plates | Blocks | Blocks |
| Ref. collected | 3047 | 3355 | 2679 | 5450 | 3406 | 4613 | 4635 |
| Independent ref. | 2558 | 2463 | 2254 | 4571 | 2671 | 3184 | 3613 |
| $R_1$ (observed) | 0.0392 | 0.0589 | 0.0441 | 0.0390 | 0.0423 | 0.0450 | 0.0387 |
| $wR_2$ (all) | 0.1072 | 0.1574 | 0.1053 | 0.1070 | 0.1098 | 0.1256 | 0.1048 |
| $R_1$ (all) | 0.0477 | 0.0865 | 0.0441 | 0.0478 | 0.0556 | 0.0785 | 0.0552 |
| Goodness of fit | 1.060 | 1.018 | 1.048 | 1.053 | 1.035 | 1.007 | 1.037 |
| No. of Parameters | 181 | 196 | 168 | 305 | 255 | 309 | 326 |
| Δρ max/min | -0.24; 0.37 | -0.31; 0.80 | -0.25; 0.29 | -0.39; 0.43 | -0.38; 0.31 | -0.55; 0.37 | -0.39; 0.41 |

**Table 2S Hydrogen bond geometry for the SA structures**

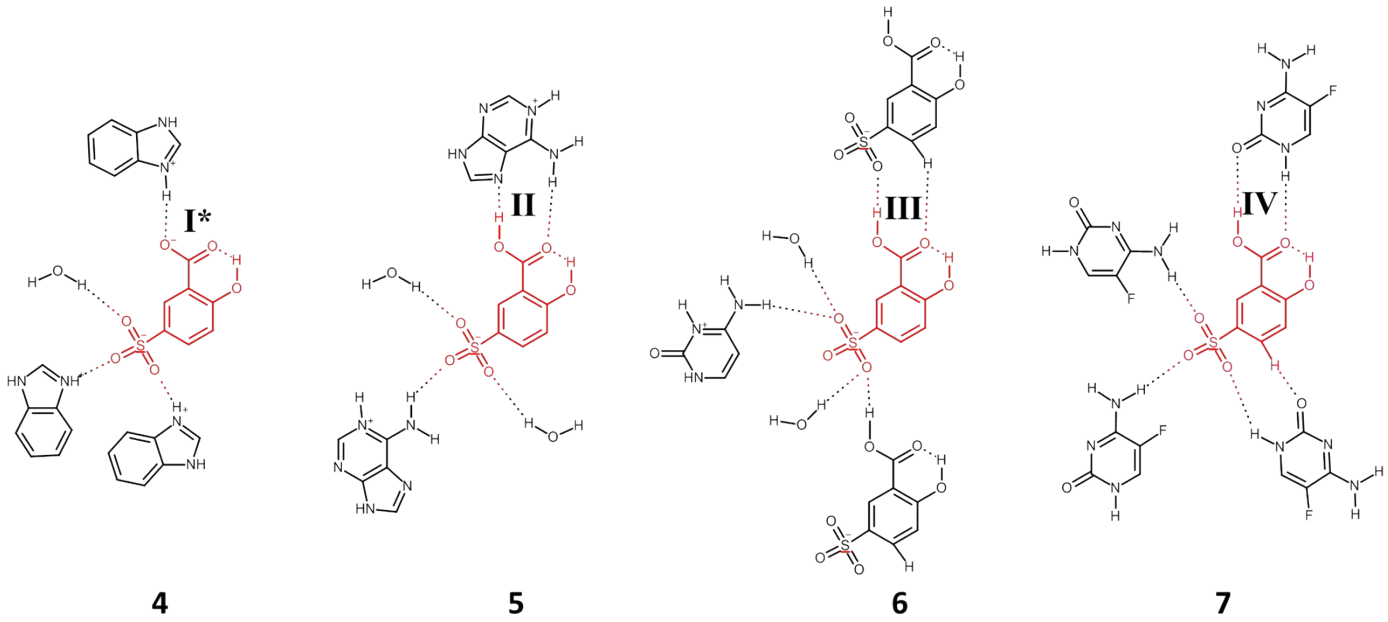
| **1** | D-H/Å | H···A/Å | D···A/Å | D-H···A/° |
|---|---|---|---|---|
| O10-H10···O9 | 0.84 | 1.81 | 2.549(4) | 146 |
| N11-H11···O8 | 0.98 | 1.65 | 2.622(1) | 170 |
| N18-H18···O9$^{i}$ | 0.97 | 1.70 | 2.646(6) | 167 |
| C19-H19···O8$^{ii}$ | 0.95 | 2.18 | 3.100(2) | 163 |
| **2** | | | | |
| O10-H10···O9 | 1.01 | 1.50 | 2.502(1) | 173 |
| N11-H11···O9 | 0.93 | 1.73 | 2.656(4) | 177 |
| N15-H15···O21 | 0.96 | 1.75 | 2.692(4) | 168 |
| N20-H20A···O8 | 0.88 | 1.90 | 2.779(5) | 178 |
| O21-H21A···N17$^{iii}$ | 0.88 | 1.94 | 2.820(2) | 173 |
| O21-H21B···O10$^{iv}$ | 0.93 | 1.99 | 2.878(5) | 159 |
| **3** | | | | |
| O10-H10···O9 | 0.84 | 1.80 | 2.545(6) | 146 |
| N11-H11···O8 | 0.85 | 1.88 | 2.736(3) | 178 |
| N13-H13···O8$^{v}$ | 0.91 | 1.80 | 2.699(3) | 169 |
| N17-H17A···O18$^{vi}$ | 0.88 | 2.00 | 2.876(5) | 176 |
| N17-H17B···O9$^{v}$ | 0.88 | 1.87 | 2.748(1) | 176 |

Symmetry codes: (i) -x, 1-y, -z; (ii) -x, 2-y, -z; (iii) x-1, y, z; (iv) 1-x, y-½, $^3/_2$-z; (v) ½-x, y-½, ½-z; (vi) x-½, ½-y, z-½.

**Table 3S Hydrogen bond geometry for the SSA structures**

| **4** | D-H/Å | H···A/Å | D···A/Å | D-H···A/° |
|---|---|---|---|---|
| O10-H10···O9 | 0.95 | 1.62 | 2.527(2) | 158 |
| N11A-H11A···O8 | 0.95 | 1.71 | 2.660(2) | 176 |
| N11B-H11B···O13 | 0.92 | 1.81 | 2.713(2) | 168 |
| N18A-H18A···O11$^{i}$ | 0.86 | 1.92 | 2.741(6) | 161 |
| N18B-H18B···O20$^{ii}$ | 0.97 | 1.66 | 2.627(3) | 173 |
| O20-H20A···O12 | 0.85 | 1.91 | 2.751(7) | 171 |
| O20-H20B···O8$^{iii}$ | 0.84 | 1.84 | 2.676(8) | 169 |
| **5** | | | | |
| O10-H10···O9 | 0.92 | 1.76 | 2.607(2) | 151 |
| O8-H8···N17 | 0.90 | 1.70 | 2.576(4) | 165 |
| N11-H11···O21$^{iv}$ | 0.96 | 1.67 | 2.626(7) | 175 |
| N15-H15···N13$^{v}$ | 0.89 | 1.97 | 2.839(4) | 167 |
| N20-H20A···O13$^{vi}$ | 0.92 | 1.96 | 2.803(2) | 151 |
| N20-H20B···O9 | 0.91 | 2.00 | 2.897(1) | 172 |
| O21-H21B···O11 | 0.86 | 1.92 | 2.772(2) | 173 |
| **6** | | | | |
| O10-H10···O9 | 0.95 | 1.73 | 2.602(6) | 152 |
| O8-H8···O11$^{vi}$ | 0.97 | 1.64 | 2.585(1) | 164 |
| N11A-H11A···N11B$^{vii}$ | 0.90 | 1.94 | 2.836(2) | 178 |
| N13A-H13A···O18B | 0.86 | 1.97 | 2.821(4) | 174 |
| N13B-H13B···O18A | 0.83 | 1.98 | 2.812(8) | 176 |
| N17A-H17A···O18B$^{vii}$ | 0.88 | 1.91 | 2.785(1) | 175 |
| N17A-H17B···O19$^{viii}$ | 0.88 | 2.10 | 2.908(3) | 152 |
| N17B-H17C···O18A$^{vi}$ | 0.88 | 2.01 | 2.885(3) | 175 |
| N17B-H17D···O13$^{vi}$ | 0.88 | 2.05 | 2.878(9) | 157 |
| O19-H19A···O9$^{v}$ | 0.87 | 2.43 | 3.095(8) | 134 |
| O19-H19A···O11$^{ii}$ | 0.87 | 2.16 | 2.819(3) | 132 |
| O19-H19B···O13 | 0.87 | 2.00 | 2.834(1) | 161 |
| **7** | | | | |
| O10-H10···O9 | 0.83 | 1.91 | 2.626(3) | 145 |
| O8-H8···O18B | 0.94 | 1.59 | 2.518(8) | 168 |
| N11A-H11A···N11B | 0.87 | 1.98 | 2.854(2) | 178 |
| N13A-H13A···O13$^{viiii}$ | 0.97 | 1.80 | 2.718(3) | 157 |
| N13B-H13B···O9 | 0.91 | 2.03 | 2.910(2) | 165 |
| N17A-H17A···O18B | 0.89 | 1.92 | 2.797(6) | 173 |
| N17A-H17B···O12$^{x}$ | 0.87 | 1.98 | 2.815(8) | 162 |
| N17B-H17C···O11$^{xi}$ | 0.83 | 2.46 | 3.206(7) | 150 |
| N17B-H17C···F1A$^{xii}$ | 0.83 | 2.52 | 3.113(1) | 130 |
| N17B-H17D···O18A | 0.94 | 2.00 | 2.930(7) | 173 |

Symmetry code: (i) -x, 1-y, 1-z; (ii) -x, -y, -z; (iii) x, 1+y, z; (iv) 1-x, -y, 1-z; (v) 1-x, -y, 1-z; (vi) 1+x, 1+y, z; (vii) x-1, y, z; (viii) 1-x, 1-y, -z; (viiii) x, y-1, z; (x) x, 1+y, z; (xi) -x-1, 1-y, 1-z; (xii) x, 1+y, 1+z.




**Scheme 3S Synthons observed in the SSA structures.**