Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics

Experimental and theoretical study of the metastable decay of negatively charged nucleosides in gasphase

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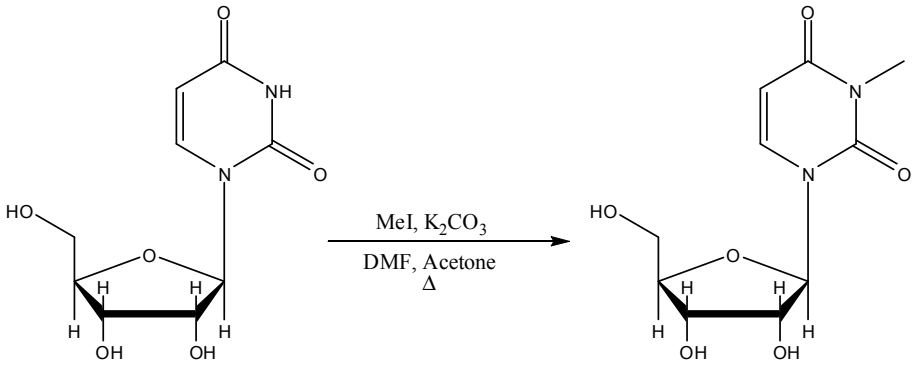
Experimental

General

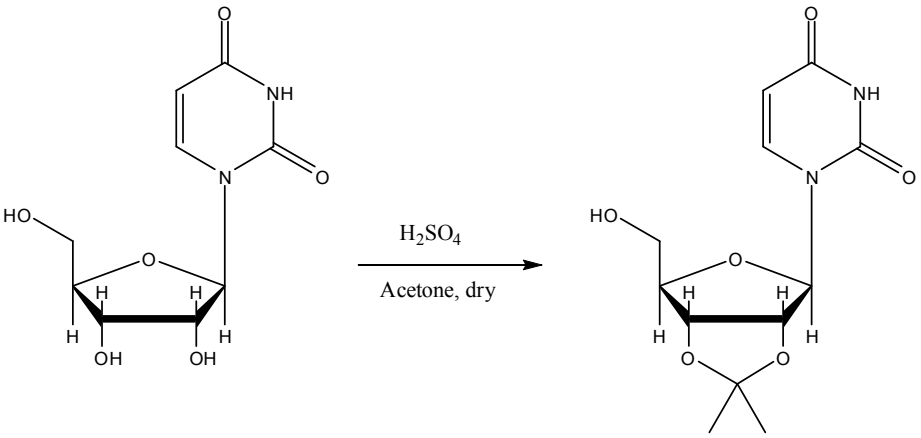
Solvents were purchased from Sigma-Aldrich. Those specified as dry in the synthesis procedure (acetone, DMSO and DMF) were dried over molecular sieves. All glass equipment was flame dried under reduced pressure. H-NMR (FT-NMR, Avance™, Bruker) was measured for all the synthesized compounds, and the chemical shifts reported relative to the deuterated solvent used (DMSO, 2.500 ppm; H2O, 4.800 ppm). HRMS (microTOF Q™, Bruker) was measured for those compounds not previously reported.

Synthesis of 3N-methyl uridine (1)



The synthesis was essentially performed as previously described. [1] The uridine (117.2 mg, 0.479 mmol) was suspended in a mixture of dry DMF (0.48 mL) and dry acetone (0.48 mL) along with K_2CO_3 (115 mg, 1.57 mmol). MeI (0.0295 mL, 0.473 mmol) was added dropwise to the suspension. The system was then refluxed over night. The solvent removed under reduced pressure and the compound purified on column with silica gel (6-12% MeOH/CH_2Cl_2), which yielded **1** (104.2 mg, 84.3% yield). H-NMR (Avance™, Bruker, 400 MHz, DMSO, 25°C): 7.960 (d, J = 8.1, 1H), 5.816 (d, J = 4.974, 1H), 5.774 (d, J = 8.1, 1H) , 5.378 (d, J = 5.6, 1H), 5.110 (t, J = 5.1, 1H), 5.085 (d, J = 5.3, 1H), 4.030 (q, J = 5.2, 1H), 4.964 (q, J = 4.9, 1H), 3.857 (dd, J = 3.1, 7.4, 1H), 3.671-3.532 (m, 2H), 3.158 (s, 3H) ppm.

Synthesis of 2',3'-O-isopropylidene uridine (2)

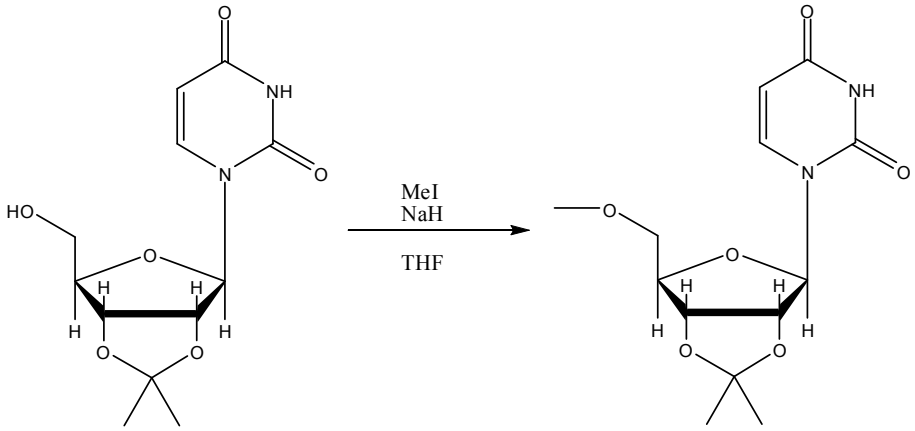


The synthesis was performed as previously described. [2] Synthesis yielded **2** (355 mg, 75.7%). H-NMR (Avance™, Bruker, 400 MHz, DMSO, 25°C): 11.371 (br s, 1H), 7.788 (d, J = 8.1, 1H), 5.828 (d, J = 2.7, 1H), 5.631 (d, J = 8.1, 1H), 5.073 (t, J = 5.3, 1H), 4.892 (dd, J = 2.7, 6.3, 1H), 4.741 (dd, J = 3.6, 6.3, 1H), 4.093-4.037 (m, 1H), 3.618-3.518 (m, 2H), 1.483 (s, 3H), 1.285 (s, 3H) ppm.

Synthesis of 2',3'-O-$d_6$isopropylidene uridine (2a)

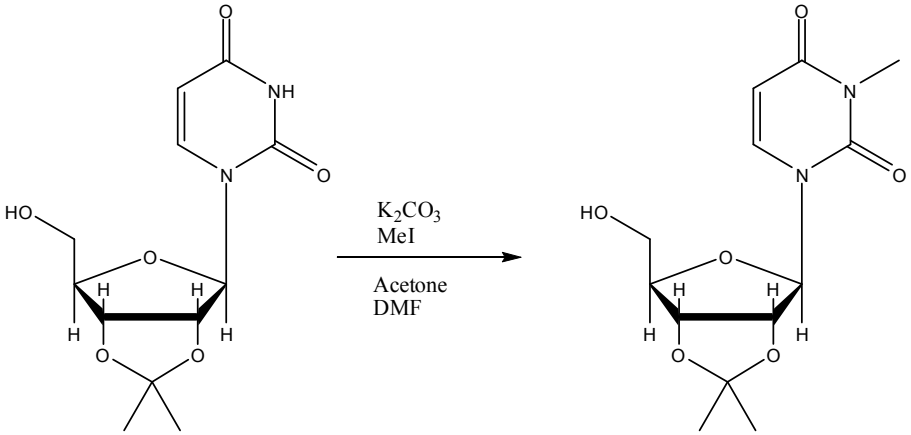
2a was prepared in the same manner as **2**. Fully deuterated acetone was used instead of acetone as a solvent and reactant. HRMS (microTOF Q™, Bruker), formula mass for $[C_{12}H_{10}D_6N_2O_6+H]^+$ is 291.1458 amu, mass found is 291.1467 amu. -NMR (Avance™, Bruker, 400 MHz, DMSO, 25°C): 11.373 (br s, 1H), 7.788 (d, J = 8.1, 1H), 5.827 (d, J = 2.664, 1H), 5.638 (br d, J = 8.1, 1H), 5.071 (t, J = 5.3, 1H), 4.889 (dd, J = 2.7, 6.4, 1H), 4.738 (dd, J = 3.6, 6.4, 1H), 4.060 (dt, J = 3.7, 4.3, 1H), 3.619-3.519 (m, 2H) ppm.

Synthesis of 2',3'-O-isopropylidene, 5'-O-methyl Uridine (3)



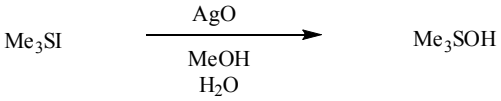
Synthesis was performed as previously described.[3] The synthesis yielded 111.1 mg of a mixture of mono and dimethylated sample 90% of which was **3**. The mixture was used without further purification. H-NMR (Avance™, Bruker, 400 MHz, DMSO, 25°C): 11.362 (br s, 1H), 7.674 (d, J = 8.1, 1H), 5.796 (d, J = 2.4, 1H), 5.637 (d, J = 8.1, 1H), 4.924 (dd, J = 2.4, 6.3, 1H), 4.716 (dd, J = 3.7, 6.3, 1H), 4.166 (dt, J = 5.2, 4.1, 1H), 3.617-3.584 (m, 1H), 3.554-3.486 (m, 2H), 3.274 (s, 3H), 1.479 (s, 3H), 1.283 (s, 3H) ppm.

Synthesis of 2',3'-O-isopropylidene 3 N methyl Uridine (4)



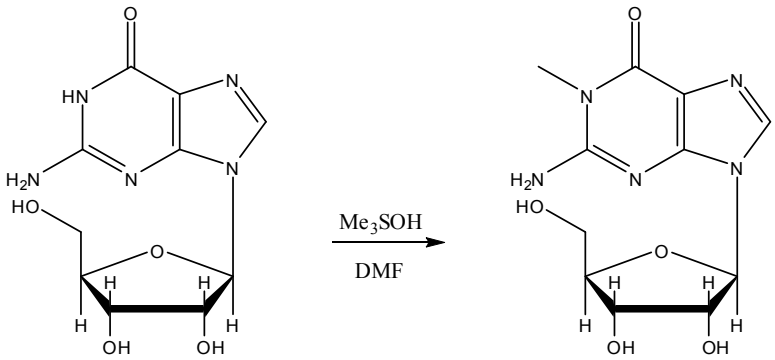
Synthesis was essentially performed as previously described.[4] 2 (80 mg, 0.28 mmol) was suspended in a mixture of acetone (0.42 mL) and DMF (0.42 mL) along with K_2CO_3 (50 mg, 0.42 mmol). MeI (0.027 mL, .42 mmol) was added dropwise to the solution. The mixture was stirred for 3 h, the solvent removed under reduced pressure and the residue purified on a column (10% methanol in dichloromethane) to give 50 mg of pure **4** (0.168 mmol, 60% yield). H-NMR (Avance™, Bruker, 400 MHz, DMSO, 25°C) = 7.844 (d, J = 8.1, 1H), 5.861 (d, J = 2.5, 1H), 5.764 (d, J = 8.1, 1H), 5.087 (t, J = 5.3, 1H), 4.898 (dd, J = 2.5, 6.3, 1H), 4.754 (dd, J = 6.3, 3.5, 1H), 4.100 (dd, J = 4.4, 8.1, 1H), 3.634-3.527 (m, 2H), 3.154 (s, 3H), 1.488 (s, 3H), 1.284 (s, 3H) ppm.

Preparation of Trimethylsulfoniumhydroxide



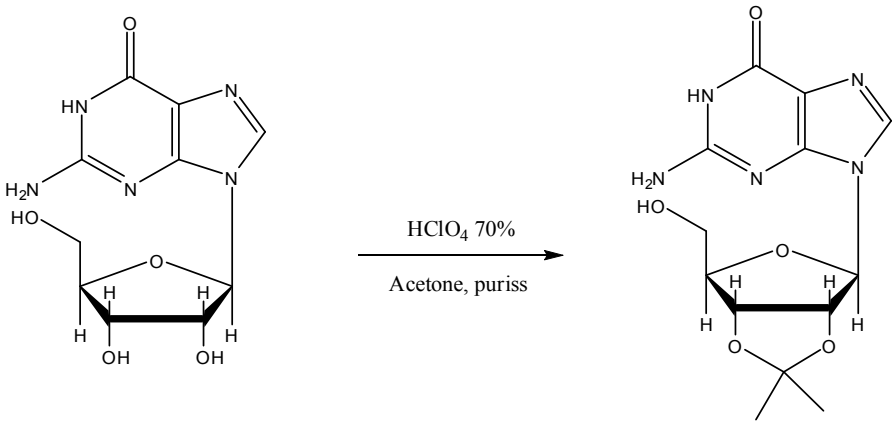
Performed as previously described. A concentration of 0.987 M was aquired.

Synthesis of 1-N methyl guanosine (5)



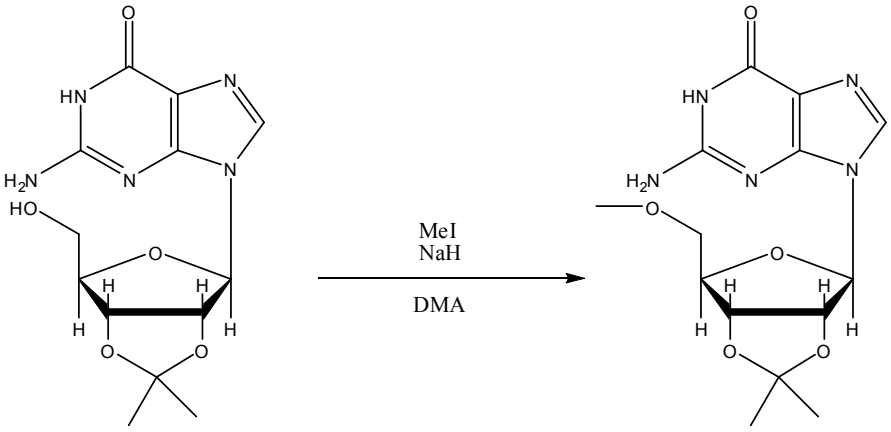
The synthesis was essentially performed as described by Yamauchi et al. [5] Guanosine (291.7 mg, 1.031 mmol) was added to the $Me_3SOH_{(aq)}$ solution (1.25 mL, 1.237 mmol). The mixture was concentrated on rotavapor to give a oily solid mixture which was dissolved in DMF (4 mL). The solution was heated to 80 °C and stirred for 40 min. The solvent was removed under reduced pressure. The residue dissolved in methanol and purified on preparatory TLC plate (30% methanol in dichloromethane). Yielding 141.6 mg of **5** (46.3% yield). HRMS (microTOF Q™, Bruker), formula mass for $[C_{11}H_{15}N_5O_5+Na]^+$ is 320.0965 amu, mass found is 320.0953 amu. H-NMR (Avance™, Bruker, 400 MHz, D_2O, 25°C): 8.000 (s, 1H), 5.922 (d, J = 5.992, 1H), 4.768 (t, J = 5.7, 1H), 4.430 (dd, J = 3.7, 5.3, 1H), 4.248 (dt, J = 3.7, 3.3, 1H), 3.905 (dd, J = 3.1, 12.7, 1H), 3.834 (dd, J = 4.1, 12.7, 1H), 3.491 (s, 3H) ppm.

Synthesis of 2',3'-O-isopropylidene guanosine (6)



Synthesis was essentially performed as previously described [6]. Guanosine (1000 mg, 3.53 mmol) was suspended in dry acetone (60 mL) and hypochloric acid (0.70 mL) added. The solution was stirred at room temperature for 20 min., neutralized with TEA, solvent removed under reduced pressure and the residue purified on a silica column (gradient 0-5% MeOH/CH_2Cl_2) yielding 579.3 mg of pure **6** (55.2% yield). H-NMR (Avance™, Bruker, 400 MHz, DMSO, 25°C): 10.676 (s, 1H), 7.906 (s, 1H), 6.559 (s, 2H), 5.918 (d, J = 2.8, 1H), 5.184 (dd, J = 6.3, 2.8, 1H), 5.041 (t, J = 5.5, 1H), 4.965 (dd, J = 3.0, 6.3, 1H), 4.126-4.084 (m, 1H), 3.558-3.487 (m, 2H), 1.501 (s, 3H), 1.313 (s, 3H) ppm.

Synthesis of 2',3'-O-isopropylidene 5'-O-methyl guanosine (7)



NaH (154.9 mg, 6.45 mmol) suspended in DMF (3 mL), 6 (139 mg, 0.43 mmol) added to the solution and stirred for 15 min. MeI (0.0268 mL, 0.43 mmol) was added dropwise to the solution and stirred at room temperature for 60 min. A concentrated solution of Na_2SO_3 in H_2O (20 mL) was added and aqueous solution extracted with CH_2Cl_2 (3x20 mL). The organic layer was dried under Na_2SO_3, filtered and the solvent removed under reduced pressure. Purification by column chromatography (10% MeOH/CH_2Cl_2). Synthesis yield was 61.8 mg of **7** (42.6% yield). HRMS (microTOF Q™, Bruker), formula mass for $[C_{11}H_{15}N_5O_5+H]^+$ is 338.1459 amu, mass found is 338.1454 amu. H-NMR (Avance™, Bruker, 400 MHz, DMSO, 25°C): 10.667 (br s, 1H), 7.841 (s, 1H), 6.527 (br s, 2H), 5.939 (d, J = 2.3, 1H), 5.226 (dd, J = 6.2, 2.3, 1H), 4.978 (dd, J = 3.1, 6.2, 1H), 4.226-4.192 (m, 1H), 3.422-3.505 (m, 2H), 3.241 (s, 3H), 1.507 (s, 3H), 1.312 (s, 3H) ppm.

References

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