Electronic Supplementary Material (ESI) for ChemComm.

SUPPLEMENTARY INFORMATION

Visible-Light-Mediated Oxidative Demethylation of N^6-Methyl Adenines

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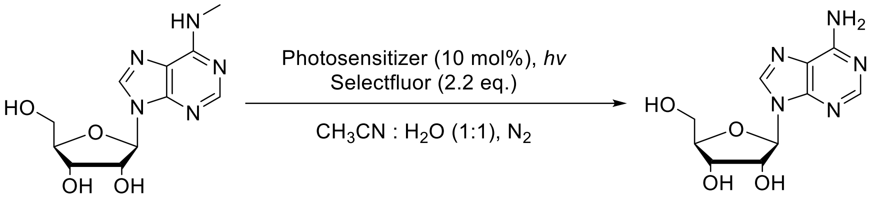
1. General information

Unless otherwise noted, all reagents were obtained from commercial suppliers and were used without further purification. Tetrahydrofuran (THF), toluene and diethyl ether (Et_2O) were distilled from sodium/benzophenone. Dry dichloromethane (CH_2Cl_2) was distilled over calcium hydride. *N*,*N*-dimethylformate (DMF), dimethyl sulphoxide (DMSO) were dried over molecular sieves 3Å.

The ^1H NMR and ^{13}C NMR spectra were collected with a Bruker Avance III 300 (300 MHz) spectrometers. Chemical shifts are given in ppm relative to tetramethylsilane (TMS). Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), triplet (t), quartet (q), multiplet (m).

HPLC data was collected with Waters ACQUITY H-Class or Shimadzu CTO_10ASVP. The HPLC-ESI-IT-MS analysis was performed on an UltiMate 3000 UHPLC system equipped with a diode-array detector and an LCQ Fleet mass spectrometer (ThermoFisher, San Jose, CA, USA). The reaction was monitored on a HPLC system equipped with an Agilent Eclipse Plus C_{18} 5 μm analysis column (250 × 4.6 mm) with mobile phase H_2O/CH_3OH (85/15) with a flow rate of 1 mL/min at room temperature. The detection wavelength was set as 260 nm. For LC-MS analysis, the reaction was monitored with a ThermoFisher Hypersil-gold C_{18} column with 3 μm particle diameter (column dimensions 100 × 2.1 mm) with a flow rate of 0.2 mL/min at room temperature. 0.1% Formic acid in H_2O (buffer A) and 0.1% formic acid in CH_3CN (buffer B) were applied as mobile phase. A gradient of 10 min 3%-30% B, 3 min 8% B, 3 min 3% B was used.

2. Optimization of photo-induced demethylation



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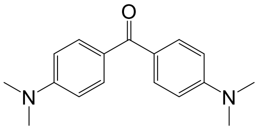
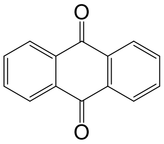
1		365	20	N. R.
2		365	3	56
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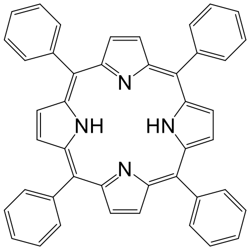
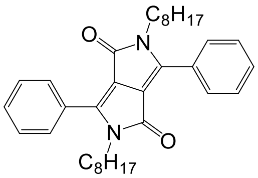
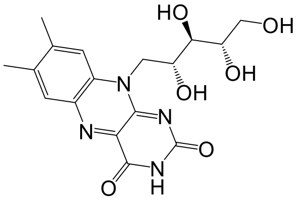
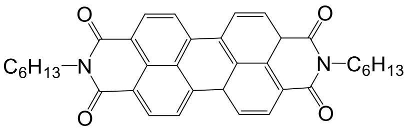
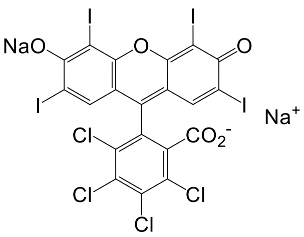
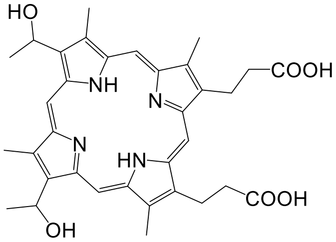
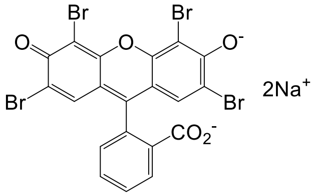
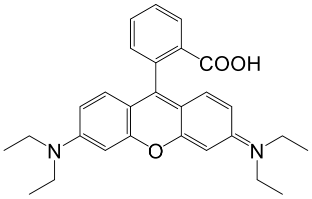
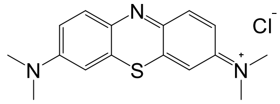
4		470	18	7
5		470	12	N. R.
6		**470**	**2**	**86**
7		530	22	11

8		530	12	trace
9		530	12	trace
10		530	12	trace
11		530	24	11
12		620	22	71

3. Experimental details

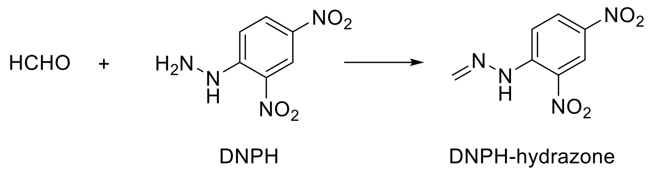
To a reaction tube was added *N*^{6}-methyladenosine **1** (m^{6}A, 28.1mg, 0.1mmol), Selectfluor (2.2 eq., 0.22 mmol, 78 mg) and riboflavin **2a** (0.1 eq., 3.8 mg, 0.01 mmol), CH_3CN:H_2O (1/1, 2 mL total) was then added under nitrogen protection and the reaction mixture was stirred under illumination. After the disappearance of m^{6}A, saturated $NaHCO_3$ solution was added to the aqueous solution until pH = 7. The residue was concentrated in vacuum and purified by column chromatography (SiO_2, CH_2Cl_2/CH_3OH = 12/1 as eluents) to yield 23 mg of adenosine A **3** (yield 86%). ^{1}H NMR (DMSO-*d*$_6$, 300 MHz) δ 8.34 (s, 1H), 8.13 (s, 1H), 7.33 (s, 2H), 5.88 (d, *J* = 6.0 Hz, 1H), 5.44-5.39 (m, 2H), 5.18-5.16 (d, *J* = 4.5 Hz, 1H), 4.63-4.58 (m, 1H), 4.16-4.12 (m, 1H), 3.96-3.95 (m, 1H), 3.70-3.64 (m, 1H), 3.58-3.52 (m, 1H). ^{13}C NMR (DMSO-*d*^{6}, 75 MHz) δ 156.6, 152.8, 149.5, 140.4, 119.8, 88.4, 86.3, 73.9, 71.1, 62.1.[1]

To a reaction tube was added *N*^{6},*N*^{6}-dimethyladenosine **4** (m^{6,6}A, 29.5 mg, 0.1 mmol), Selectfluor (2.2 eq., 78 mg, 0.22 mmol) and riboflavin **2a** (0.1 eq., 3.8 mg, 0.01 mmol), CH_3CN:H_2O (1/1, 2 mL total) was then added under nitrogen protection and the reaction mixture was stirred under illumination. After the disappearance of m^{6,6}A, saturated $NaHCO_3$ solution was added to the aqueous solution until pH = 7. The residue was concentrated in vacuum and purified by column chromatography (SiO_2, CH_2Cl_2/CH_3OH = 12/1 as eluents) to yield 5 mg of *N*^{6}-methyladenosine m^{6}A **1** (yield 17%) and 21 mg of adenosine **3** (yield 78%).

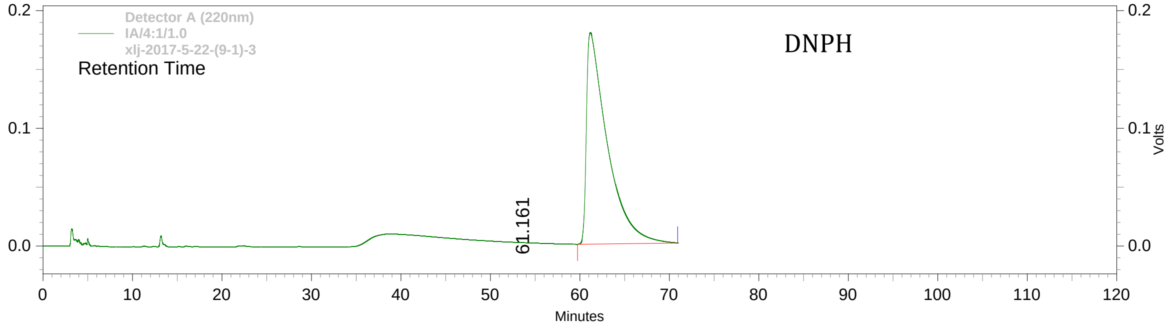
To a reaction tube was added *N*^{6}-methyl-2'-deoxy-adenosine **5** (m^{6}dA, 29.5mg, 0.1mmol), Selectfluor (2.2 eq., 78 mg, 0.22 mmol) and riboflavin **2a** (0.1eq., 3.8 mg, 0.01 mmol), CH_3CN:H_2O (1/1, 2 mL total) was then added under nitrogen protection and the reaction mixture was stirred under illumination for 3 hours. After the disappearance of m^{6}dA, saturated $NaHCO_3$ solution was added to the aqueous solution until pH = 7. The residue was concentrated in vacuum and purified by column chromatography (SiO_2, CH_2Cl_2/CH_3OH = 12/1 as eluents) to yield 2'-deoxy-adenosine dA 15mg (yield 60%). ^{1}H NMR (DMSO-*d*$_6$, 300 MHz) δ 8.33 (s, 1H), 8.13 (s, 1H), 7.31 (s, 2H), 6.36-6.31 (m, 1H), 5.31 (d, *J* = 4.2 Hz, 1H), 5.26-5.22 (m, 1H), 4.42-4.38 (m, 1H), 3.89-3.86 (m, 1H), 3.65-3.60 (m, 1H), 3.58-3.48 (m, 1H).

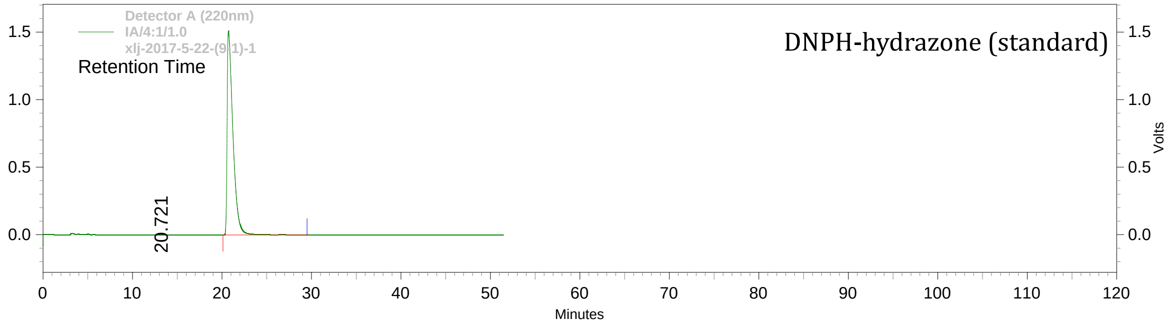
To a reaction tube was added *N*^{6}-methyladenine **6** (29.8 mg, 0.2 mmol), Selectfluor (2.2 eq., 156 mg, 0.44 mmol,) and riboflavin **2a** (0.1 eq., 7.5 mg, 0.02 mmol), CH_3CN:H_2O (1/1, 2 mL total) was then added under nitrogen protection and the reaction mixture was stirred under illumination for 3 hours. After the disappearance of *N*^{6}-methyladenine, saturated $NaHCO_3$ solution was added to the aqueous solution until pH = 7. The residue was concentrated in vacuum and purified by column chromatography (SiO_2, CH_2Cl_2/CH_3OH = 12/1 as eluents) to yield 19mg of adenine (yield 71%). ^1H NMR (DMSO-*d*^{6}, 300 MHz) δ 12.8 (s, 1H), 8.1 (d, *J* = 5.4 Hz, 2H), 7.1 (s, 2H)[2].

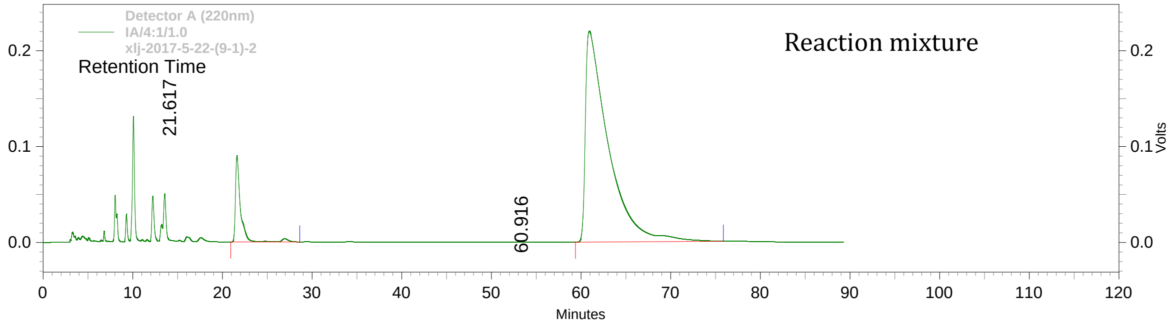
4. HPLC assay for the detection of HCHO



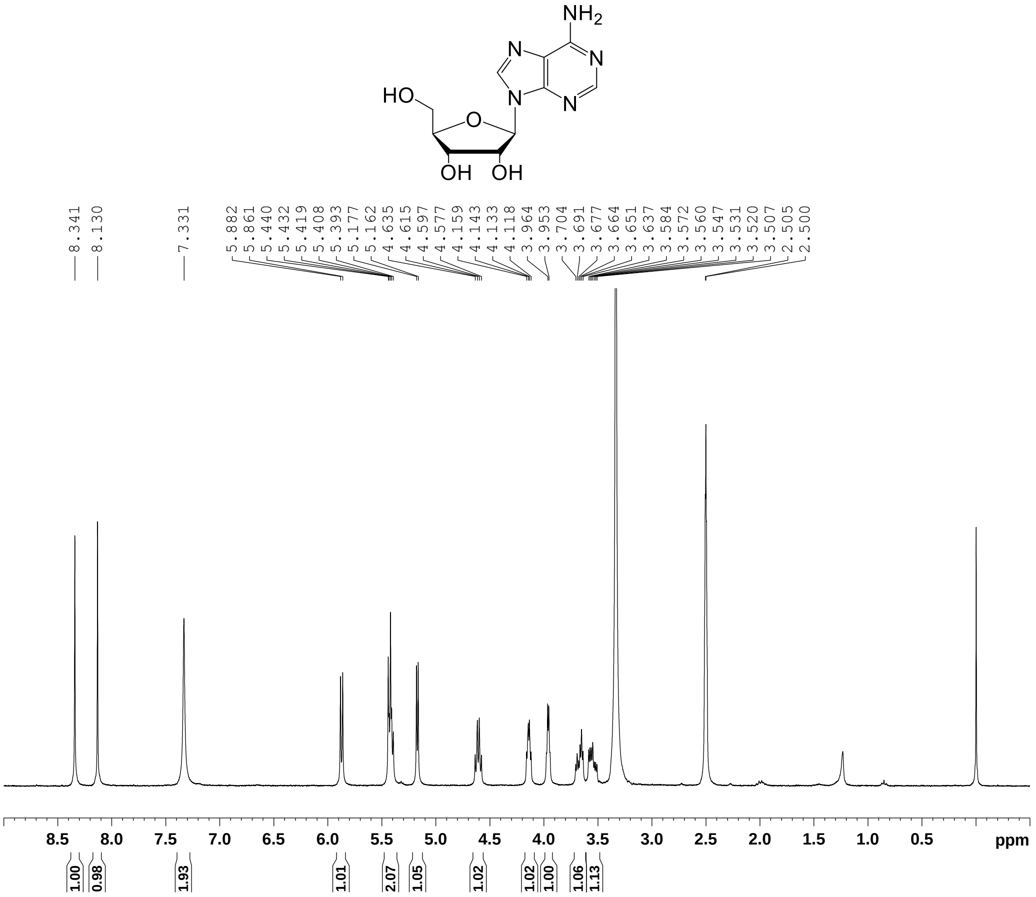
After completion of the demethylation process, excess (2,4-dinitrophenyl)hydrazine (DNPH) was added to the reaction mixture, and then analyzed on a HPLC system equipped with a Chiralpak AD-H 5 µm column (250 × 4.6 mm) with the mobile phase *n*-butanol/cyclohexane (1:9) in a flow rate of 1 mL/min at room temperature. The detection wavelength was set as 220 nm.

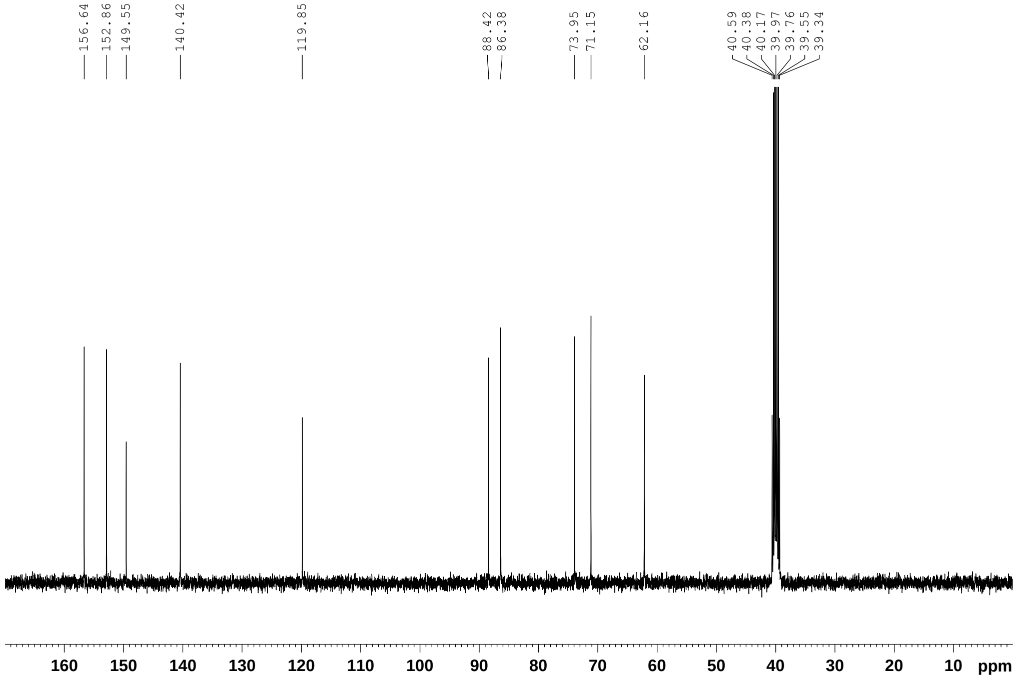


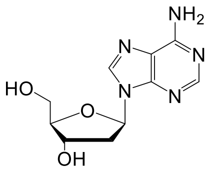




5. NMR spectra







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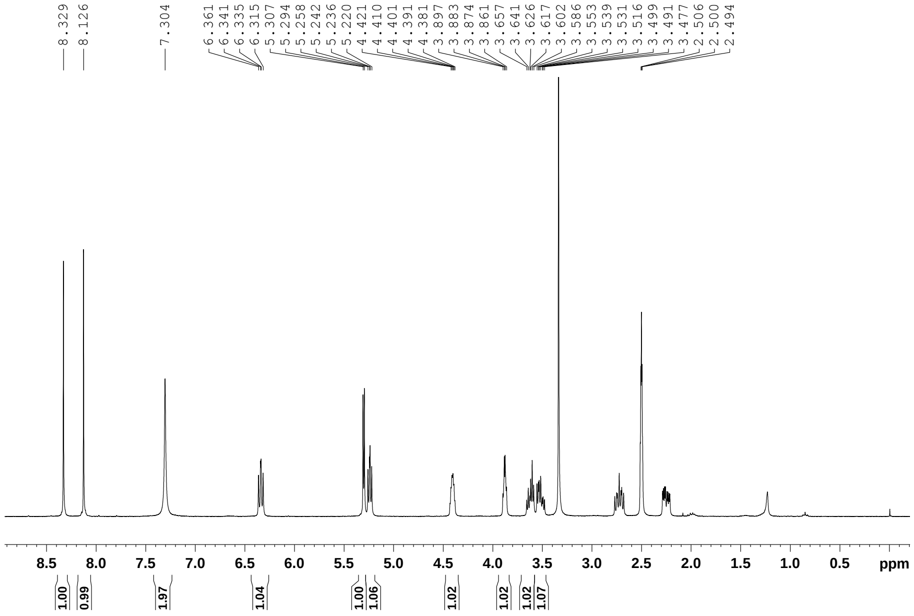
N
N
N
HO
O
OH



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8.126
7.304
6.361
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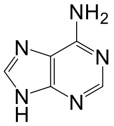

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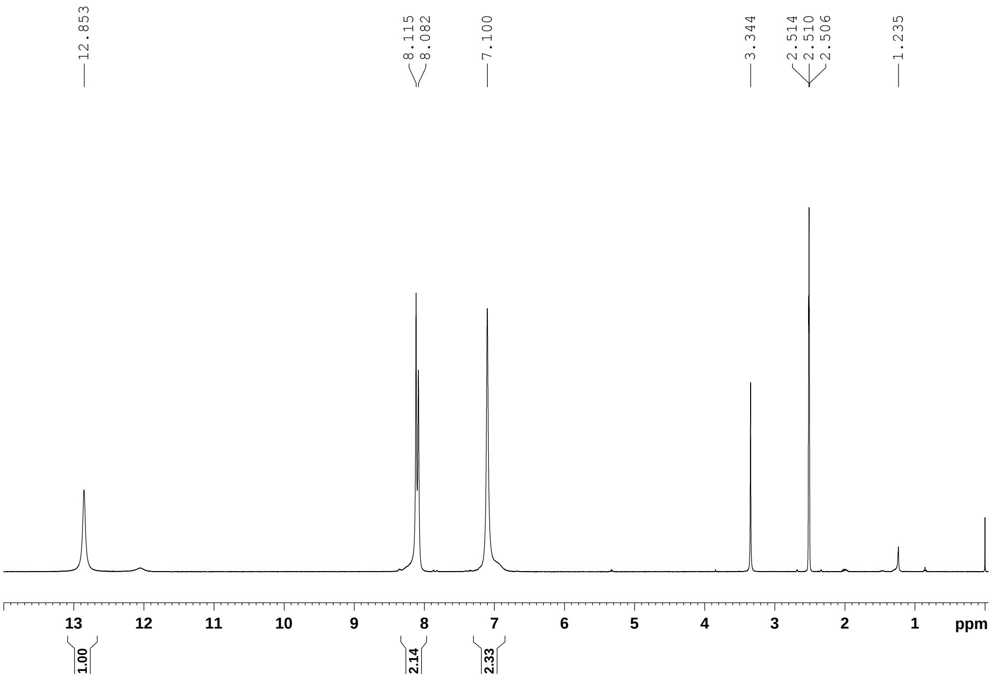
N
H



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13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.00
2.14
2.33

6. References

[1]. J. Wu, H. Xiao, T. Wang, T. Hong, B. Fu, D. Bai, Z. He, S. Peng, X. Xing, J. Hu, P. Gao and X. Zhou, *Chem. Sci.*, 2015, **6**, 3013.

[2]. R. Liu, H. Luo, Y. Li, M. Yang, X. Xu, H. Li, Y. Shen, C. Zhang, J. Su and W. Zhang, *Chem. Nat. Compd.*, 2009, **45**, 599.