A novel nucleophilic approach to 1-alkyladenosines. A two-step synthesis of [1-^{15}N]adenosine from inosine

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2',3',5'-Tri-*O*-acetyl-1-(2,4-dinitrobenzenesulphonyl)inosine (2a).
^{1}H NMR ($CDCl_3$, 400 MHz) 2.10 (s, 3H), 2.14 (s, 3H), 2.16 (s, 3H), 4.38 (dd, *J* = 4.2, 12.3 Hz, 1H), 4.42 (dd, *J* = 3.1, 12.3 Hz, 1H), 4.48 (m, 1H), 5.54 (dd, *J* = 5.6, 4.5 Hz, 1H), 5.75 (dd, *J* = 5.4, 5.6 Hz, 1H), 6.17 (d, *J* = 5.4 Hz, 1H), 8.02 (s, 1H), 8.62 (s, 1H), 8.66 (d, *J* = 2.1 Hz, 1H), 8.70 (dd, *J* = 2.1, 8.8 Hz, 1H), 8.96 (d, *J* = 8.8, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) 20.2, 20.4, 20.7, 62.8, 70.4, 73.6, 80.7, 86.5, 120.4, 124.2, 126.9, 134.6, 138.6, 139.3, 143.8, 146.9, 148.5, 151.2, 153.5, 169.2, 169.5, 170.2. HRMS (FAB) calcd for $C_{22}H_{21}N_6O_{14}S$ $(M+H)^+$ 625.0836, found 625.0860.

3',5'-Di-*O*-acetyl-2'-deoxy-1-(2,4-dinitrobenzenesulphonyl)inosine (2b).
^{1}H NMR ($CDCl_3$, 400 MHz) 2.09 (s, 3H), 2.15 (s, 3H), 2.69 (ddd, *J* = 6.0, 2.6, 14.2 Hz, 1H), 2.81 (ddd, *J* = 7.6, 6.4, 14.2 Hz, 1H), 4.32-4.40 (m, 3H), 5.40 (m, 1H), 6.40 (dd, *J* = 6.0, 7.6 Hz, 1H), 8.00 (s, 1H), 8.61 (s, 1H), 8.67 (d, *J* = 2.1 Hz, 1H), 8.70 (dd, *J* = 2.1, 8.8 Hz, 1H), 8.98 (d, *J* = 8.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) 20.7, 20.9, 38.4, 63.5, 74.1, 82.9, 84.9, 120.3, 124.2, 126.9, 134.8, 138.7, 139.1, 143.5, 146.7, 148.6, 151.2, 153.6, 170.2, 170.3. HRMS (FAB) calcd for $C_{20}H_{19}N_6O_{12}S$ $(M+H)^+$ 567.0782, found 567.0755.

[1-^{15}N]-2',3',5'-Tri-*O*-acetyl-1-(2,4-dinitrobenzenesulphonyl)inosine (2a).
^{1}H NMR ($CDCl_3$, 400 MHz) 2.10 (s, 3H), 2.14 (s, 3H), 2.16 (s, 3H), 4.36-4.49 (m, 3H), 5.54 (dd, *J* = 5.6, 4.5 Hz, 1H), 5.75 (dd, *J* = 5.4, 5.6 Hz, 1H), 6.16 (d, *J* = 5.4 Hz, 1H), 7.98 (s, 1H), 8.63 (d, *J* = 6.4 Hz, 1H), 8.66 (d, *J* = 2.1 Hz, 1H), 8.70 (dd, *J* = 8.8, 2.1 Hz, 1H), 8.98 (d, *J* = 8.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) 20.3, 20.5, 20.7, 62.8, 70.4, 73.6, 80.7, 86.5, 120.3, 124.4 (d, *J* = 9.2 Hz), 126.8, 134.8 (d, *J* = 4.6 Hz), 138.9, 139.2, 143.8 (d, *J* = 3.8 Hz), 147.0, 148.7, 151.2, 153.5 (d, *J* = 3.8 Hz), 169.2, 169.5, 170.2. ^{15}N NMR ($CDCl_3$, 30 MHz) -168.1 (10 M $H^{15}NO_3$ as the external reference). HRMS (FAB) calcd for $C_{22}H_{21}N_5{}^{15}NO_{14}S$ $(M+H)^+$ 626.0807, found 626.0809.

[6-^{18}O]-2',3',5'-Tri-*O*-acetyl-1-(2,4-dinitrobenzenesulphonyl)inosine (2a$^{\lozenge}$).
HRMS (FAB) calcd for $C_{22}H_{21}N_6O_{13}{}^{18}OS$ $(M+H)^+$ 627.0879, found 627.0873.

[1-^{15}N]-2',3',5'-Tri-*O*-acetyladenosine (3a*).
^{1}H NMR ($CDCl_3$, 400 MHz) 2.09 (s, 3H), 2.13 (s, 3H), 2.15 (s, 3H), 4.38 (dd, *J* = 5.4, 11.2 Hz, 1H), 4.43-4.47 (m, 2H), 5.67 (dd, *J* = 5.4, 4.6 Hz, 1H), 5.82 (bs, 2H), 5.93 (dd,

J = 5.4, 5.3 Hz, 1H), 6.18 (d, *J* = 5.3 Hz, 1H), 7.97 (s, 1H), 8.37 (d, *J* = 15.2 Hz, 1H). ^{13}C NMR ($CDCl_3$,100 MHz) 20.4, 20.5, 20.7, 63.1, 70.6, 73.2, 80.3, 86.2, 120.1 (d, *J* = 2.5 Hz), 138.9, 149.8 (d, *J* = 3.0 Hz), 152.9 (d, *J* = 2.0 Hz), 155.3 (d, *J* = 5.4 Hz), 169.4, 169.6, 170.3. ^{15}N NMR ($CDCl_3$, 30 MHz) -175.4 (10 M $H^{15}NO_3$ as the external reference). HRMS (FAB) calcd for $C_{16}H_{20}N_4{}^{15}NO_7$ $(M+H)^+$ 395.1333, found 395.1333.

[1-^{15}N]-3',5'-Di-*O*-acetyl-2'-deoxyadenosine (3b*).
^{1}H NMR ($CDCl_3$, 400 MHz) 2.09 (s, 3H), 2.11 (s, 3H), 2.63 (ddd, *J* = 5.9, 2.5, 14.3 Hz, 1H), 2.96 (ddd, *J* = 8.0, 6.4, 14.3 Hz, 1H), 4.33-4.44 (m, 3H), 5.44 (m, 1H), 5.82 (bs, 2H), 6.44 (dd, *J* = 5.9, 8.0, 1H), 7.99 (s, 1H), 8.35 (d, *J* = 15.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) 20.8, 20.9, 37.5, 63.7, 74.5, 82.5, 84.5, 120.1 (d, *J* = 2.0 Hz), 138.5, 149.6 (d, *J* = 2.6 Hz), 153.1 (d, *J* = 1.5 Hz), 155.5 (d, *J* = 4.6 Hz), 170.3, 170.4. ^{15}N NMR ($CDCl_3$, 30 MHz) -184.0 (10 M $H^{15}NO_3$ as the external reference). HRMS (FAB) calcd for $C_{14}H_{18}N_4{}^{15}NO_5$ $(M+H)^+$ 337.1278, found 337.1266.

[6-$^{15}NH_2$]-2',3',5'-Tri-*O*-acetyladenosine (3a).
^{1}H NMR ($CDCl_3$, 400 MHz) 2.09 (s, 3H), 2.13 (s, 3H), 2.15 (s, 3H), 4.36-4.47 (m, 3H), 5.67 (dd, *J* = 5.4, 4.6 Hz, 1H), 5.91 (d, *J* = 90.4 Hz, 2H), 5.93 (dd, *J* = 5.4, 5.3 Hz, 1H), 6.19 (d, *J* = 5.3, 1H), 7.98 (s, 1H), 8.37 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) 20.4, 20.5, 20.7, 63.1, 70.6, 73.2, 80.3, 86.3, 120.1, 139.0, 149.7, 152.9 (d, *J* = 2.0 Hz), 155.3 (d, *J* = 20.6 Hz), 169.4, 169.6, 170.3. ^{15}N NMR ($CDCl_3$, 30 MHz) -273.4 (10 M $H^{15}NO_3$ as the external reference). HRMS (FAB) calcd for $C_{16}H_{20}N_4{}^{15}NO_7$ $(M+H)^+$ 395.1333, found 395.1331.

2',3',5'-Tri-*O*-acetyl-1-benzyladenosine (4a).
^{1}H NMR ($CDCl_3$, 400 MHz) 2.09 (s, 3H), 2.12 (s, 6H), 4.30-4.43 (m, 3H), 5.26 (s, 2H), 5.61 (dd, *J* = 5.5, 4.8 Hz, 1H), 5.86 (dd, *J* = 5.5, 5.0 Hz, 1H), 6.00 (d, *J* = 5.0 Hz, 1H), 7.30-7.36 (m, 5H), 7.73 (s, 1H), 7.74 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) 20.4, 20.5, 20.7, 49.9, 63.0, 70.4, 73.2, 80.1, 86.5, 124.4, 127.8, 128.0, 128.9, 136.0, 136.9, 141.3, 147.7, 154.5, 169.3, 169.5, 170.3. HRMS (FAB) calcd for $C_{23}H_{26}N_5O_7$ $(M+H)^+$ 484.1832, found 484.1833.

2',3',5'-Tri-*O*-acetyl-1-ethyladenosine (4b).
^{1}H NMR ($CDCl_3$, 400 MHz) 1.45 (t, *J* = 7.0 Hz, 3H), 2.09 (s, 3H), 2.12 (s, 3H), 2.14 (s, 3H), 4.19 (q, *J* = 7.0 Hz, 2H), 4.32-4.45 (m, 3H), 5.62 (dd, *J* = 5.5, 4.8 Hz, 1H), 5.90 (dd, *J* = 5.5, 5.1 Hz, 1H), 6.03 (d, *J* = 5.1 Hz, 1H), 7.78 (s, 1H), 7.95 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) 14.4, 20.4, 20.5, 20.7, 45.9, 63.1, 70.5, 73.1, 80.2, 86.7, 124.0, 138.1, 143.8, 147.0, 153.4, 169.3, 169.5, 170.4. HRMS (FAB) calcd for $C_{18}H_{24}N_5O_7$ $(M+H)^+$ 422.1676, found 422.1679.

2',3',5'-Tri-*O*-acetyl-1-butyladenosine (4c).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.97 (t, *J* = 7.4 Hz, 3H), 1.42 (m, 2H), 1.81 (m, 2H), 2.10 (s, 3H), 2.12 (s, 3H), 2.14 (s, 3H), 4.06 (t, *J* = 7.4 Hz, 2H), 4.33-4.45 (m, 3H), 5.61 (dd, *J* = 5.5, 4.8 Hz, 1H), 5.88 (dd, *J* = 5.5, 5.1 Hz, 1H), 6.01 (d, *J* = 5.1 Hz, 1H), 7.70 (s, 1H), 7.79 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.7, 19.8, 20.4, 20.5, 20.7, 30.7, 48.0, 63.1, 70.5, 73.1, 80.1, 86.5, 124.1, 137.2, 141.7, 147.5, 154.0, 169.3, 169.5, 170.3. HRMS (FAB) calcd for $C_{20}H_{28}N_5O_7$ $(M+H)^+$ 450.1989, found 450.1995.

2',3',5'-Tri-*O*-acetyl-1-isopropyladenosine (4d).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.46 (d, *J* = 6.8 Hz, 6H), 2.10 (s, 3H), 2.12 (s, 3H), 2.13 (s, 3H), 4.32-4.45 (m, 3H), 5.45 (hp, *J* = 6.8 Hz, 1H), 5.64 (dd, *J* = 5.3, 5.1 Hz, 1H), 5.89 (dd, *J* = 5.3, 5.1 Hz, 1H), 6.00 (d, *J* = 5.1 Hz, 1H), 7.73 (s, 1H), 7.80 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.4, 20.5, 20.7, 22.4, 46.8, 63.1, 70.5, 73.1, 80.1, 86.8, 123.4, 138.0, 144.2, 150.0, 154.0, 169.3, 169.5, 170.4. HRMS (FAB) calcd for $C_{19}H_{26}N_5O_7$ $(M+H)^+$ 436.1832, found 436.1836.

2,4-Dinitrophenol (6).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34 (d, *J* = 9.2 Hz, 1H), 8.46 (dd, *J* = 2.8, 9.2 Hz, 1H), 9.08 (d, *J* = 2.8 Hz, 1H), 11.03 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 121.2, 121.9, 131.6, 132.6, 140.3, 159.0. HRMS (EI) calcd for $C_6H_4N_2O_5$ (M) 184.0120, found 184.0123.

[^{18}O]-2,4-Dinitrophenol (6$^{\diamond}$).
HRMS (EI) calcd for $C_6H_4N_2{}^{18}OO_4$ (M) 186.0163, found 186.0158.

2',3',5'-Tri-*O*-acetyl-6-benzyladenosine.
^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.08 (s, 3H), 2.12 (s, 3H), 2.14 (s, 3H), 4.35-4.47 (m, 3H), 4.87 (bs, 2H), 5.68 (dd, *J* = 5.6, 4.4 Hz, 1H), 5.93 (dd, *J* = 5.6, 5.2 Hz, 1H), 6.13 (bs, 1H), 6.18 (d, *J* = 5.2 Hz, 1H), 7.26-7.40 (m, 5H), 7.89 (s, 1H), 8.42 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.4, 20.5, 20.8, 44.5, 63.1, 70.7, 73.2, 80.2, 86.1, 120.2, 127.6, 127.7, 128.7, 138.1, 138.3, 140.8, 153.5, 154.7, 169.4, 169.6, 170.4. HRMS (FAB) calcd for $C_{23}H_{26}N_5O_7$ $(M+H)^+$ 484.1832, found 484.1835.