

Microwave Assisted Synthesis of 6-Substituted Aminopurine Analogs in Water

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General procedure for the synthesis of 6-substituted aminopurine analogs **1-7,a-e** and **8a, 8a', 9a**

Amine (6 mmol) is added to a stirred suspension of 6-chloropurine derivatives **1-9** (2 mmol) in water (10 mL) in a 50 mL round-bottomed flask. After vibration, the flask is moved into microwave oven and irradiated at 200 W for 10 minutes. At each interval, TLC monitors the reaction progress. When the reaction completed, the mixture is cooled to room temperature and desired 6-substituted aminopurine analogs **1-3,a-e** and **7,a-e** precipitate out. Then filter the solid directly followed by washing with cold water (3×5 mL). The filtrate is concentrated to 1/3 volume, and collects the products crystallized again from the mixture. The products **4-6,a-e** and **8a, 8a', 9a** are purified by column chromatography with CHCl₃/CH₃OH (9/1, v/v) for **4-6,a-e** and CHCl₃/CH₃OH (97/3, v/v) for **8a, 8a', 9a** after the concentration of the reaction mixtures.

Physical data of the known compounds had been partly reported in the literatures (see references 23-27 in the original manuscript) and melting points of **2a** and **3a** are not identified with the literatures (see references 23 and 24 in the original manuscript) although the NMR spectra have proved their structures.

6-cyclohexylamino purine (**1a**)

White crystal; mp 210-211°C (lit. 210-211°C).²⁶ ¹H NMR (DMSO-*d*₆) δ 1.131-1.953 (m, 10H, H cyclohexyl), 4.089 (s, 1H, H-1 cyclohexyl), 7.287 (d, 1H, *J* 8.4 Hz, NH), 8.083 (s, 1H, H-2), 8.162 (s, 1H, H-8).

6-phenylamino purine (**1b**)

White crystal; mp 279-282 °C (lit. 278-281°C).²⁷ ¹H NMR (DMSO-*d*₆) δ 7.032 (t, 1H, *J* 7.2Hz, H_{Ar}), 7.334 (t, 2H, *J* 8.0 Hz, H_{Ar}), 7.966 (d, 2H, *J* 8.0 Hz, H_{Ar}), 8.307 (s, 1H, H-2), 8.405 (s, 1H, H-8), 9.796 (s, 1H, NH). ¹³C NMR

(DMSO-*d*₆) δ 118.83 (5-C), 120.96, 122.86, 128.57, 128.86, 129.13, 129.44 (C_{Ar}), 140.24 (8-C), 140.79 (6-C), 151.82 (4-C), 152.17 (2-C).

6-(*p*-tolylamino) purine (**1c**)

White needle crystal; mp 259-260 °C (lit. 242-243°C).²⁶ ¹H NMR (DMSO-*d*₆) δ 2.278 (s, 3H, CH₃), 7.134 (d, 2H, *J* 8.4 Hz, H_{Ar}), 7.820 (d, 2H, *J* 8.4 Hz, H_{Ar}), 8.268 (s, 1H, H-2), 8.359 (s, 1H, H-8), 9.640 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆) δ 20.90 (CH₃), 118.95 (5-C), 121.07, 129.26, 131.77, 137.68 (C_{Ar}), 140.53 (8-C), 148.46 (6-C), 151.95 (4-C), 152.26 (2-C).

6-(*p*-methoxyphenylamino) purine (**1d**)

Colorless needle crystal; mp 279-280 °C. ¹H NMR (DMSO-*d*₆) δ 3.750 (s, 3H, OCH₃), 6.916 (d, 2H, *J* 8.8 Hz, H_{Ar}), 7.806 (d, 2H, *J* 8.8 Hz, H_{Ar}), 8.232 (s, 1H, H-2), 8.307 (s, 1H, H-8), 9.603 (s, 1H, NH), 13.095 (br, 1H, H-9). ¹³C NMR (DMSO-*d*₆) δ 55.65 (OCH₃), 119.66 (5-C), 114.04, 122.92, 133.27 (C_{Ar}), 139.96 (8-C), 150.64 (6-C), 152.37 (4-C), 155.38 (2-C).

6-(*p*-ethoxyphenylamino) purine (**1e**)

White needle crystal; mp 270-272 °C. ¹H NMR (DMSO-*d*₆) δ 1.323 (t, 3H, *J* 6.8 Hz, CH₂CH₃), 4.001 (q, 2H, *J* 7.2 Hz, OCH₂CH₃), 6.899 (d, 2H, *J* 9.2 Hz, H_{Ar}), 7.793 (d, 2H, *J* 9.2 Hz, H_{Ar}), 8.243 (s, 1H, H-2), 8.320 (s, 1H, H-8), 9.578 (s, 1H, NH), 13.090 (br, 1H, H-9). ¹³C NMR (DMSO-*d*₆) δ 15.17 (CH₂CH₃), 63.55 (CH₂CH₃), 119.13 (5-C), 114.62, 122.80, 133.15 (C_{Ar}), 140.20 (8-C), 149.68 (6-C), 152.36 (4-C), 154.63 (2-C).

2-chloro-6-cyclohexylamino purine (**2a**)

White powder; mp 290-294 °C. ¹H NMR (DMSO-*d*₆) δ 1.044-1.884 (m, 10H, H cyclohexyl), 3.978 (s, 1H, H-1 cyclohexyl), 7.885 (d, 1H, NH), 8.204 (s, 1H, H-8).

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2-chloro-6-phenylamino purine (2b**)**

White needle crystal; mp>300 °C. ^1H NMR (DMSO- d_6) δ 7.096 (t, 1H, J 7.6 Hz, H_{Ar}), 7.369 (t, 2H, J 7.6 Hz, H_{Ar}), 7.848 (d, 2H, J 7.6 Hz, H_{Ar}), 8.303 (s, 1H, H-8), 10.126 (s, 1H, NH), 13.313 (bs, 1H, H-9). ^{13}C NMR (DMSO- d_6) δ 118.47 (5-C), 121.16, 123.74, 128.99, 139.37 (C_{Ar}), 141.01 (8-C), 151.68 (6-C), 152.02 (4-C), 152.57 (2-C).

2-chloro-6-(*p*-tolylamino) purine (2c**)**

White powder; mp>300 °C. ^1H NMR (DMSO- d_6) δ 2.294 (s, 3H, CH₃), 7.169 (d, 2H, J 8.0 Hz, H_{Ar}), 7.697 (d, 2H, J 8.0 Hz, H_{Ar}), 8.276 (s, 1H, H-8), 10.081 (s, 1H, NH), 13.272 (br, 1H, H-9). ^{13}C NMR (DMSO- d_6) δ 20.92 (CH₃), 118.86 (5-C), 121.67, 129.40, 132.85, 136.75 (C_{Ar}), 140.84 (8-C), 149.56 (6-C), 151.97 (4-C), 152.66 (2-C).

2-chloro-6-(*p*-methoxyphenylamino) purine (2d**)**

White powder; mp>300 °C. ^1H NMR (DMSO- d_6) δ 3.761 (s, 3H, OCH₃), 6.950 (d, 2H, J 8.8 Hz, H_{Ar}), 7.696 (d, 2H, J 8.8 Hz, H_{Ar}), 8.260 (s, 1H, H-8), 10.021 (s, 1H, NH), 13.224 (br, 1H, H-9). ^{13}C NMR (DMSO- d_6) δ 55.67 (OCH₃), 118.76 (5-C), 114.23, 123.34, 132.23 (C_{Ar}), 140.95 (8-C), 149.43 (6-C), 152.76 (4-C), 156.04 (2-C).

2-amino-6-cyclohexylamino purine (3a**)**

Lustrous white flakes; mp 184-187 °C. ^1H NMR (DMSO- d_6) δ 1.182-1.869 (m, 10H, H cyclohexyl), 4.071 (s, 1H, H-1 cyclohexyl), 5.599 (s, 2H, NH₂), 6.693 (d, 1H, NH), 7.638 (s, 1H, H-8).

2-amino-6-phenylamino purine (3b**)**

White powder; mp 290 °C. ^1H NMR (DMSO- d_6) δ 6.000 (s, 2H, NH₂), 6.966 (t, 1H, J 7.6Hz, H_{Ar}), 7.275 (t, 2H, J 7.6 Hz, H_{Ar}), 7.816 (s, 1H, H-8), 8.015 (d, 2H, J 7.6 Hz, H_{Ar}), 9.254 (s, 1H, NH), 12.274 (bs, 1H, H-9). ^{13}C NMR (DMSO- d_6) δ 113.55 (5-C), 120.43, 122.07, 128.73, 136.89 (C_{Ar}), 140.92 (8-C), 152.38 (6-C), 153.32 (4-C), 160.18 (2-C).

2-amino-6-(*p*-tolylamino) purine (3c**)**

Lustrous flakes; mp 242-245 °C. ^1H NMR (DMSO- d_6) δ 2.262 (s, 3H, CH₃), 5.942 (s, 2H, NH₂), 7.075 (d, 2H, J 8.4 Hz, H_{Ar}), 7.869 (d, 2H, J 8.4 Hz, H_{Ar}), 8.085 (s, 1H, H-8), 9.132 (s, 1H, NH). ^{13}C NMR (DMSO- d_6) δ 20.87 (CH₃), 119.75 (5-C), 120.57, 123.67, 129.13, 130.85,

136.50, 138.37 (C_{Ar}), 141.75 (8-C), 149.48 (6-C), 155.41 (4-C), 160.29 (2-C).

2-amino-6-(*p*-methoxyphenylamino) purine (3d**)**

White powder; mp 290 °C (dec.). ^1H NMR (DMSO- d_6) δ 3.760 (s, 3H, OCH₃), 6.616 (s, 2H, NH₂), 6.922 (d, 2H, J 8.8 Hz, H_{Ar}), 7.846 (d, 2H, J 8.8 Hz, H_{Ar}), 8.043 (s, 1H, H-8), 9.603 (s, 1H, NH). ^{13}C NMR (DMSO- d_6) δ 55.61 (OCH₃), 119.66 (5-C), 114.04, 122.91, 133.27 (C_{Ar}), 139.96 (8-C), 150.64 (6-C), 152.37 (4-C), 155.38 (2-C).

2-amino-6-(*p*-ethoxyphenylamino) purine (3e**)**

White powder; mp 133-135 °C. ^1H NMR (DMSO- d_6) δ 1.317 (t, 3H, J 6.8 Hz, CH₂CH₃), 3.990 (q, 2H, J 6.8 Hz, OCH₂CH₃), 6.022 (s, 2H, NH₂), 6.845 (d, 2H, J 8.8 Hz, H_{Ar}), 7.653 (d, 2H, J 8.8 Hz, H_{Ar}), 8.093 (s, 1H, H-8), 9.226 (s, 1H, NH), 12.848 (br, 1H, H-9). ^{13}C NMR (DMSO- d_6) δ 15.19 (CH₂CH₃), 63.53 (CH₂CH₃), 119.16 (5-C), 114.56, 122.24, 123.67, 133.75, 136.92 (C_{Ar}), 141.77 (8-C), 149.48 (6-C), 152.77 (4-C), 154.21 (2-C).

9-β-cyanoethyl-6-cyclohexylamino purine (4a**)**

White needle crystal; mp 137-139 °C. ^1H NMR (DMSO- d_6) δ 1.112-1.881 (m, 10H, H cyclohexyl), 3.168 (t, 2H, J 6.4 Hz, CH₂CH₂CN), 4.101 (br, 1H, H cyclohexyl), 4.447 (t, 2H, J 6.4 Hz, NCH₂CH₂), 7.554 (d, 1H, J 8.0 Hz, NH), 8.187 (s, 1H, H-2), 8.219 (s, 1H, H-8). ^{13}C NMR (DMSO- d_6) δ 18.56 (CH₂CN), 39.26 (NCH₂CH₂), 24.80, 25.56, 26.25, 32.78, 33.35, 49.11 (C cyclohexyl), 118.72 (CN), 119.33 (5-C), 140.59 (8-C), 149.18 (6-C), 153.03 (4-C), 154.30 (2-C). MS (ESI) m/z [M⁺Na⁺-1 307.8], 270.8, 254.8, 228.8, 203.7, 150.8. IR (KBr) ν_{max} /cm⁻¹: 3398, 3385, 3084, 3036, 2933, 2854, 2250, 1607, 1586, 1475, 1366, 1299, 772. Anal. Calc. for C₁₄H₁₈N₆: C, 62.22; H, 6.67; N, 31.11. Found: C, 61.97; H, 6.73; N, 31.34%.

9-β-cyanoethyl-6-phenylamino purine (4b**)**

Lustrous flakes; mp 168-170 °C. ^1H NMR (DMSO- d_6) δ 3.229 (t, 2H, J 6.4 Hz, CH₂CH₂CN), 4.538 (t, 2H, J 6.4 Hz, NCH₂CH₂), 7.049 (t, 1H, J 6.4 Hz, H_{Ar}), 7.340 (t, 2H, J 6.0 Hz, H_{Ar}), 7.972 (d, 2H, J 8.8 Hz, H_{Ar}), 8.390 (s, 1H, H-2), 8.445 (s, 1H, H-8), 9.917 (s, 1H, NH). ^{13}C NMR (DMSO- d_6) δ 18.63 (CH₂CN), 39.46 (NCH₂CH₂), 118.71 (CN), 120.20 (C-5), 121.33, 123.10, 128.82, 140.06 (C_{Ar}), 141.94 (C-8), 149.75 (C-6), 150.04 (C-4), 152.53 (C-2). MS (ESI) m/z [M⁺Na⁺-1 286.7], 233.8. IR (KBr) ν_{max} /cm⁻¹: 3352, 3087, 3050, 2967, 2261, 1622, 1580, 1476, 1300,

1239, 1148, 1018, 753. Anal. Calc. for $C_{14}H_{12}N_6$: C, 63.64; H, 4.54; N, 31.82. Found: C, 63.51; H, 4.59; N, 31.93%.

*9-β-cyanoethyl-6-(*p*-tolylamino) purine (4c)*

Broken-white powder; mp 173-174 °C. 1H NMR (DMSO- d_6) δ 2.284 (s, 3H, CH_3), 3.218 (t, 2H, J 6.4 Hz, CH_2CH_2CN), 4.521 (t, 2H, J 6.4 Hz, NCH_2CH_2), 7.141 (d, 2H, J 8.4 Hz, H_{Ar}), 7.816 (d, 2H, J 8.4 Hz, H_{Ar}), 8.364 (s, 1H, H-2), 8.403 (s, 1H, H-8), 9.811 (s, 1H, NH). ^{13}C NMR (DMSO- d_6) δ 18.60 (CH_2CN), 20.91 (CH_3), 39.42 (NCH_2CH_2), 118.71 (CN), 120.07 (C-5), 121.42, 129.23, 132.06, 137.46 (C_{Ar}), 141.78 (C-8), 149.93 (C-6), 151.23 (C-4), 152.56 (C-2). MS (ESI) m/z [M $^+Na^+$ -1 300.7], 145.9. IR (KBr) ν_{max} /cm $^{-1}$: 3386, 3089, 2919, 2860, 2249, 1616, 1585, 1476, 1367, 821. Anal. Calc. for $C_{15}H_{14}N_6$: C, 64.75; H, 5.04; N, 30.22. Found: C, 64.49; H, 5.21; N, 30.35%.

*9-β-cyanoethyl-6-(*p*-methoxyphenylamino) purine (4d)*

Colorless column crystal; mp 80-82 °C. 1H NMR (DMSO- d_6) δ 3.216 (t, 2H, J 6.4 Hz, CH_2CH_2CN), 3.750 (s, 3H, OCH_3), 4.517 (t, 2H, J 6.4 Hz, NCH_2CH_2), 6.924 (d, 2H, J 8.8 Hz, H_{Ar}), 7.794 (d, 2H, J 9.2 Hz, H_{Ar}), 8.344 (s, 1H, H-2), 8.370 (s, 1H, H-8), 9.765 (s, 1H, NH). ^{13}C NMR (DMSO- d_6) δ 18.62 (CH_2CN), 39.41 (NCH_2CH_2), 55.64 (OCH_3), 118.72 (CN), 119.91 (C-5), 114.06, 123.23, 132.95, 152.63 (C_{Ar}), 141.61 (C-8), 149.82 (C-6), 152.67 (C-4), 155.61 (C-2). MS (ESI) m/z [M $^+Na^+$ -1 316.7], 263.7. IR (KBr) ν_{max} /cm $^{-1}$: 3466, 3301, 3204, 3101, 2978, 2881, 2253, 1620, 1587, 1512, 1471, 1294, 1035, 797. Anal. Calc. for $C_{15}H_{14}N_6O$: C, 61.22; H, 4.76; N, 28.57. Found: C, 61.09; H, 4.84; N, 28.64%.

*9-β-cyanoethyl-6-(*p*-ethoxyphenylamino) purine (4e)*

Gray flakes; mp 146-148 °C. 1H NMR (DMSO- d_6) δ 1.328 (t, 3H, J 7.2 Hz, CH_2CH_3), 3.215 (t, 2H, J 6.4 Hz, CH_2CH_2CN), 4.009 (q, 2H, J 7.2 Hz, OCH_2CH_3), 4.513 (t, 2H, J 6.4 Hz, NCH_2CH_2), 6.907 (d, 2H, J 9.2 Hz, H_{Ar}), 7.783 (d, 2H, J 8.8 Hz, H_{Ar}), 8.343 (s, 1H, H-2), 8.365 (s, 1H, H-8), 9.758 (s, 1H, NH). ^{13}C NMR (DMSO- d_6) δ 15.16 (OCH_2CH_3), 18.60 (CH_2CN), 39.42 (NCH_2CH_2), 118.72 (CN), 119.90 (C-5), 114.60, 123.15, 132.88, 152.62 (C_{Ar}), 141.61 (C-8), 149.81 (C-6), 154.84 (C-4), 158.64 (C-2). MS (ESI) m/z [M $^+Na^+$ -1 330.8], 308.8. IR (KBr) ν_{max} /cm $^{-1}$: 3309, 3231, 3107, 2979, 1930, 2881, 2252, 1618, 1587, 1512, 1479, 1299, 1048, 840. Anal. Calc. for $C_{16}H_{16}N_6O$: C, 62.34; H, 5.19; N, 27.27. Found: C, 62.11; H, 5.31; N, 27.46%.

2-chloro-9-β-cyanoethyl-6-cyclohexylamino purine (5a)

White powder; mp 179-181 °C. 1H NMR (DMSO- d_6) δ 1.107-1.923 (m, 10H, H cyclohexyl), 3.135 (t, 2H, J 6.4Hz, CH_2CH_2CN), 4.005 (br, 1H, H cyclohexyl), 4.411 (t, 2H, J 6.4 Hz, NCH_2CH_2), 8.163 (d, 1H, J 8.0 Hz, NH), 8.199 (s, 1H, H-8). ^{13}C NMR (DMSO- d_6) δ 18.62 (CH_2CN), 25.13, 25.36, 25.56, 32.47, 33.48, 49.45 (C cyclohexyl), 38.76 (NCH_2CH_2), 118.38 (C-5), 118.65 (CN), 141.15 (C-8), 150.13 (C-6), 153.79 (C-4), 154.66 (C-2). MS (ESI) m/z [M $^+Na^+$ -1, 286.7], 233.8. Anal. Calc. for $C_{14}H_{17}ClN_6$: C, 55.17; H, 5.62; N, 27.57. Found: C, 54.97; H, 5.69; N, 27.73%.

2-chloro-9-β-cyanoethyl-6-phenylamino purine (5b)

White powder; mp 266-268 °C. 1H NMR (DMSO- d_6) δ 3.187 (t, 2H, J 6.4 Hz, CH_2CH_2CN), 4.492 (t, 2H, J 6.4 Hz, NCH_2CH_2), 7.113 (t, 1H, J 7.2 Hz, H_{Ar}), 7.374 (t, 2H, J 7.6 Hz, H_{Ar}), 7.845 (d, 2H, J 8.0 Hz, H_{Ar}), 8.388 (s, 1H, H-8), 10.348 (s, 1H, NH). ^{13}C NMR (DMSO- d_6) δ 18.64 (CH_2CN), 39.94 (NCH_2CH_2), 118.65 (CN), 119.20 (C-5), 121.81, 124.03, 128.97, 139.14 (C_{Ar}), 142.49 (C-8), 149.32 (C-6), 151.15 (C-4), 152.91 (C-2). MS (ESI) m/z [M $^+Na^+$ -1, 320.7], 298.8, 256.9, 101.9, 88.0. IR (KBr) ν_{max} /cm $^{-1}$: 3346, 3087, 3062, 2973, 2935, 2258, 1622, 1578, 1500, 1452, 1318, 1284, 756. Anal. Calc. for $C_{14}H_{11}ClN_6$: C, 56.28; H, 3.69; N, 28.14. Found: C, 55.97; H, 3.81; N, 28.36%.

*2-chloro-9-β-cyanoethyl-6-(*p*-tolylamino) purine (5c)*

Lustrous needle crystal; mp 254-256 °C. 1H NMR (DMSO- d_6) δ 2.297 (s, 3H, CH_3), 3.180 (t, 2H, J 6.4Hz, CH_2CH_2CN), 4.480 (t, 2H, J 6.4 Hz, NCH_2CH_2), 7.174 (d, 2H, J 8.0 Hz, H_{Ar}), 7.690 (d, 2H, J 8.4 Hz, H_{Ar}), 8.363 (s, 1H, H-8), 10.256 (s, 1H, NH). ^{13}C NMR (DMSO- d_6) δ 18.63 (CH_2CN), 20.94 (CH_3), 39.99 (NCH_2CH_2), 118.65 (CN), 119.08 (C-5), 121.99, 129.39, 133.18, 136.51 (C_{Ar}), 142.32 (C-8), 149.54 (C-6), 151.04 (C-4), 152.98 (C-2). MS (ESI) m/z [M $^+Na^+$ -1, 334.7], 271.9, 227.9, 145.8, 96.9. IR (KBr) ν_{max} /cm $^{-1}$: 3339, 3055, 2930, 2264, 1623, 1579, 1514, 1456, 1252, 818. Anal. Calc. for $C_{15}H_{13}ClN_6$: C, 57.60; H, 4.16; N, 26.88. Found: C, 57.51; H, 4.22; N, 26.93%.

*2-chloro-9-β-cyanoethyl-6-(*p*-methoxyphenylamino) purine (5d)*

Lustrous flakes; mp 239-240 °C. 1H NMR (DMSO- d_6) δ 3.178 (t, 2H, J 6.4 Hz, CH_2CH_2CN), 3.764 (s, 3H, OCH_3), 4.476 (t, 2H, J 6.4 Hz, NCH_2CH_2), 6.954 (d, 2H,

J 8.8 Hz, H_{Ar}), 7.691 (d, 2H, *J* 8.8 Hz, H_{Ar}), 8.343 (s, 1H, H-8), 10.205 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆) δ 18.65 (CH₂CN), 39.49 (NCH₂CH₂), 55.68 (OCH₃), 118.65 (CN), 118.94 (C-5), 114.20, 123.71, 131.96, 150.91 (C_{Ar}), 142.15 (C-8), 153.06 (C-6), 153.12 (C-4), 156.23 (C-2). MS (ESI) *m/z* [M⁺Na⁺-1, 350.7], 328.8, 292.8, 239.8, 224.7, 196.7. IR (KBr) ν_{max} /cm⁻¹: 3337, 3063, 2962, 2935, 2835, 2258, 1624, 1589, 1512, 1478, 1309, 1248, 1048, 827. Anal. Calc. for C₁₅H₁₅CIN₆O: C, 54.79; H, 3.96; N, 25.57. Found: C, 54.66; H, 4.03; N, 25.64%.

2-amino-9-β-cyanoethyl-6-cyclohexylamino purine (**6a**)

White powder; mp 135-136 °C. ¹H NMR (DMSO-*d*₆) δ 1.085-1.861 (m, 10H, H cyclohexyl), 3.088 (t, 2H, *J* 6.4 Hz, CH₂CH₂CN), 4.060 (br, 1H, H cyclohexyl), 4.243 (t, 2H, *J* 6.4 Hz, NCH₂CH₂), 5.846 (s, 2H, NH₂), 6.914 (s, 1H, NH), 7.742 (s, 1H, H-8). ¹³C NMR (DMSO-*d*₆) δ 18.34 (CH₂CN), 25.51, 25.69, 33.13, 48.54 (C cyclohexyl), 38.76 (NCH₂CH₂), 113.48 (C-5), 118.85 (CN), 137.04 (C-8), 152.31 (C-6), 154.63 (C-4), 160.76 (C-2). MS (ESI) *m/z* [M⁺Na⁺-1, 307.8], 285.9, 254.8, 203.7, 150.8. IR (KBr) ν_{max} /cm⁻¹: 3331, 3218, 3103, 2929, 2854, 2246, 1637, 1602, 1486, 1399, 791. Anal. Calc. for C₁₄H₁₉N₇: C, 58.95; H, 6.67; N, 34.39. Found: C, 58.82; H, 6.79; N, 34.45%.

2-amino-9-β-cyanoethyl-6-phenylamino purine (**6b**)

Colorless flake crystal; mp 246-247 °C. ¹H NMR (DMSO-*d*₆) δ 3.141 (t, 2H, *J* 6.4 Hz, CH₂CH₂CN), 4.313 (t, 2H, *J* 6.4 Hz, NCH₂CH₂), 6.204 (s, 2H, NH₂), 6.981 (t, 1H, *J* 7.2 Hz, H_{Ar}), 7.280 (t, 2H, *J* 8.0 Hz, H_{Ar}), 7.910 (s, 1H, H-8), 8.017 (d, 2H, *J* 8.0 Hz, H_{Ar}), 9.380 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆) δ 18.36 (CH₂CN), 38.87 (NCH₂CH₂), 118.83 (CN), 120.65 (C-5), 114.17, 122.25, 128.71, 138.13 (C_{Ar}), 140.77 (C-8), 152.18 (C-6), 152.82 (C-4), 160.44 (C-2). MS (ESI) *m/z* [M⁺Na⁺-1, 301.6], 248.7. IR (KBr) ν_{max} /cm⁻¹: 3445, 3391, 3329, 3202, 3099, 2984, 2935, 2252, 1645, 1617, 1579, 1498, 1439, 787. Anal. Calc. for C₁₄H₁₃N₇: C, 60.22; H, 4.66; N, 35.13. Found: C, 60.13; H, 4.73; N, 35.19%.

2-amino-9-β-cyanoethyl-6-(*p*-tolylamino) purine (**6c**)

White needle crystal; mp 208-209 °C. ¹H NMR (DMSO-*d*₆) δ 2.269 (s, 3H, CH₃), 3.134 (t, 2H, *J* 6.4 Hz, CH₂CH₂CN), 4.305 (t, 2H, *J* 6.4 Hz, NCH₂CH₂), 6.153 (s, 2H, NH₂), 7.083 (d, 2H, *J* 8.4 Hz, H_{Ar}), 7.864 (d, 2H, *J* 8.4 Hz, H_{Ar}), 7.889 (s, 1H, H-8), 9.271 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆) δ 18.36 (CH₂CN), 20.89 (CH₃), 38.86 (NCH₂CH₂), 118.83 (CN), 120.82 (C-5), 114.10, 129.14, 131.13, 137.98 (C_{Ar}), 138.17 (C-8), 152.06 (C-6), 152.87 (C-4), 160.46 (C-2). MS (ESI)

m/z [M⁺Na⁺-1, 315.8], 293.8, 245.9, 228.8, 198.7, 156.8, 144.7, 117.9, 82.0, 65.1. IR (KBr) ν_{max} /cm⁻¹: 3457, 3337, 3104, 2944, 2855, 2252, 1627, 1597, 1513, 1482, 1417, 825, 788. Anal. Calc. for C₁₅H₁₅N₇: C, 61.43; H, 5.12; N, 33.45. Found: C, 61.36; H, 5.17; N, 33.48%.

2-amino-9-β-cyanoethyl-6-(*p*-methoxyphenylamino) purine (**6d**)

Colorless needle crystal; mp 174-176 °C. ¹H NMR (DMSO-*d*₆) δ 3.133 (t, 2H, *J* 6.4 Hz, CH₂CH₂CN), 3.738 (s, 3H, OCH₃), 4.303 (t, 2H, *J* 6.4 Hz, NCH₂CH₂), 6.116 (s, 2H, NH₂), 6.863 (d, 2H, *J* 8.8 Hz, H_{Ar}), 7.856 (d, 2H, *J* 8.8 Hz, H_{Ar}), 7.877 (s, 1H, H-8), 9.249 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆) δ 18.37 (CH₂CN), 38.86 (NCH₂CH₂), 55.61 (OCH₃), 118.84 (CN), 120.15 (C-5), 113.95, 122.46, 133.82, 137.86, 152.92 (C_{Ar}), 141.59 (C-8), 151.96 (C-6), 154.98 (C-4), 160.50 (C-2). MS (ESI) *m/z* [M⁺Na⁺-1, 331.7], 309.8, 292.8, 267.8, 252.7, 224.7, 214.7, 199.7, 160.8, 92.4. IR (KBr) ν_{max} /cm⁻¹: 3483, 3327, 3203, 3008, 2946, 2848, 2250, 1596, 1514, 1486, 1243, 1031, 786. Anal. Calc. for C₁₅H₁₅N₇O: C, 58.25; H, 4.85; N, 31.72. Found: C, 58.16; H, 4.78; N, 31.91%.

2-amino-9-β-cyanoethyl-6-(*p*-ethoxyphenylamino) purine (**6e**)

White needle crystal; mp 177-178 °C. ¹H NMR (DMSO-*d*₆) δ 1.324 (t, 3H, *J* 6.8 Hz, OCH₂CH₃), 3.131 (t, 2H, *J* 6.4 Hz, CH₂CH₂CN), 3.998 (q, 2H, *J* 6.8 Hz, OCH₂CH₃), 4.301 (t, 2H, *J* 6.4 Hz, NCH₂CH₂), 6.114 (s, 2H, NH₂), 6.846 (d, 2H, *J* 8.8 Hz, H_{Ar}), 7.851 (d, 2H, *J* 9.2 Hz, H_{Ar}), 7.876 (s, 1H, H-8), 9.243 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆) δ 15.20 (OCH₂CH₃), 18.60 (CH₂CN), 38.86 (NCH₂CH₂), 63.52 (OCH₂CH₃), 118.84 (CN), 120.15 (C-5), 113.97, 114.52, 122.41, 133.73, 137.85, 152.89 (C_{Ar}), 141.59 (C-8), 151.93 (C-6), 154.23 (C-4), 160.47 (C-2). MS (ESI) *m/z* [M⁺Na⁺-1, 323.8], 281.8, 253.7, 224.7, 200.7, 146.8, 119.8, 80.9. IR (KBr) ν_{max} /cm⁻¹: 3487, 3322, 3195, 2975, 2930, 2884, 2248, 1599, 1512, 1456, 1418, 1235, 1053, 832, 786. Anal. Calc. for C₁₆H₁₇N₇O: C, 59.44; H, 5.26; N, 30.34. Found: C, 59.35; H, 5.29; N, 30.42%.

6-cyclohexylamino-9-(²-D-ribofuranosyl) purine (**7a**)

White flake crystal; mp 187-188 °C (lit. 187-188 °C).^{7c} ¹H NMR (DMSO-*d*₆) δ 1.119-1.873 (m, 10H, H cyclohexyl), 3.529-3.586, 3.685 (m, 2H, H-5'), 3.971 (m, 1H, H-4'), 4.096 (s, 1H, H-1' cyclohexyl), 4.150 (m, 1H, H-3'), 4.612 (m, 1H, H-2'), 5.881 (d, 1H, *J* 6.4 Hz, H-1'), 7.628 (d, 1H, *J* 8.0 Hz, NH), 8.191 (s, 1H, H-2), 8.339 (s, 1H, H-8).

6-phenylamino-9-(β -D-ribofuranosyl) purine (7b**)**

White powder; mp 195-196 °C (lit. 195-196 °C).²⁷ ¹H NMR (DMSO-*d*₆) δ 3.606 (m, 2H, H-5'), 3.990 (m, 1H, H-4'), 4.192 (m, 1H, H-3'), 4.651 (m, 1H, H-2'), 5.970 (d, 1H, *J* 6.0 Hz, H-1'), 7.050 (t, 1H, *J* 4.0 Hz, H_{Ar}), 7.341 (t, 2H, *J* 4.0 Hz, H_{Ar}), 7.947 (d, 2H, *J* 4.0 Hz, H_{Ar}), 8.407 (s, 1H, H-2), 8.551 (s, 1H, H-8), 9.942 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆) δ 60.21 (5'-C), 70.99 (3'-C), 74.05 (2'-C), 86.30 (4'-C), 88.31 (1'-C), 117.19 (5-C), 120.81, 121.36, 123.17, 128.83, 129.32, 139.98 (C_{Ar}), 141.13 (8-C), 149.79 (6-C), 152.36 (4-C), 152.62 (2-C).

9-(β -D-ribofuranosyl)-6-(*p*-tolylamino)purine (7c**)**

Buff needle crystal; mp 214-215 °C (lit. 214-216 °C).^{7a} ¹H NMR (DMSO-*d*₆) δ 2.286 (s, 3H, CH₃), 3.645 (dd, 2H, *J* 12 Hz, H-5'), 3.990 (q, 1H, *J* 3.2 Hz, H-4'), 4.181 (d, 1H, *J* 3.2 Hz, H-3'), 4.646 (q, 1H, *J* 6.4 Hz, H-2'), 5.959 (d, 1H, *J* 7.0 Hz, H-1'), 7.143 (d, 2H, *J* 8.4 Hz, H_{Ar}), 7.808 (d, 2H, *J* 8.4 Hz, H_{Ar}), 8.378 (s, 1H, H-2), 8.525 (s, 1H, H-8), 9.845 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆) δ 20.92 (CH₃), 62.02 (5-C), 71.00 (3'-C), 74.04 (2'-C), 86.30 (4'-C), 88.32 (1'-C), 117.40 (5-C), 120.71, 121.48, 129.24, 132.16, 137.38 (C_{Ar}), 140.98 (8-C), 149.67 (6-C), 152.40 (4-C), 152.68 (2-C)

6-(*p*-methoxyphenylamino)-9-(β -D-ribofuranosyl) purine (7d**)**

Broken-white needle crystal; mp 206-208 °C (lit. 207-208 °C).^{7a} ¹H NMR (DMSO-*d*₆) δ 3.650 (m, 2H, H-5'), 3.753 (s, 3H, OCH₃), 3.992 (dd, 1H, *J* 3.2 and 3.6 Hz, H-4'), 4.181 (dd, 1H, *J* 3.2 and 4.8 Hz, H-3'), 4.646 (dd, 1H, *J* 4.8 and 6.0 Hz, H-2'), 5.952 (d, 1H, *J* 6.0 Hz, H-1'), 6.925 (m, 2H, H_{Ar}), 7.786 (m, 2H, H_{Ar}), 8.340 (s, 1H, H-2), 8.504 (s, 1H, H-8), 9.800 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆) δ 55.66 (OCH₃), 62.04 (5'-C), 71.02 (3'-C), 74.03 (2'-C), 86.31 (4'-C), 88.34 (1'-C), 117.42 (5-C), 114.07, 120.56, 123.26, 132.88, 149.55 (C_{Ar}), 140.86 (8-C), 152.45 (6-C), 152.77 (4-C), 155.65 (2-C).

6-(*p*-ethoxyphenylamino)-9-(β -D-ribofuranosyl) purine (7e**)**

White powder; mp 191-192 °C. ¹H NMR (DMSO-*d*₆) δ 1.330 (t, 3H, *J* 7.2 Hz, CH₂CH₃), 3.650 (dd, 2H, *J* 12 Hz, H-5'), 3.898 (m, 1H, H-4'), 4.012 (q, 2H, *J* 7.2 Hz, OCH₂CH₃), 4.183 (m, 1H, H-3'), 4.648 (m, 1H, H-2'), 5.953 (d, 1H, *J* 7.0 Hz, H-1'), 6.908 (d, 2H, *J* 8.8 Hz, H_{Ar}), 7.777 (d, 2H, *J* 8.8 Hz, H_{Ar}), 8.341 (s, 1H, H-2), 8.504 (s, 1H, H-8), 9.792 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆) δ 15.16 (CH₂CH₃), 62.05 (5'-C), 63.57 (CH₂CH₃), 71.03

(3'-C), 74.03 (2'-C), 86.32 (4'-C), 88.35 (1'-C), 117.41 (5-C), 114.61, 115.77, 120.56, 123.21, 132.78, 149.53 (C_{Ar}), 140.85 (8-C), 152.45 (6-C), 152.75 (4-C), 154.89 (2-C). MS (ESI) *m/z*+Na⁺-1 409.7, 387.8, 362.0, 318.0, 274.0, 255.8, 227.7, 199.8, 171.7, 134.8, 119.9, 108.9. IR (KBr) ν_{max} /cm⁻¹: 3338, 3223, 3151, 2983, 2930, 2871, 1645, 1596, 1512, 1478, 1240, 1058, 826, 791. Anal. Calc. for C₁₈H₂₁N₅O₅: C, 55.81; H, 5.43; N, 18.09. Found: C, 55.72; H, 5.51; N, 18.13%.

2-chloro-6-cyclohexylamino-9-(β -D-ribofuranosyl) purine (8a**)**

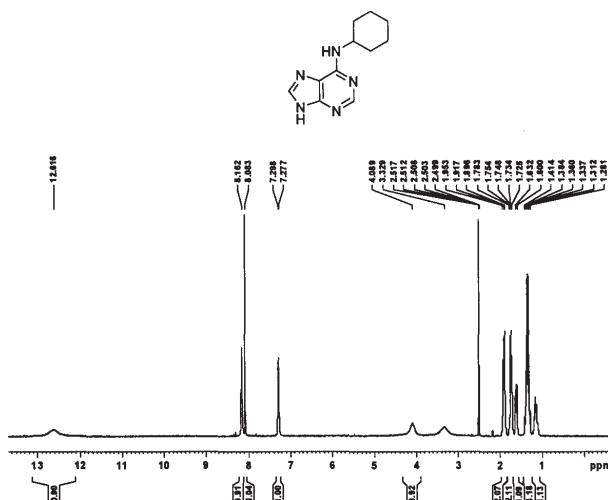
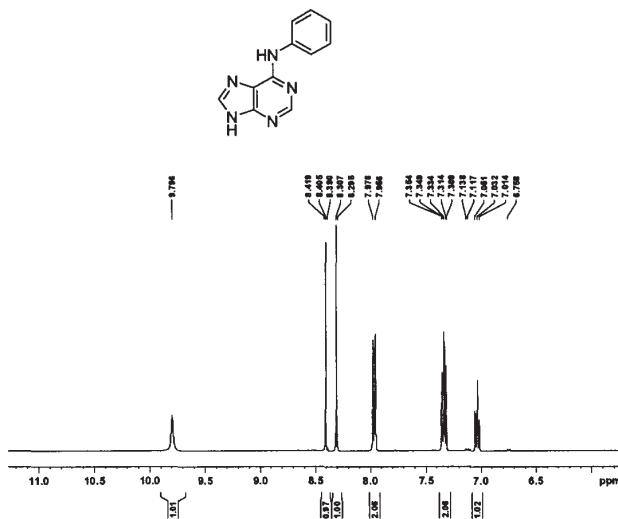
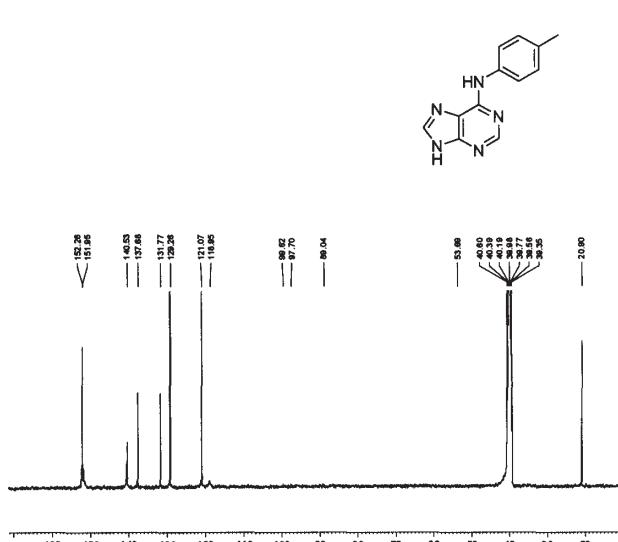
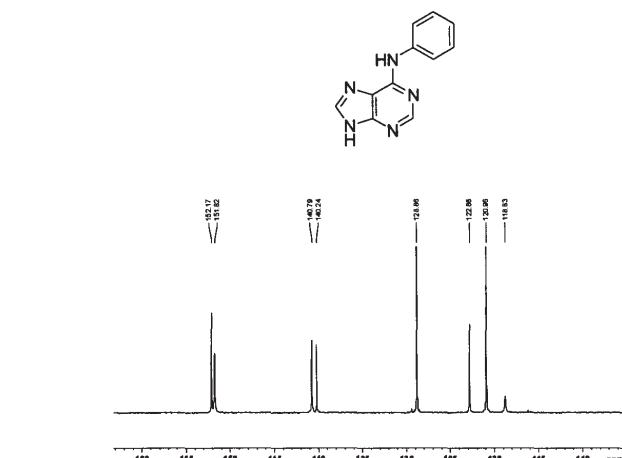
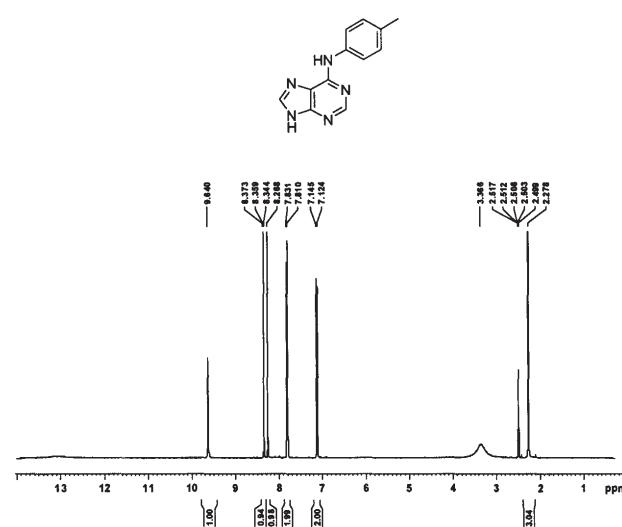
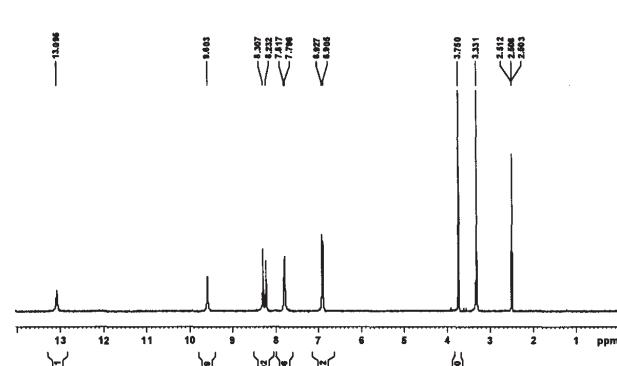
White powder; mp 108-111 °C (lit. 108-111 °C).⁶ ¹H NMR (DMSO-*d*₆) δ 1.112-1.916 (m, 10H, H cyclohexyl), 3.609 (m, 2H, H-5'), 3.946 (m, 1H, H-4'), 4.007 (s, 1H, H-1 cyclohexyl), 4.129 (m, 1H, H-3'), 4.510 (m, 1H, H-2'), 5.822 (d, 1H, *J* 6.4 Hz, H-1'), 8.193 (d, 1H, *J* 8.8 Hz, NH), 8.377 (s, 1H, H-8).

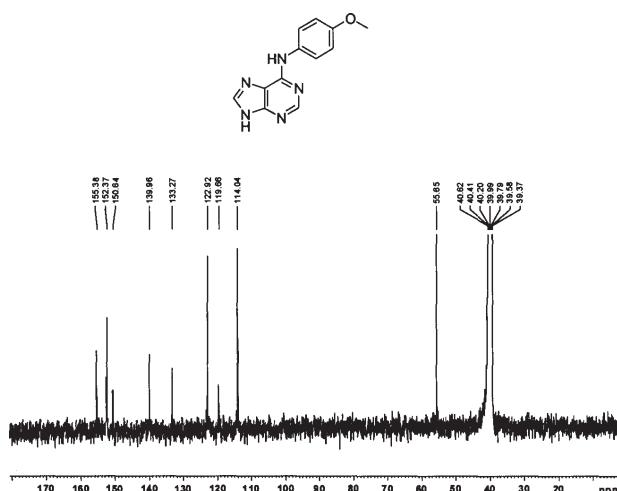
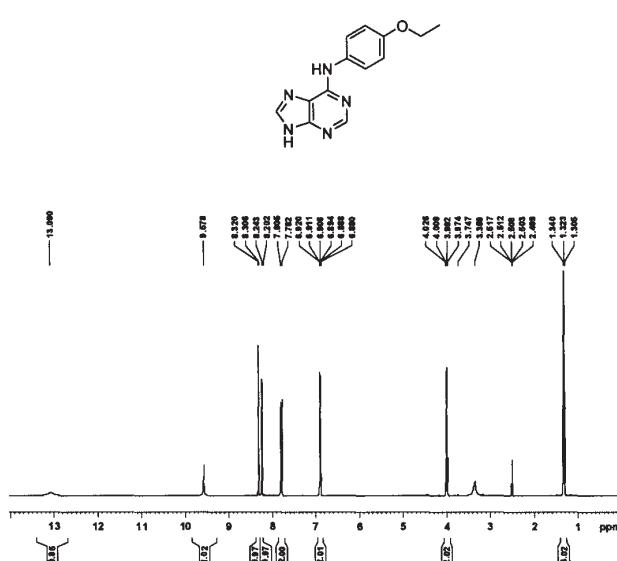
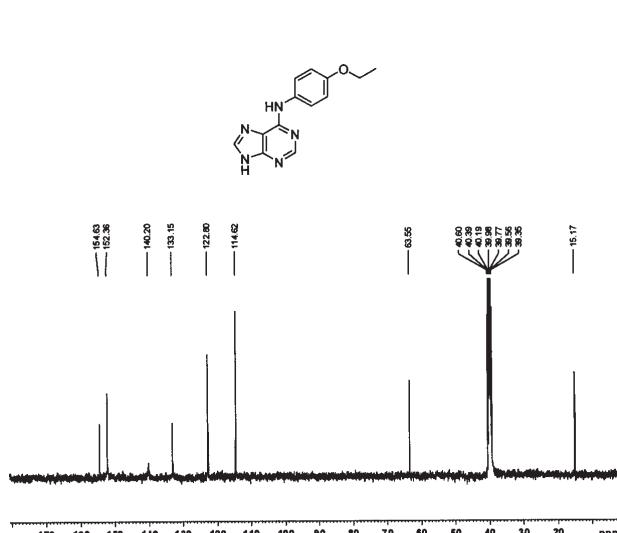
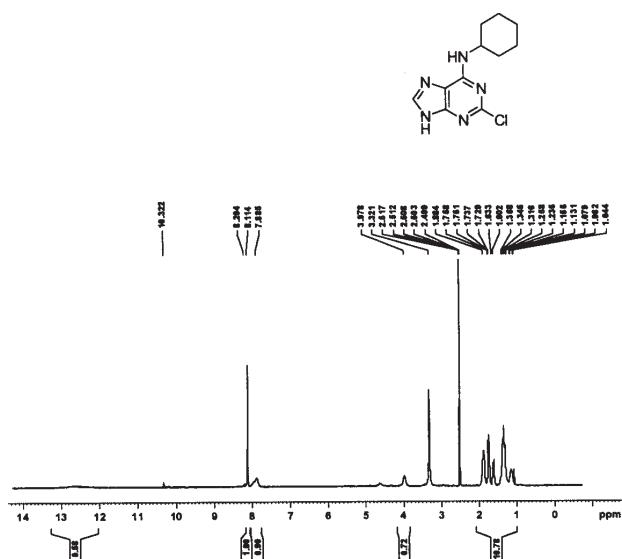
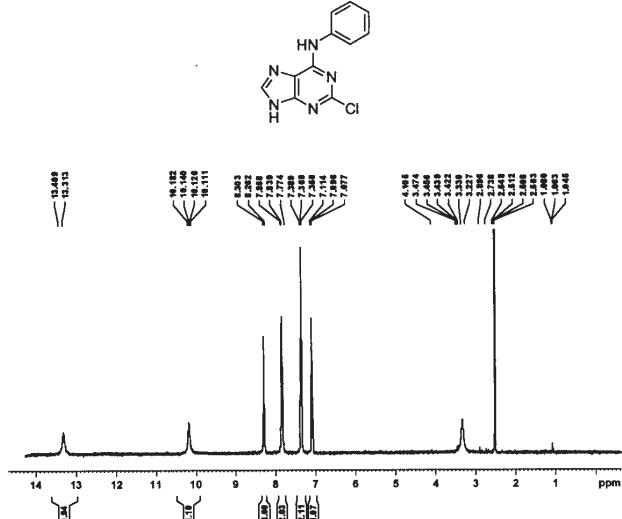
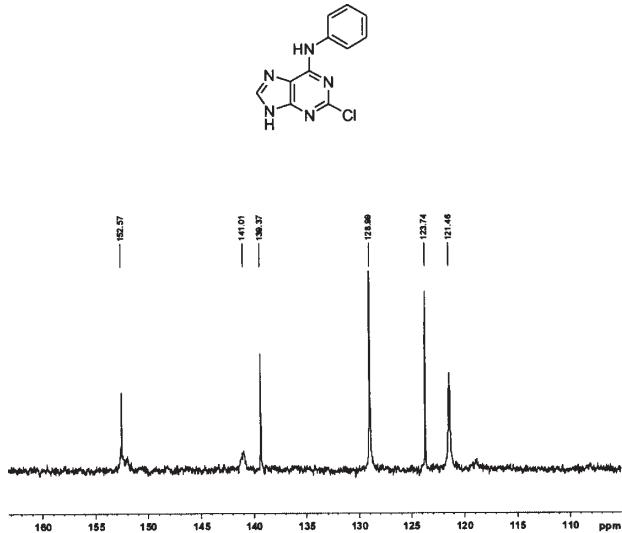
2-chloro-6-cyclohexylamino-9-(β -D-2,3,5-O-triacetyl-ribofuranosyl) purine (8a'**)**

White needle crystal; mp 186-188 °C. ¹H NMR (DMSO-*d*₆) δ 1.089-1.830 (m, 10H, H cyclohexyl), 1.864 (s, 3H, COCH₃), 1.925 (s, 3H, COCH₃), 2.028 (s, 3H, COCH₃), 3.995 (s, 1H, H-1 cyclohexyl), 4.084 (m, 2H, H-5'), 4.183 (m, 1H, H-4'), 4.307 (m, 1H, H-3'), 4.575 (m, 1H, H-2'), 5.847 (d, 1H, *J* 4.8 Hz, H-1'), 8.198 (d, 1H, *J* 8.4 Hz, NH), 8.338 (s, 1H, H-8). ¹³C NMR (DMSO-*d*₆) δ 21.02 (COCH₃), 23.19 (COCH₃), 25.04, 25.36, 25.56, 25.69, 32.96, 33.44 (C cyclohexyl), 64.23 (5'-C), 70.64 (3'-C), 73.43 (2'-C), 82.12 (4'-C), 88.11 (1'-C), 118.85 (5-C), 140.10 (8-C), 149.96 (6-C), 153.84 (4-C), 154.68 (2-C), 168.42 (COCH₃), 170.59 (COCH₃).

2-chloro-6-cyclohexylamino-9-[(2-hydroxylethoxy)methyl]purine (9a**)**

White powder; mp 165-167 °C. ¹H NMR (DMSO-*d*₆) δ 1.107-1.922 (m, 10H, H cyclohexyl), 3.493 (m, 4H, HOCH₂CH₂O), 4.004 (br, 1H, H cyclohexyl), 5.518 (s, 2H, NCH₂O), 8.154 (d, 1H, *J* 7.2 Hz, NH), 8.283 (s, 1H, H-8). ¹³C NMR (DMSO-*d*₆) δ 33.48, 32.47, 25.56, 25.35 (C cyclohexyl), 49.47 (NCH), 60.34 (HOCH₂CH₂O), 71.23 (HOCH₂CH₂O), 72.92 (NCH₂O), 118.33 (5-C), 141.77 (8-C), 150.41 (6-C), 154.08 (4-C), 154.70 (2-C). MS (ESI) *m/z* [M⁺Na⁺-1, 347.7], 325.8, 311.6, 284.0, 228.8, 101.9. IR (KBr) ν_{max} /cm⁻¹: 3441, 3236, 2937, 2923, 2857, 1621, 1310, 1216. Anal. Calc. for C₁₄H₂₀ClN₅O₂: C, 51.61; H, 6.14; N, 21.51. Found: C, 51.47; H, 6.18; N, 21.63%.

Figure S1. ^1H NMR of 1a.Figure S2. ^1H NMR of 1b.Figure S5. ^{13}C NMR of 1c.Figure S3. ^{13}C NMR of 1b.Figure S4. ^1H NMR of 1c.Figure S6. ^1H NMR of 1d.

**Figure S7.** ^{13}C NMR of **1d**.**Figure S8.** ^1H NMR of **1e**.**Figure S9.** ^{13}C NMR of **1e**.**Figure S10.** ^1H NMR of **2a**.**Figure S11.** ^1H NMR of **2b**.**Figure S12.** ^{13}C NMR of **2b**.

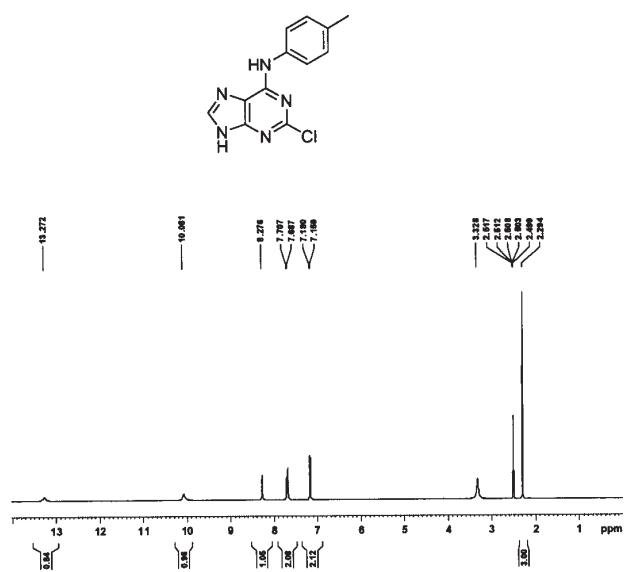


Figure S13. ¹H NMR of 2c.

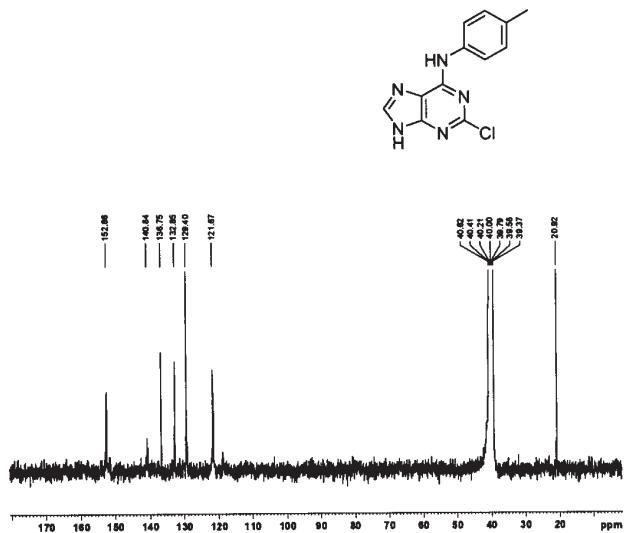


Figure S14. ¹³C NMR of 2c.

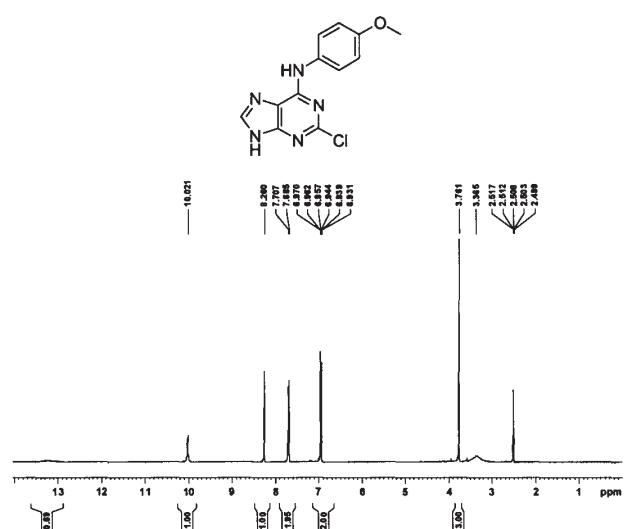


Figure S15. ¹H NMR of 2d.

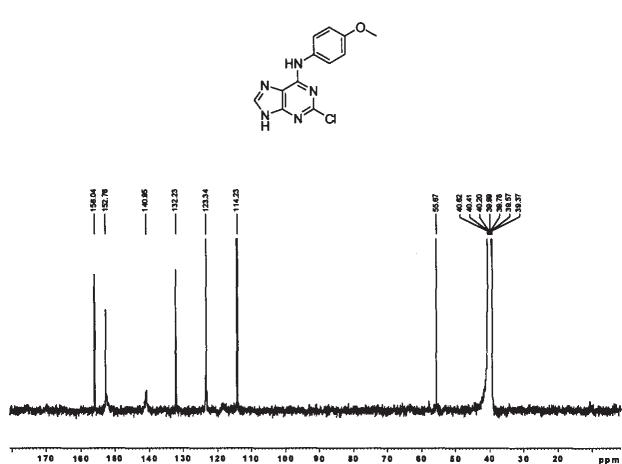


Figure S16. ¹³C NMR of 2d.

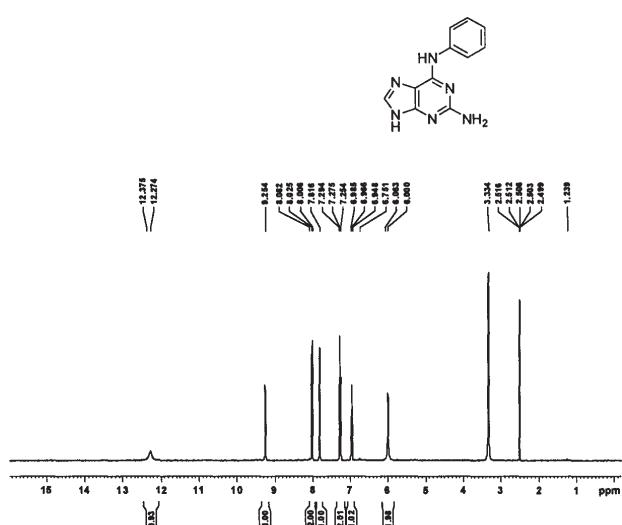


Figure S17. ¹H NMR of 3b.

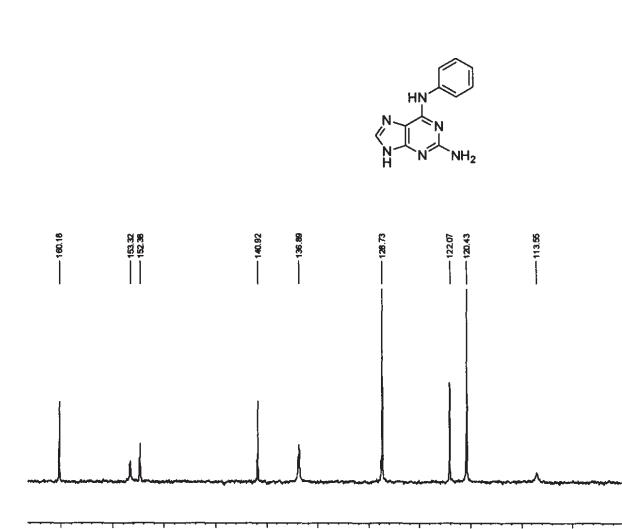
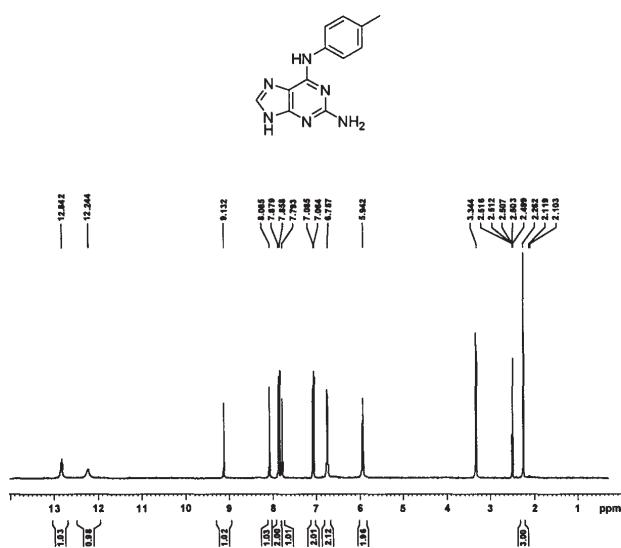
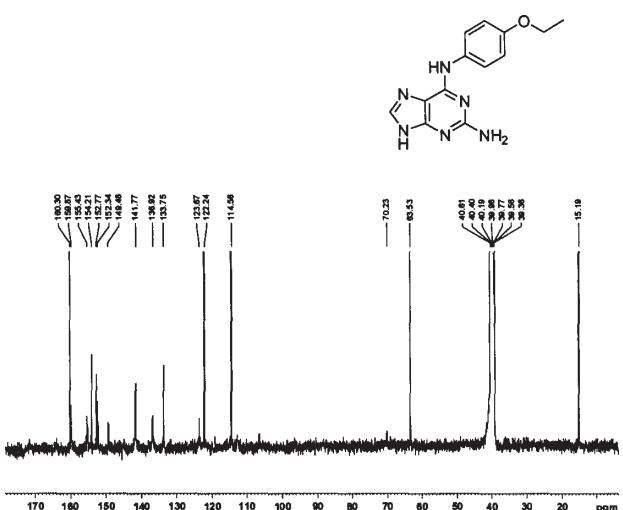
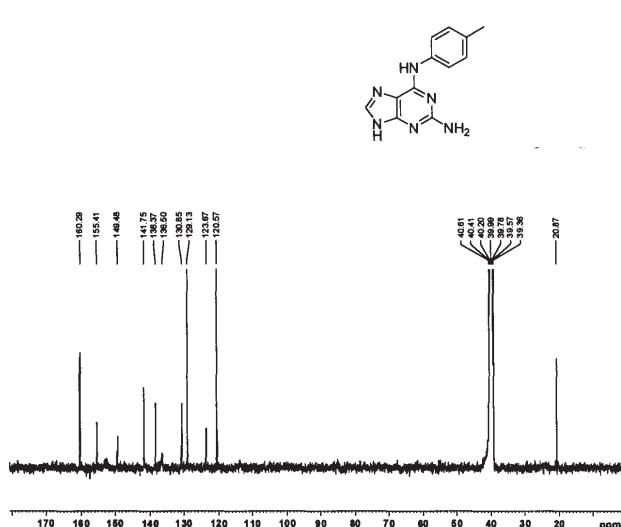
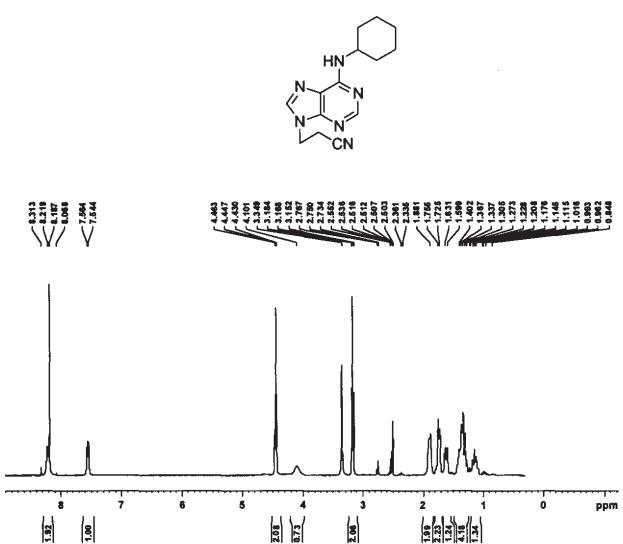
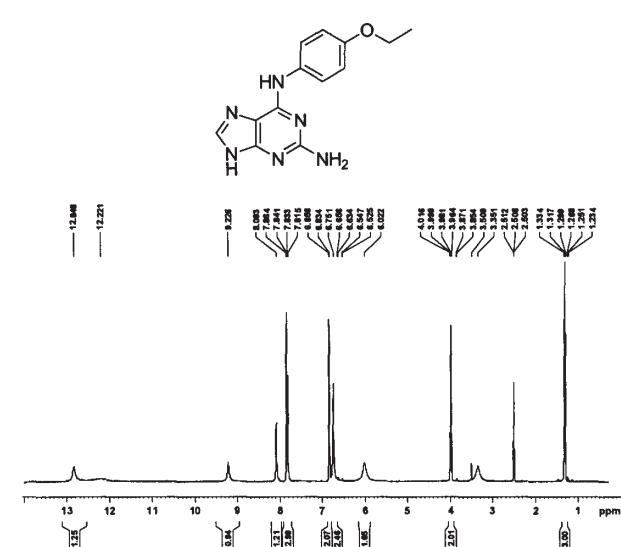
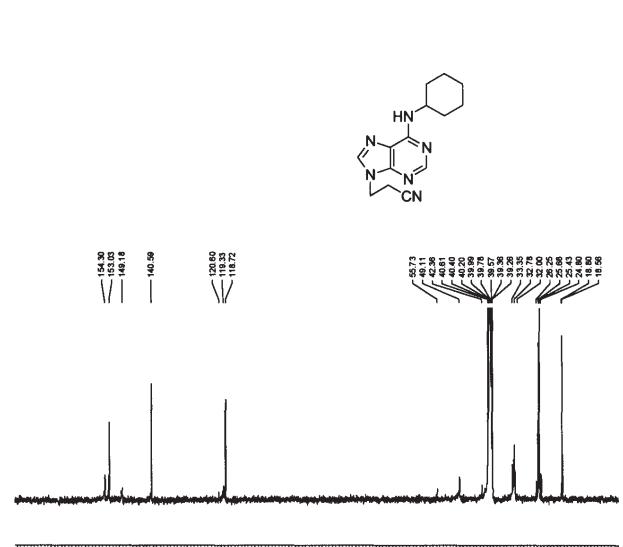


Figure S18. ¹³C NMR of 3b.

Figure S19. ¹H NMR of 3c.Figure S22. ¹³C NMR of 3e.Figure S20. ¹³C NMR of 3c.Figure S23. ¹H NMR of 4a.Figure S21. ¹H NMR of 3e.Figure S24. ¹³C NMR of 4a.

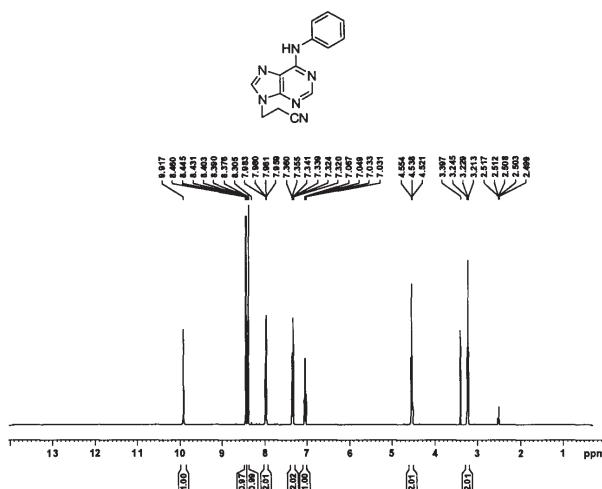


Figure S25. ^1H NMR of **4b**.

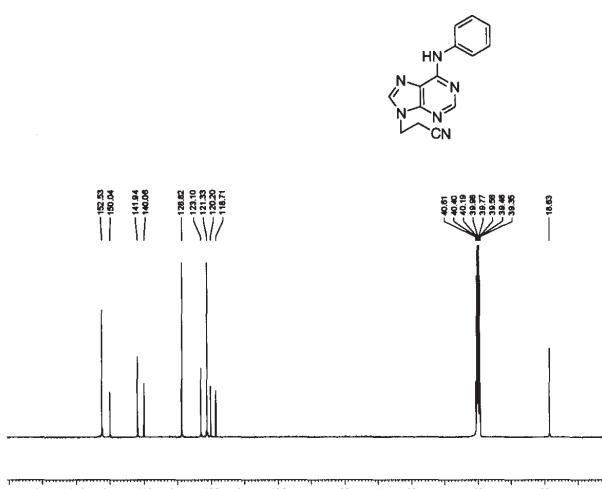


Figure S26. ^{13}C NMR of 4b.

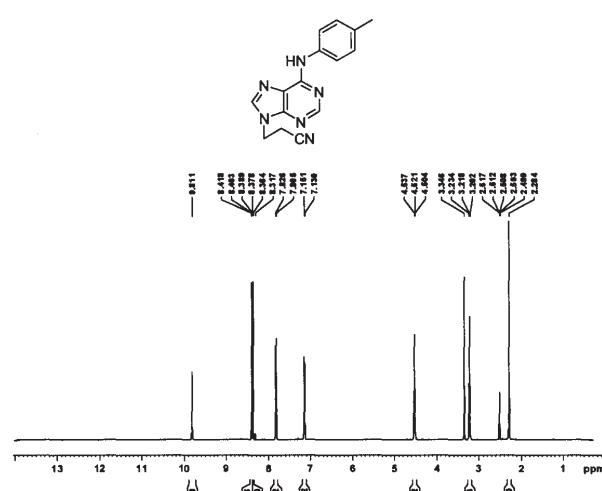


Figure S27. ^1H NMR of 4c

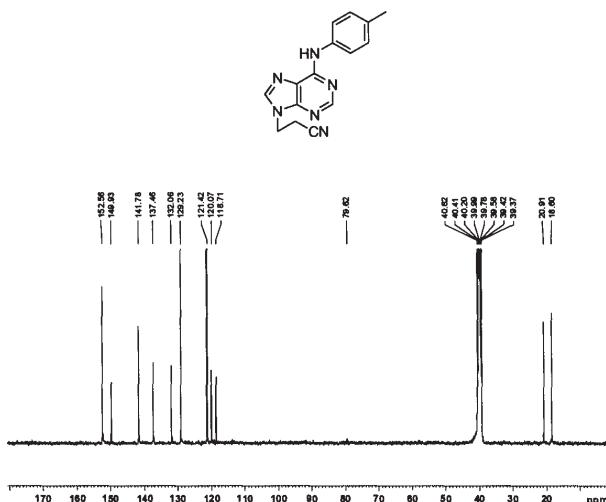


Figure S28. ^{13}C NMR of **4c**.

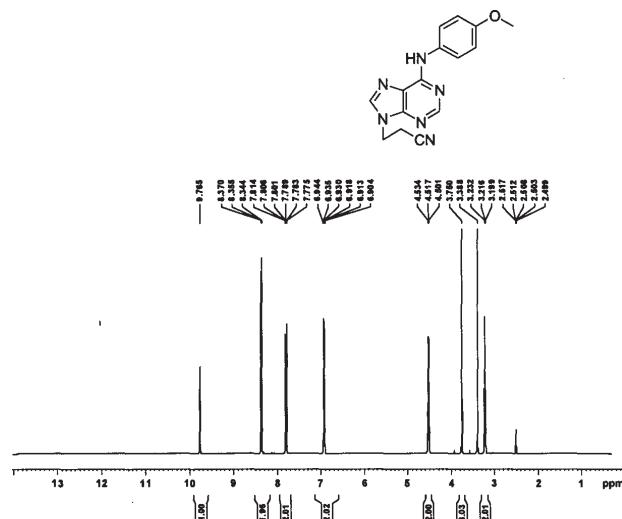


Figure S29. ^1H NMR of 4d.

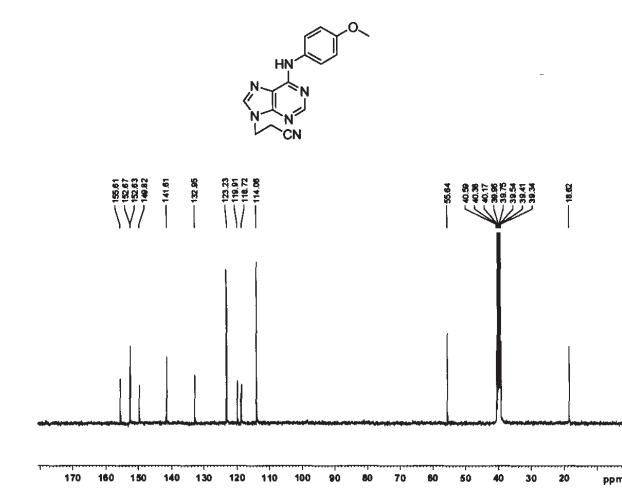


Figure S30. ^{13}C NMR of 4d.

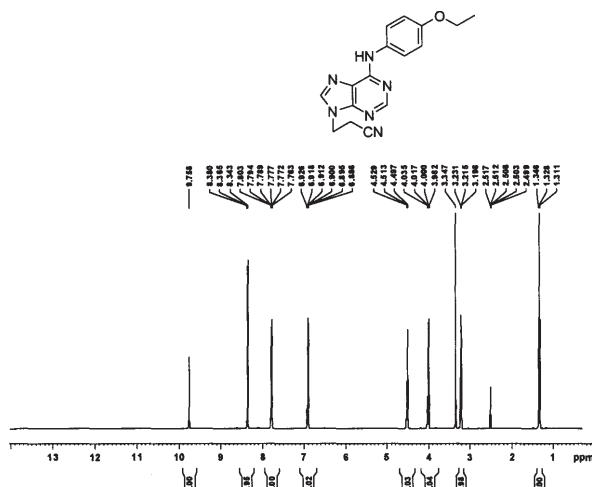


Figure S31. ^1H NMR of 4e.

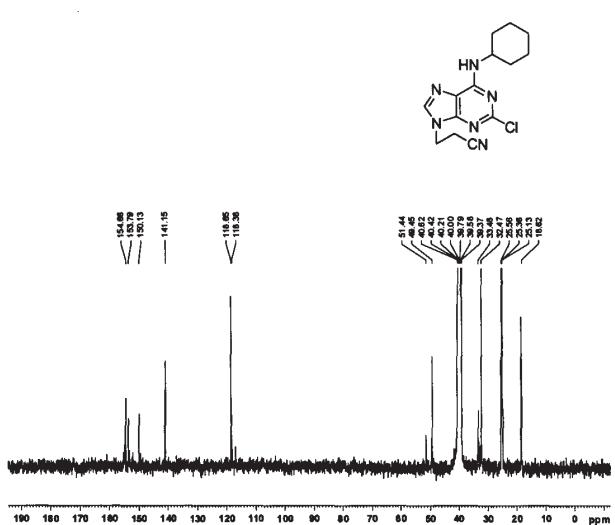


Figure S34. ^{13}C NMR of **5a**.

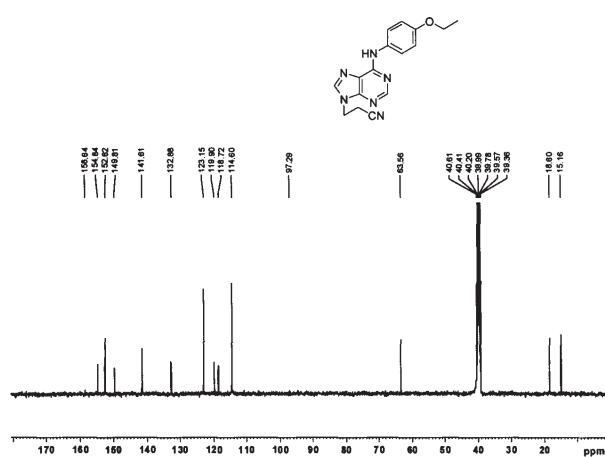


Figure S32. ^{13}C NMR of 4e.

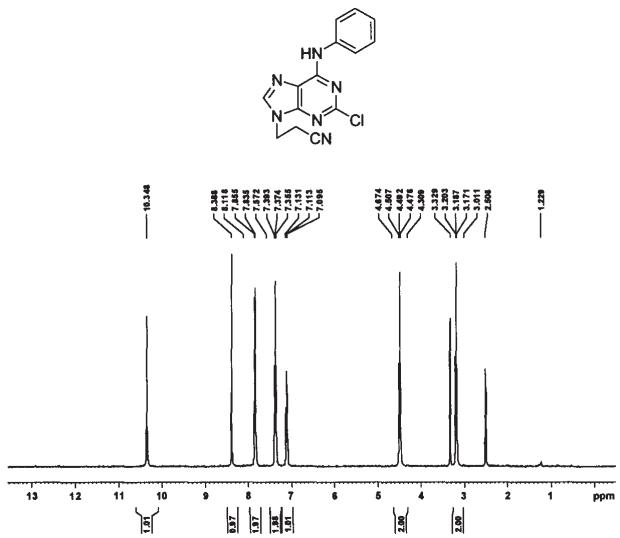


Figure S35. ^1H NMR of **5b**.

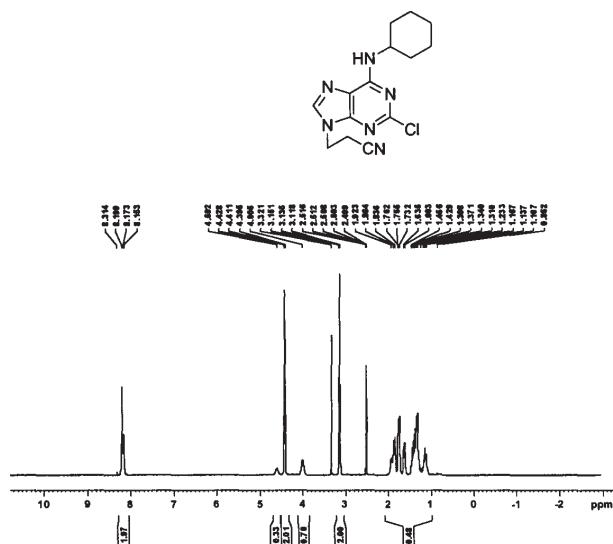


Figure S33. ^1H NMR of **5a**.

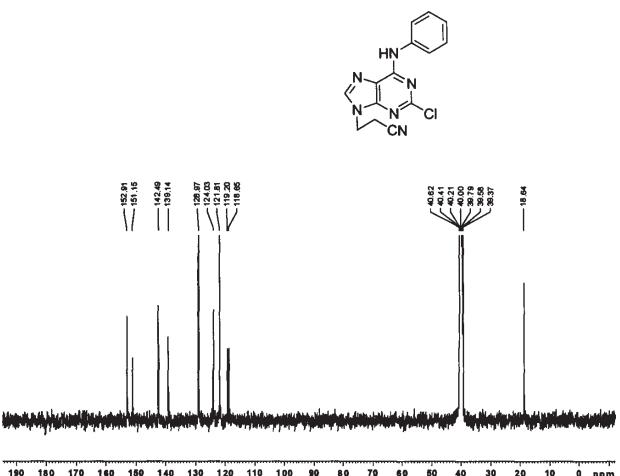


Figure S36. ^{13}C NMR of 5b.

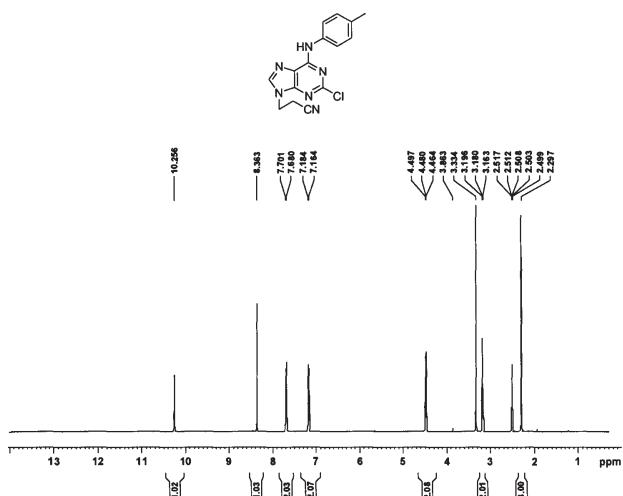


Figure S37. ^1H NMR of 5c.

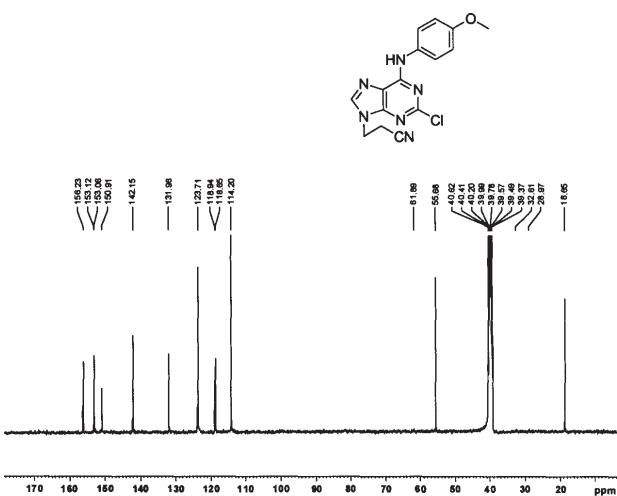


Figure S40. ^{13}C NMR of **5d**.

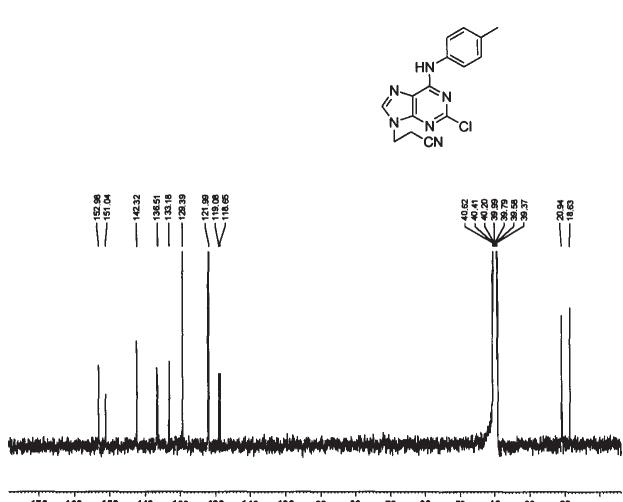


Figure S38. ^{13}C NMR of 5c.

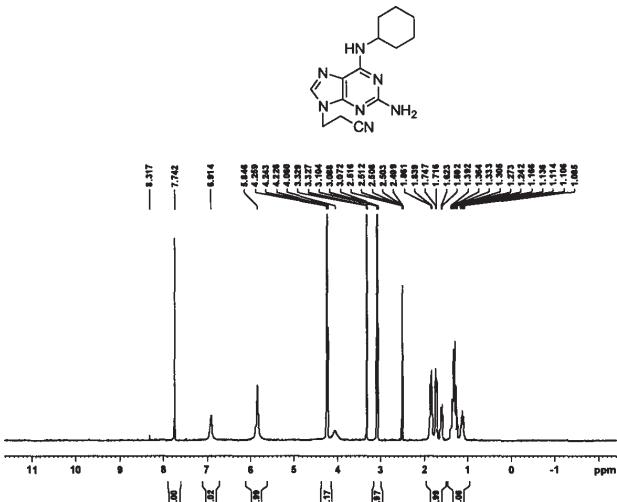


Figure S41 ^1H NMR of 6a

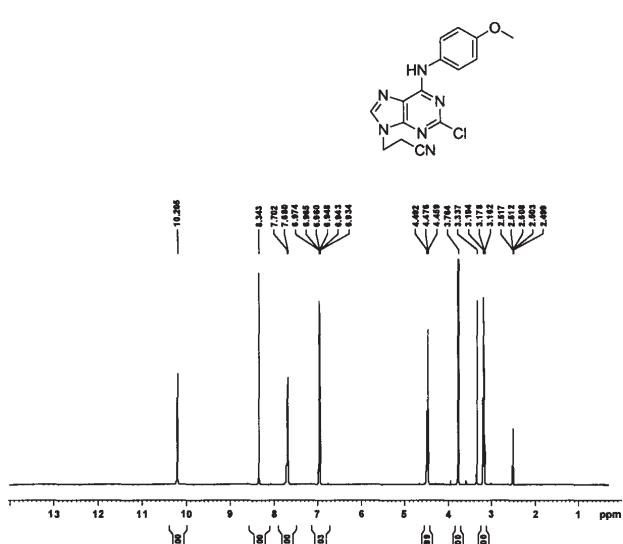


Figure S39. ^1H NMR of 5d.

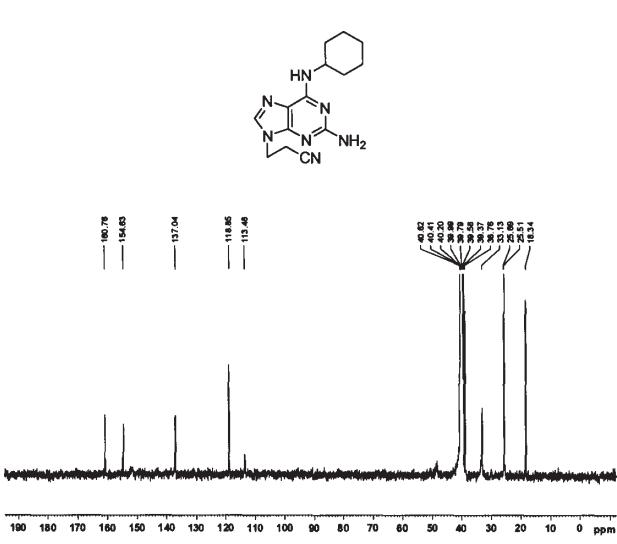
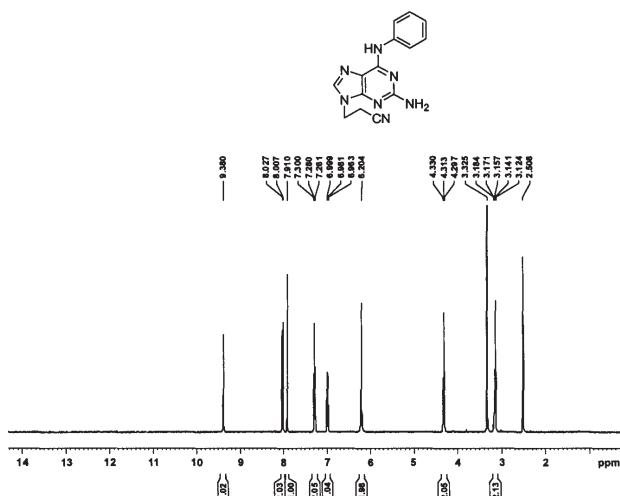
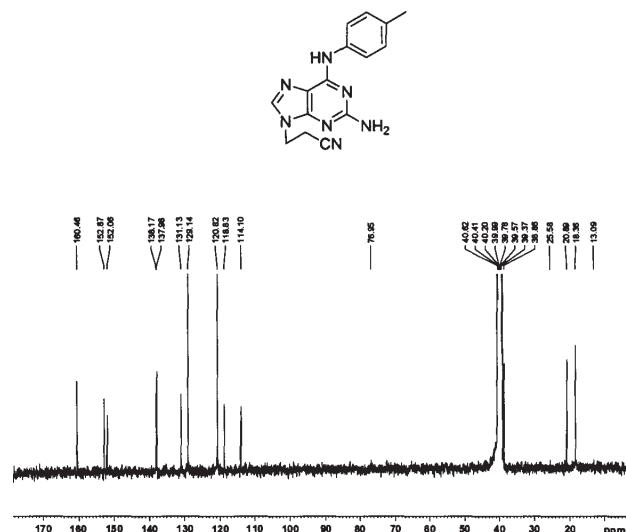
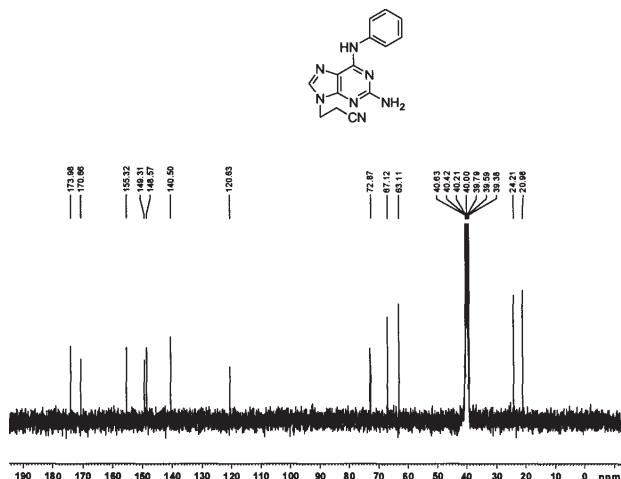
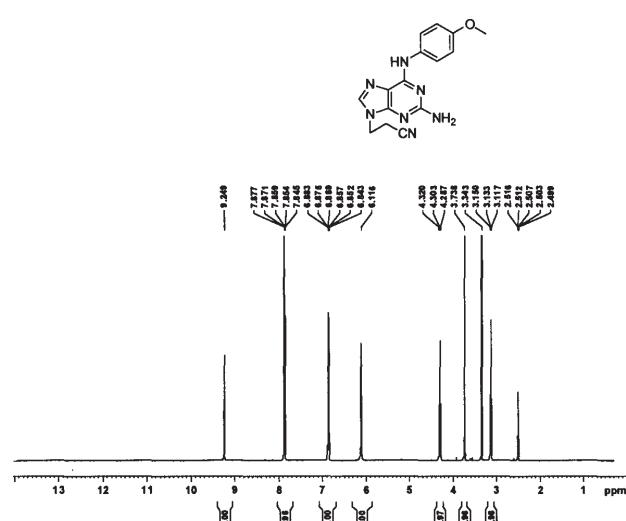
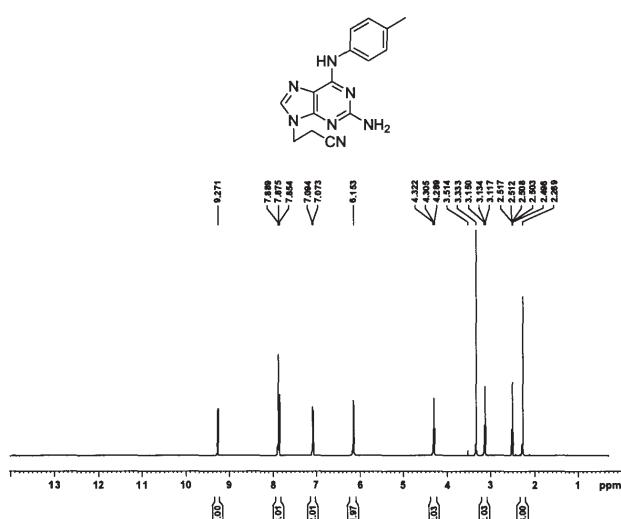
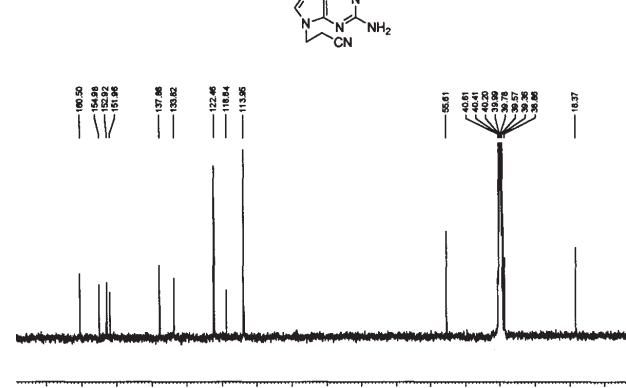


Figure S42. ^{13}C NMR of **6a**.

Figure S43. ^1H NMR of 6b.Figure S46. ^{13}C NMR of 6c.Figure S44. ^{13}C NMR of 6b.Figure S47. ^1H NMR of 6d.Figure S45. ^1H NMR of 6c.Figure S48. ^{13}C NMR of 6d.

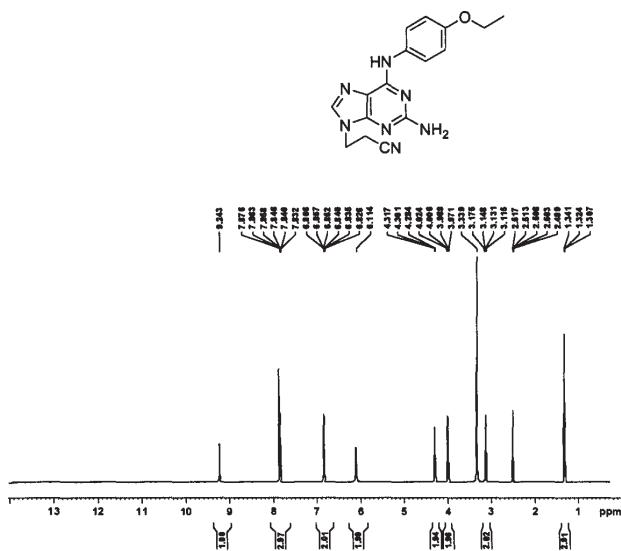


Figure S49. ^1H NMR of 6e.

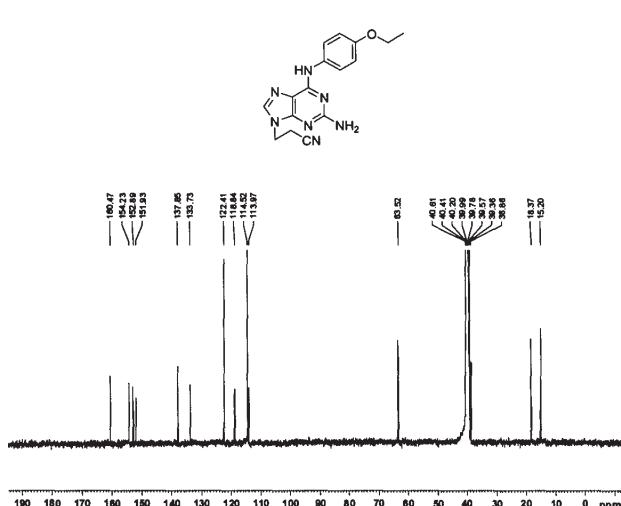


Figure S50. ^{13}C NMR of 6e.

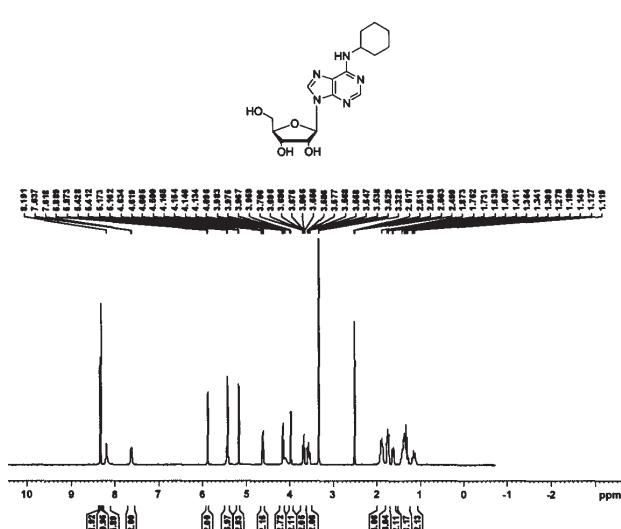


Figure S51. ^1H NMR of 7a.

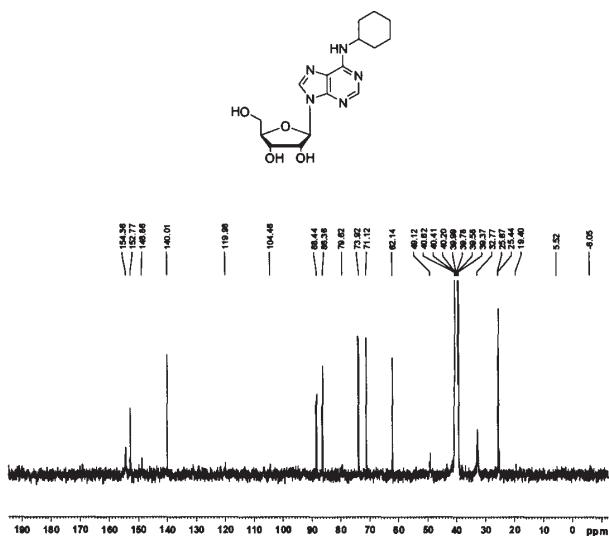


Figure S52. ^{13}C NMR of 7a.

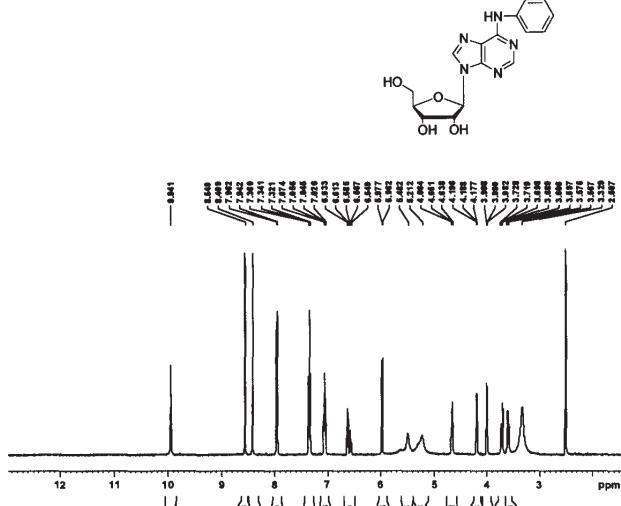


Figure S53. ^1H NMR of 7h.

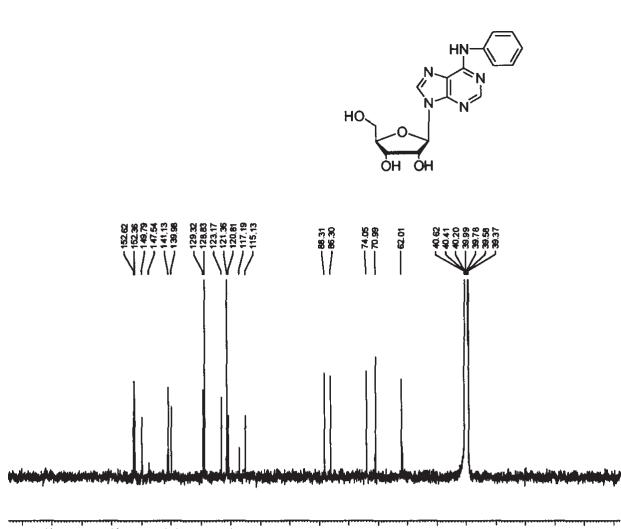
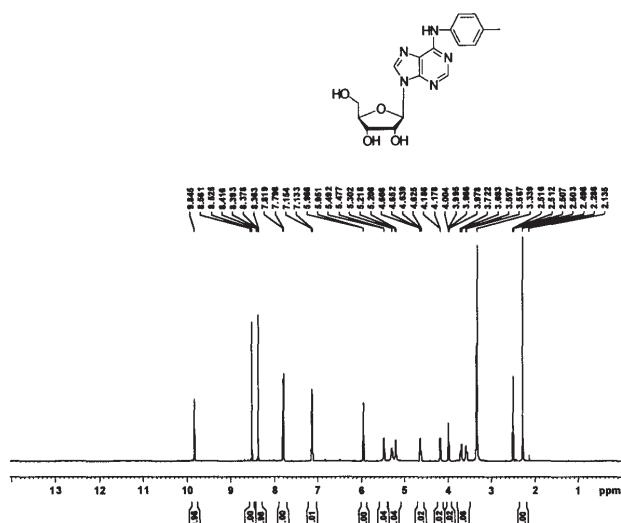
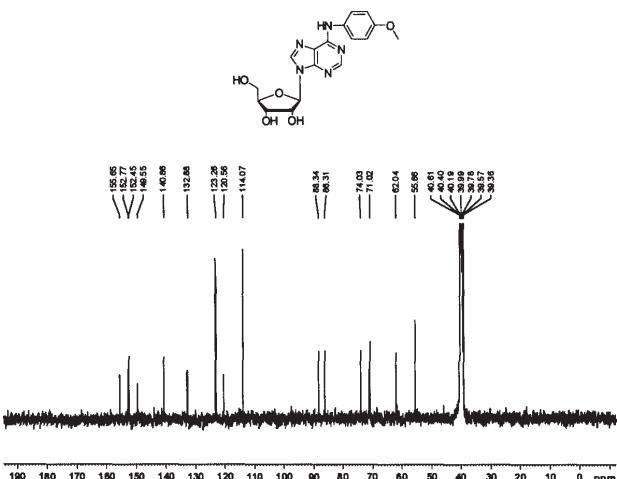
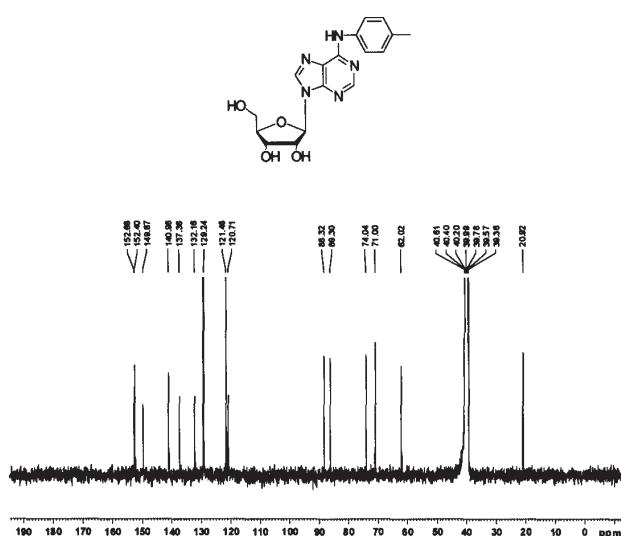
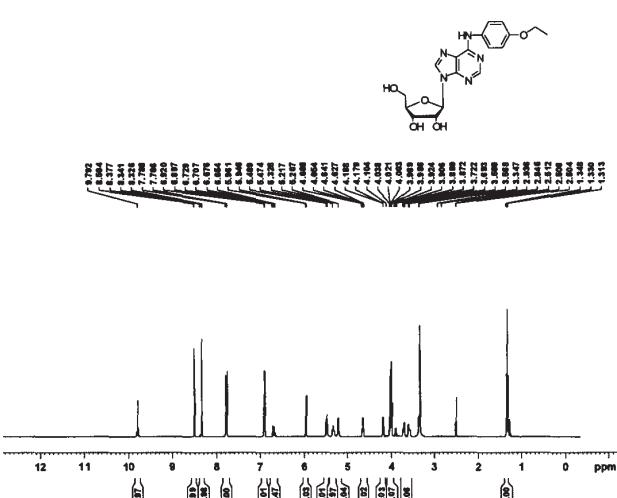
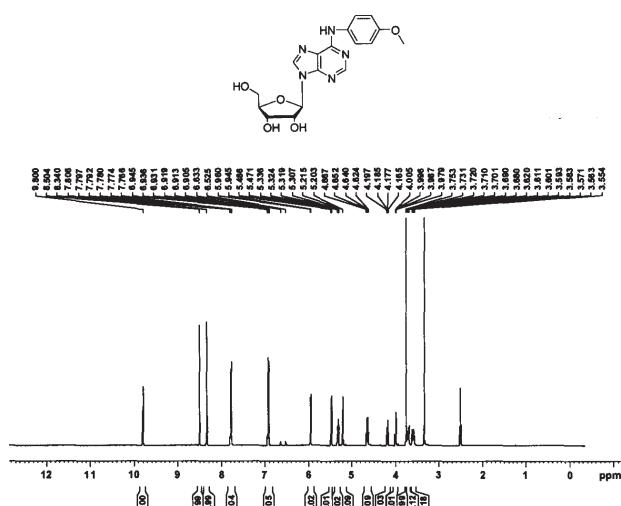
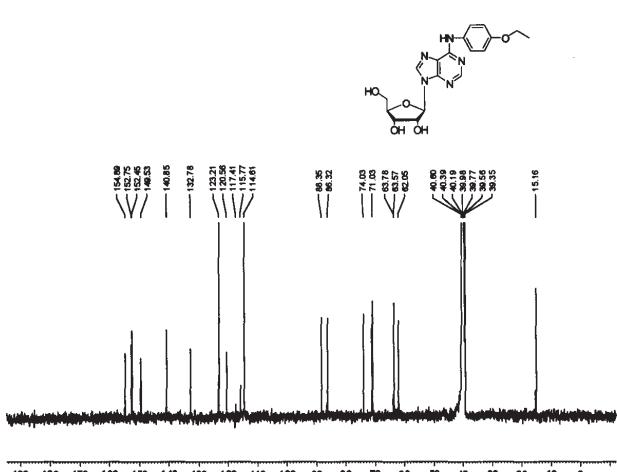


Figure S54. ^{13}C NMR of 7b.

**Figure S55.** ¹H NMR of 7c.**Figure S58.** ¹³C NMR of 7d.**Figure S56.** ¹³C NMR of 7c.**Figure S59.** ¹H NMR of 7e.**Figure S57.** ¹H NMR of 7d.**Figure S60.** ¹³C NMR of 7e.

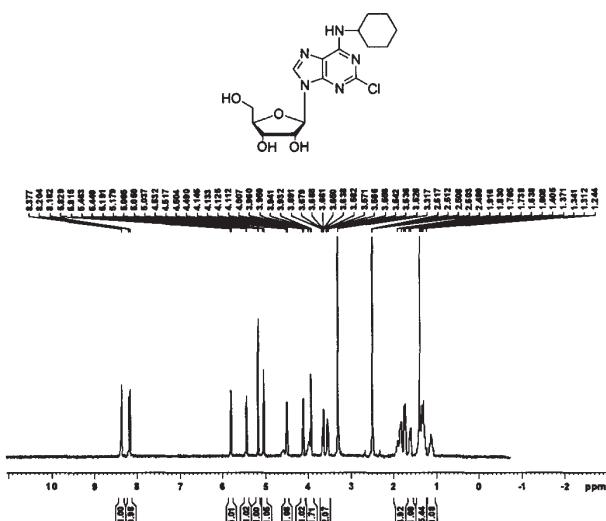


Figure S61. ^1H NMR of 8a.

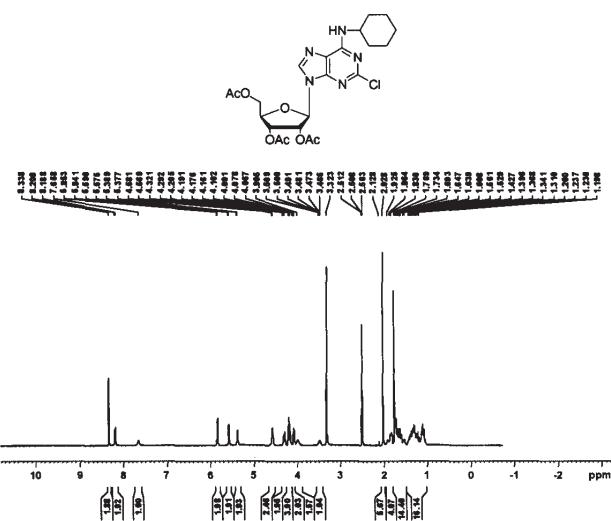


Figure S62. ^1H NMR of $8\text{a}'$.

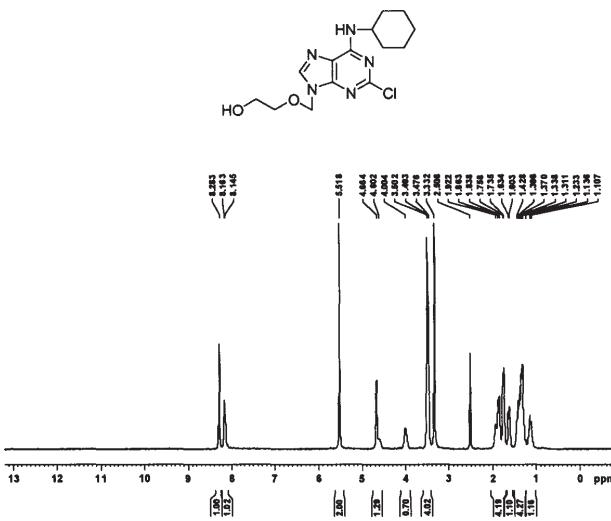


Figure S64. ^1H NMR of **9a**.

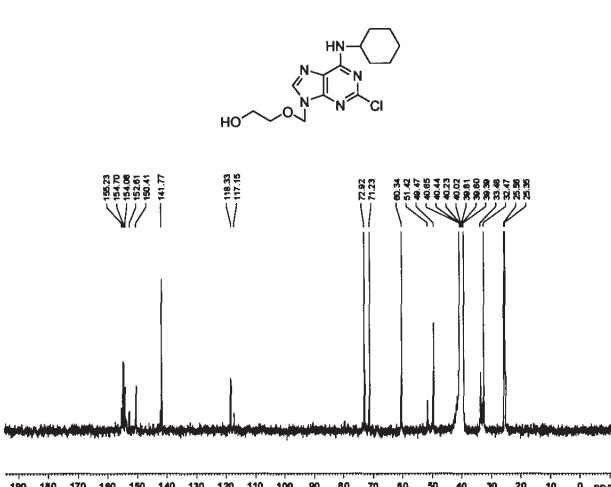


Figure S65. ^{13}C NMR of 9a.

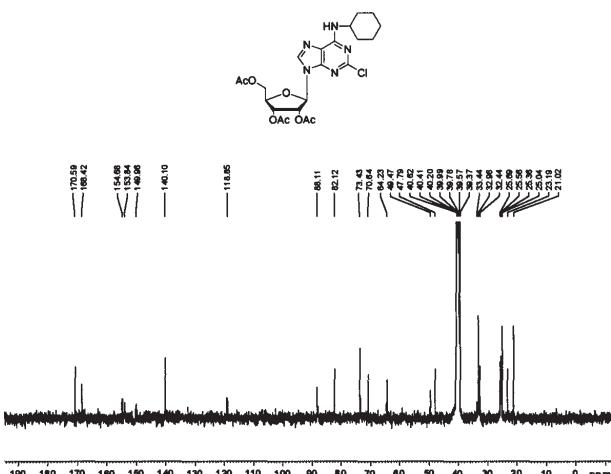


Figure S63. ^{13}C NMR of **8a'**.

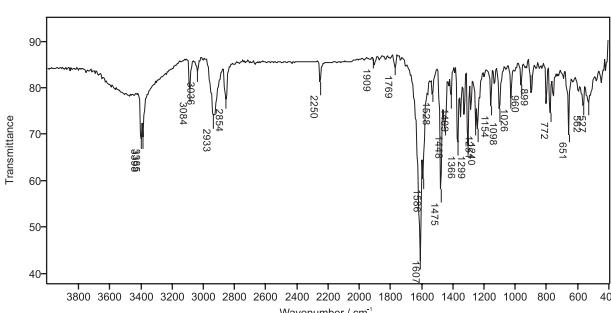


Figure S66. IR of 4a.

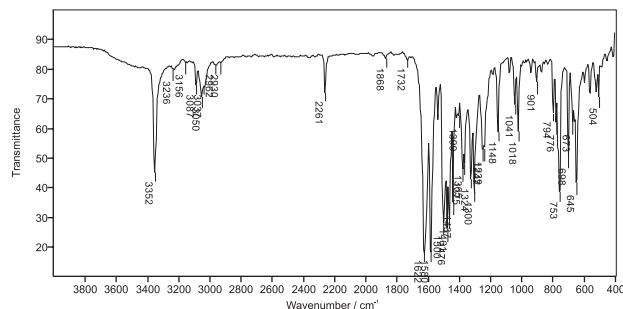


Figure S67. IR of 4b.

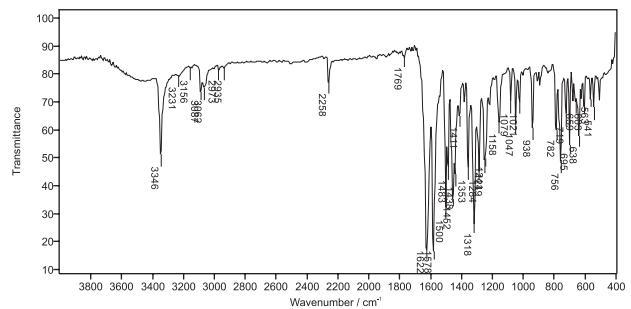


Figure S71. IR of 5b.

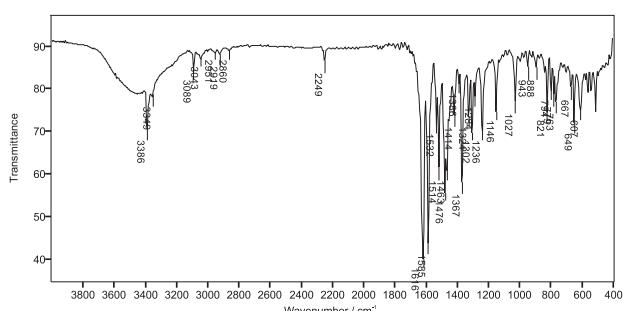


Figure S68. IR of 4c.

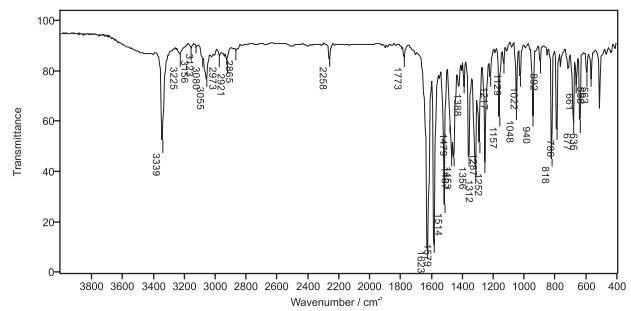


Figure S72. IR of 5c.

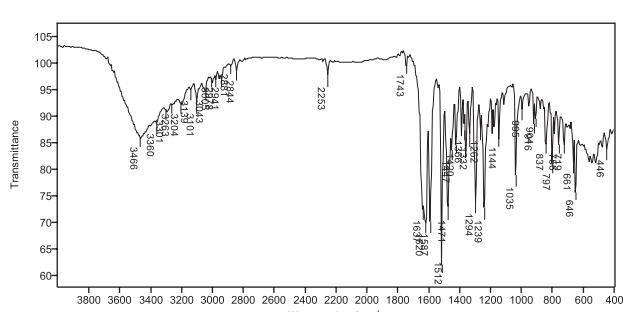


Figure S69. IR of 4d.

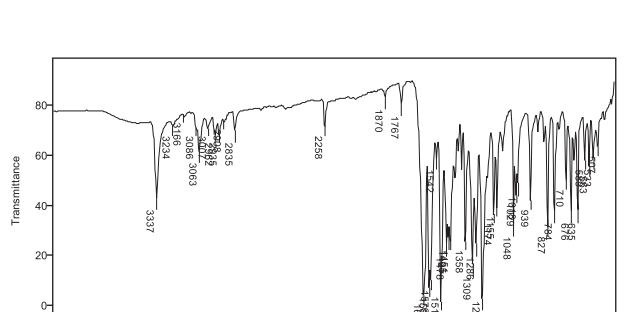


Figure S73. IR of 5d.

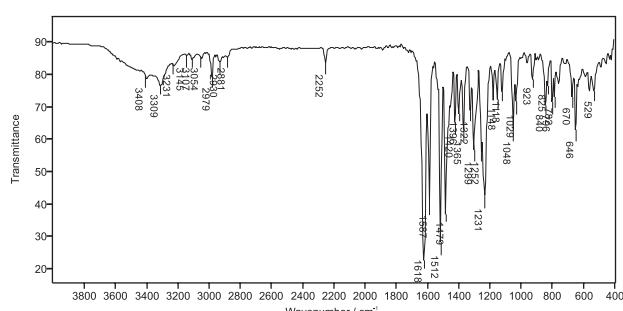


Figure S70. IR of 4e.

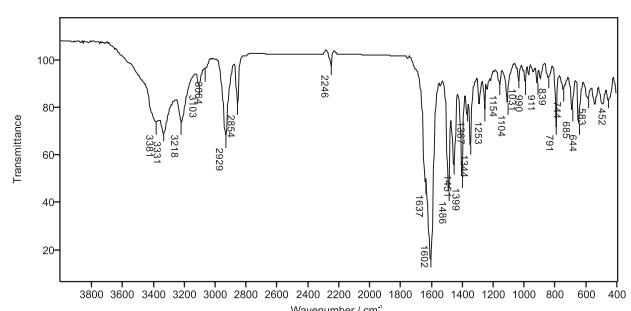


Figure S74. IR of 6a.

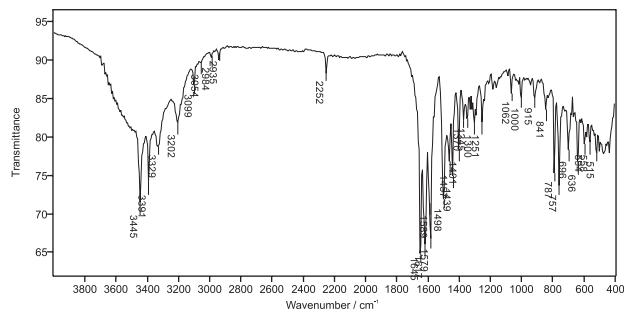


Figure S75. IR of 6b.

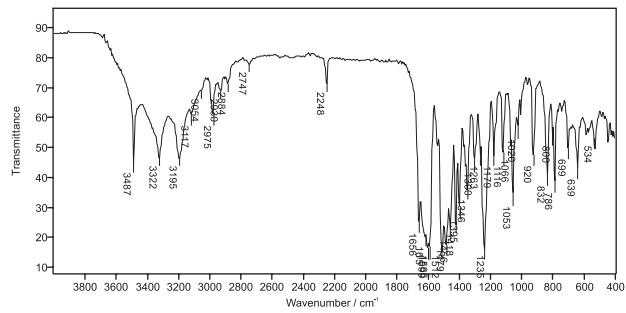


Figure S78. IR of 6e.

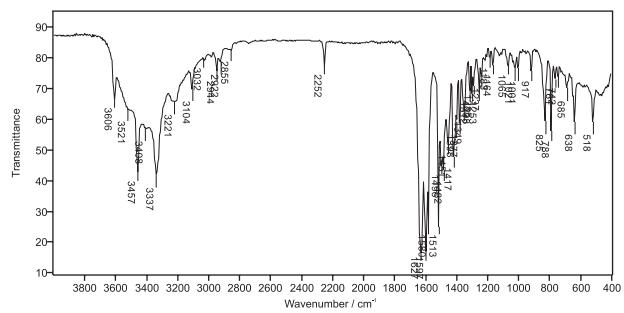


Figure S76. IR of 6c.

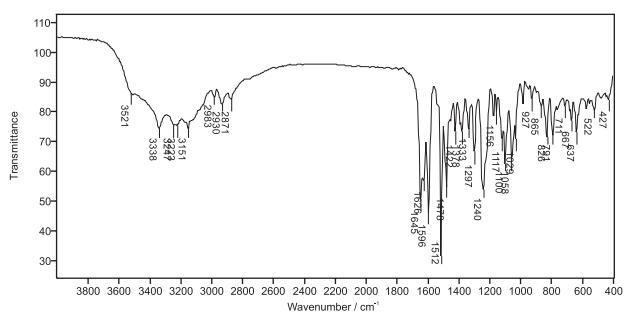


Figure S79. IR of 7e.

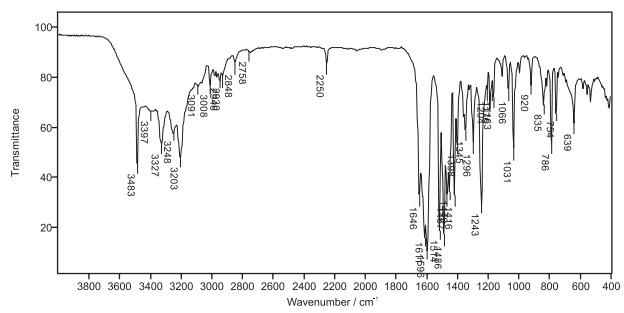


Figure S77. IR of 6d.

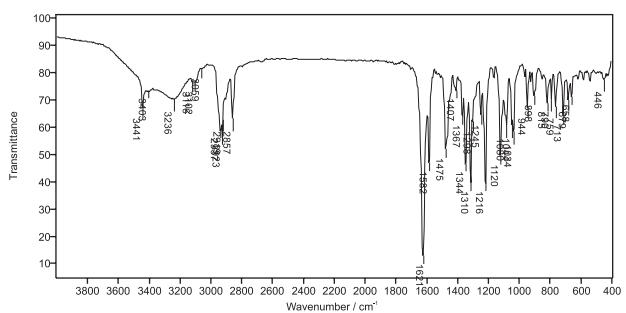


Figure S80. IR of 9a.