Palladium-Catalyzed Allylic Amination and Metathesis Reactions: Powerful Tools for the Enantioselective Synthesis of Acyclic Nucleoside Phosphonate Analogues of Cidofovir

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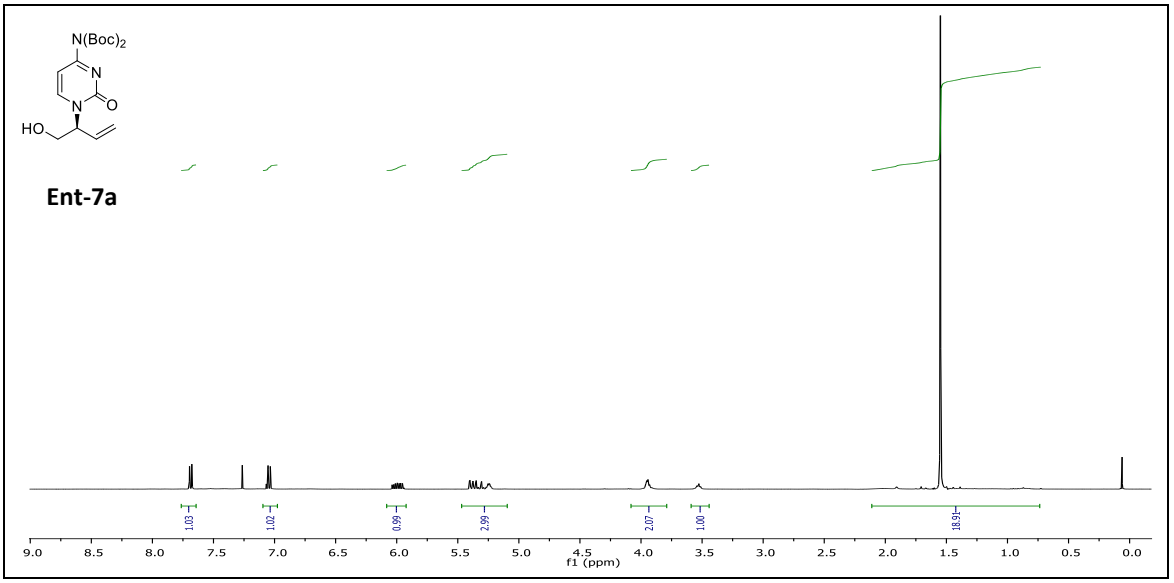
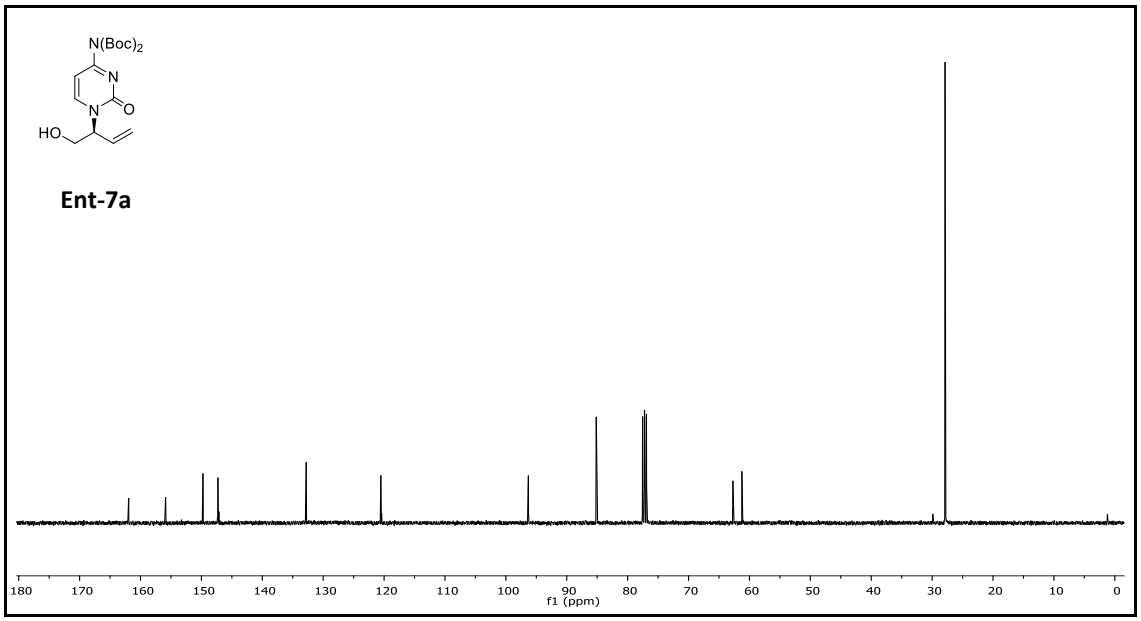
INDEX

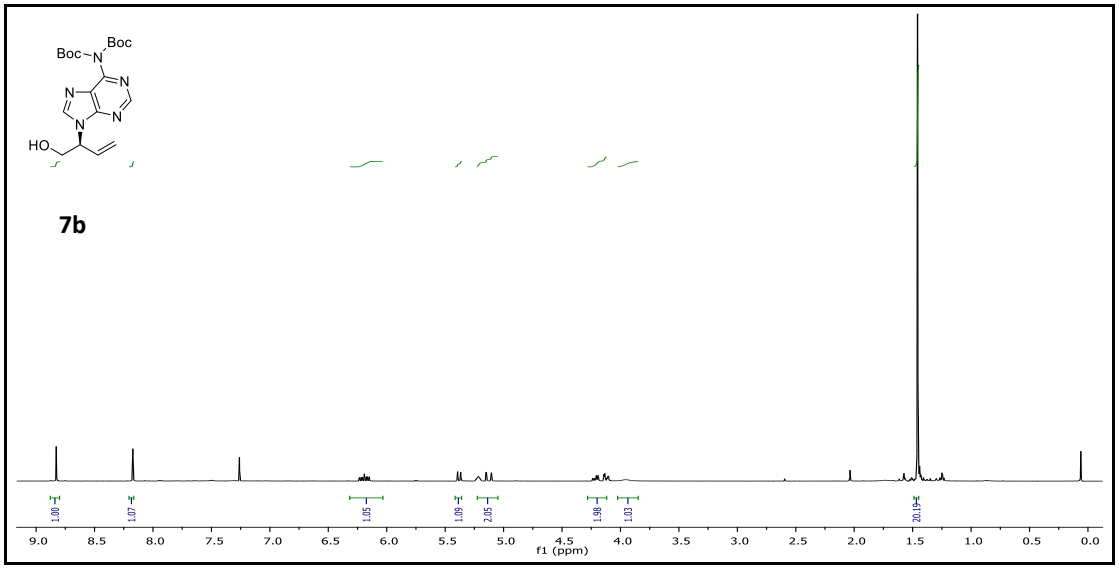
^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm) of (*R*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-1-(1-hydroxybut-3-en-2-yl)-cytosine (ent-7a).



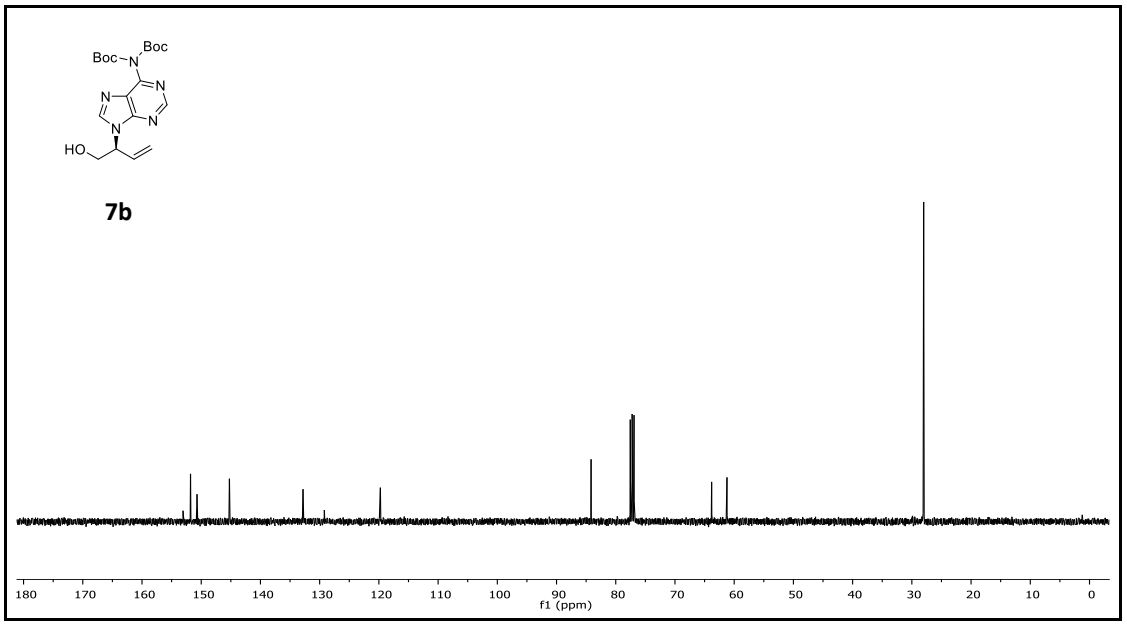
^{13}C NMR ($CDCl_3$, 100.6 MHz, δ in ppm) of (R)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-1-(1-hydroxybut-3-en-2-yl)-cytosine (ent-7a).



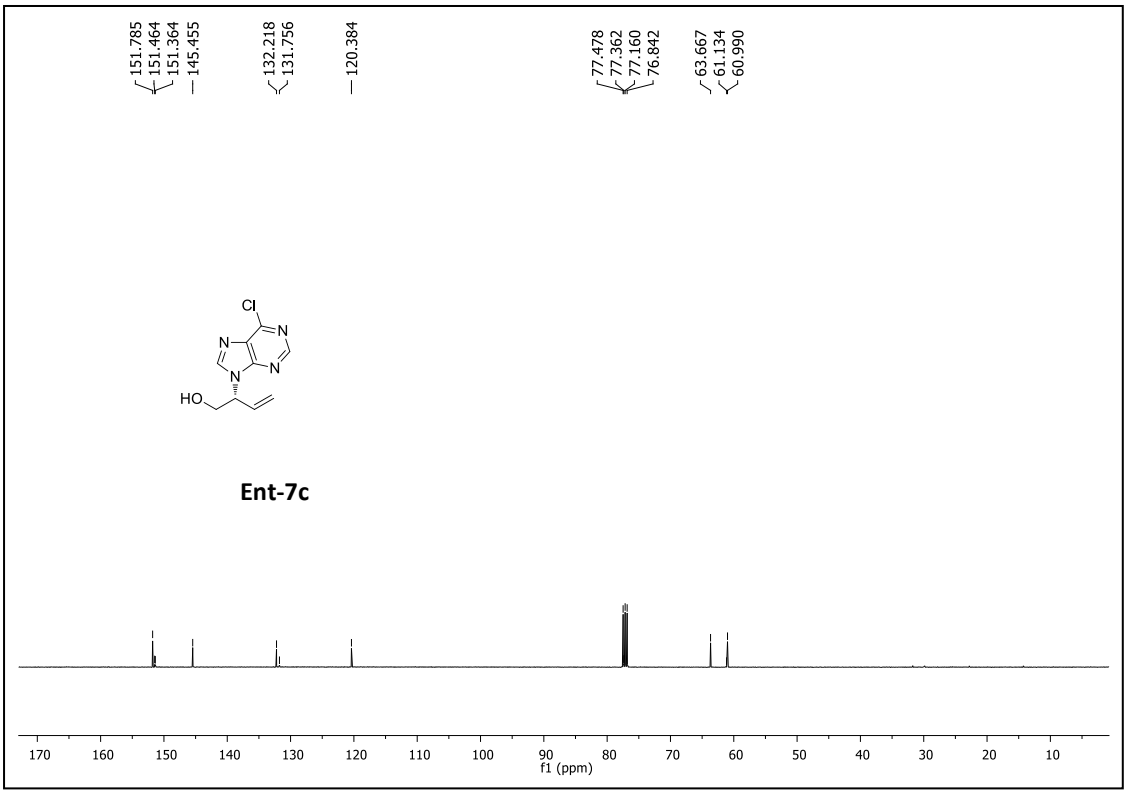
^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm) of (*S*)-*N*,*N*-Bis(tert-butoxycarbonyl)-9-(1-hydroxybut-3-en-2-yl)adenine (7b).



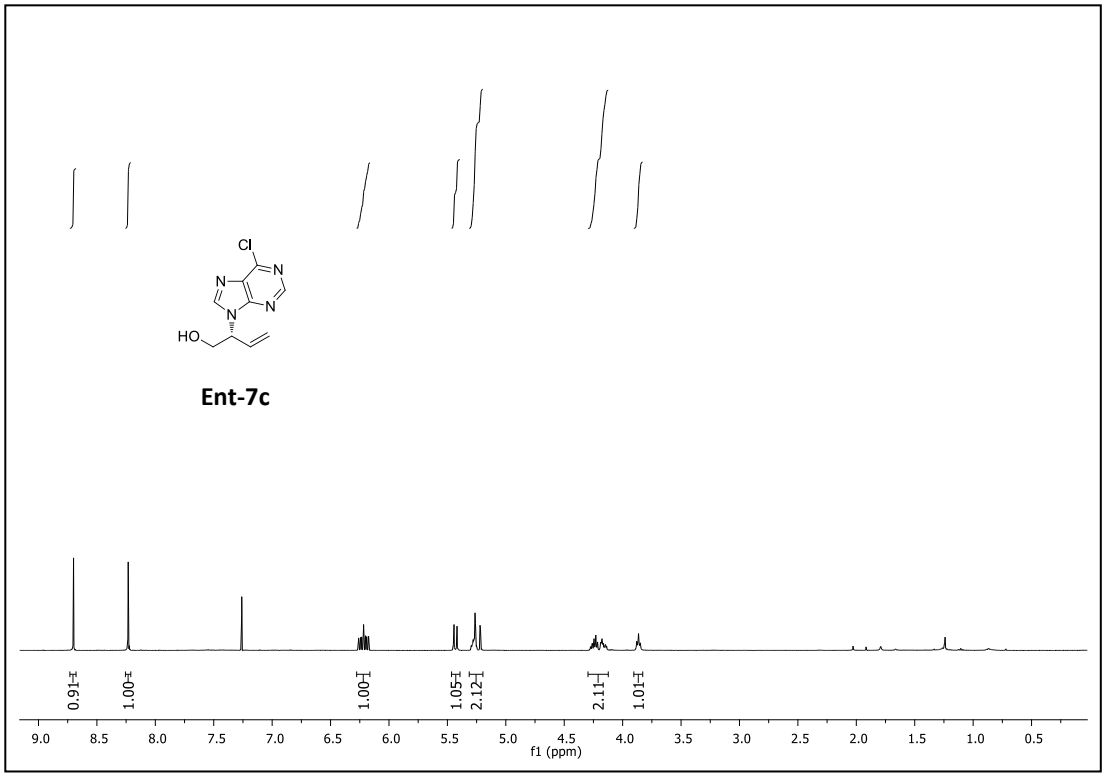
^{13}C NMR ($CDCl_3$, 100.6 MHz, δ in ppm) of (*S*)-*N*,*N*-Bis(tert-butoxycarbonyl)-9-(1-hydroxybut-3-en-2-yl)adenine (7b).



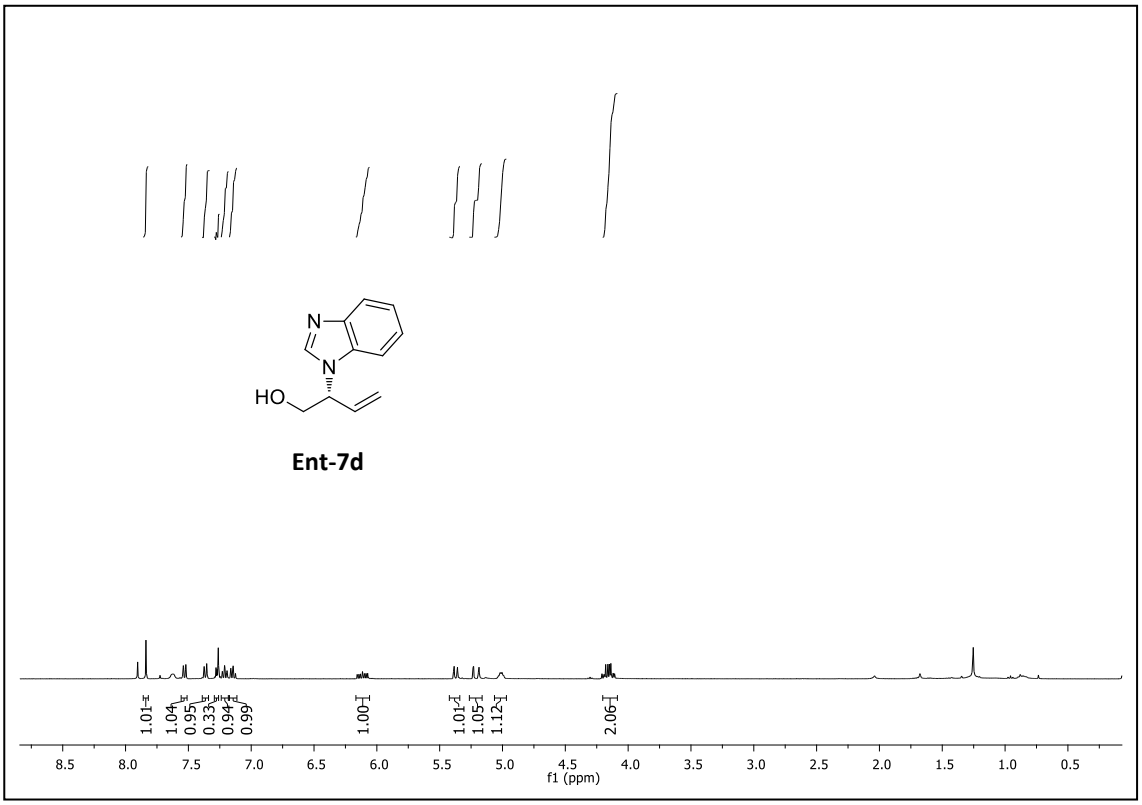
^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm) of (*R*)-6-chloro-9-(1-hydroxybut-3-en-2-yl)-9*H*-purine (ent-7c).



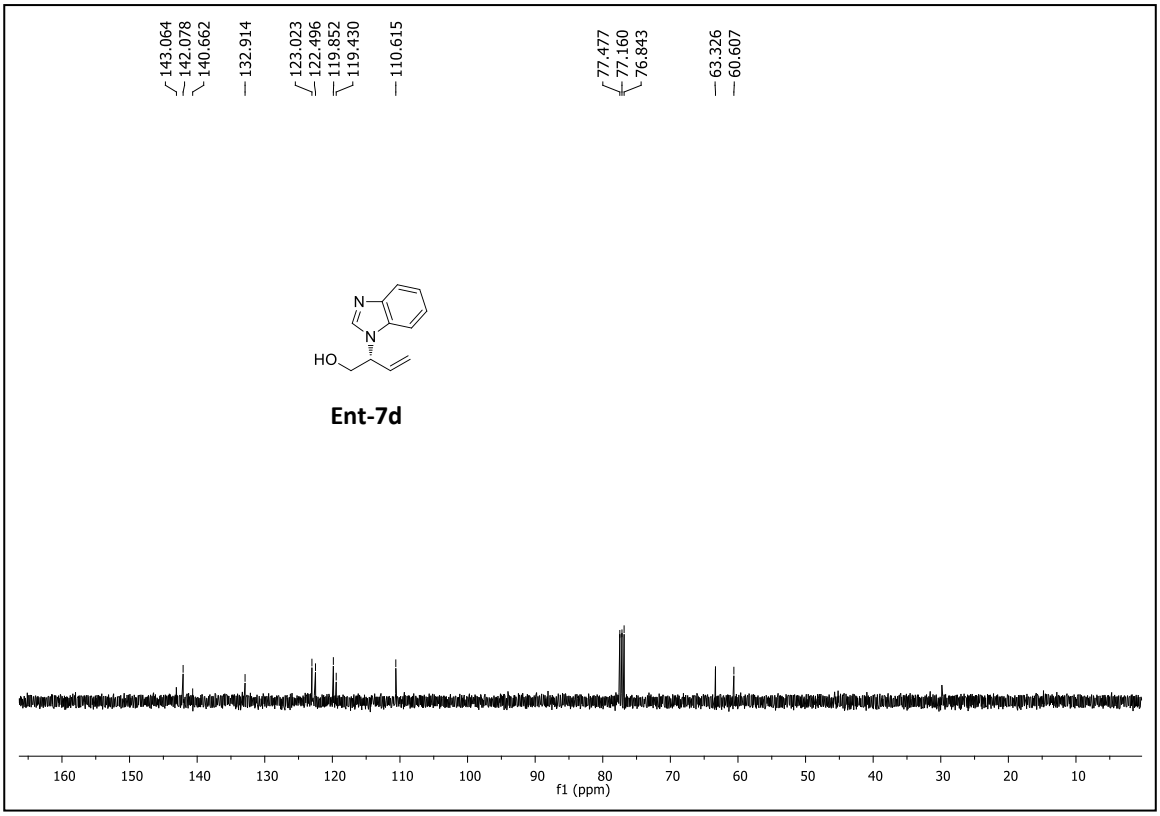
^{13}C NMR ($CDCl_3$, 100.6 MHz, δ in ppm) of of (*R*)-6-chloro-9-(1-hydroxybut-3-en-2-yl)-9*H*-purine (ent-7c)



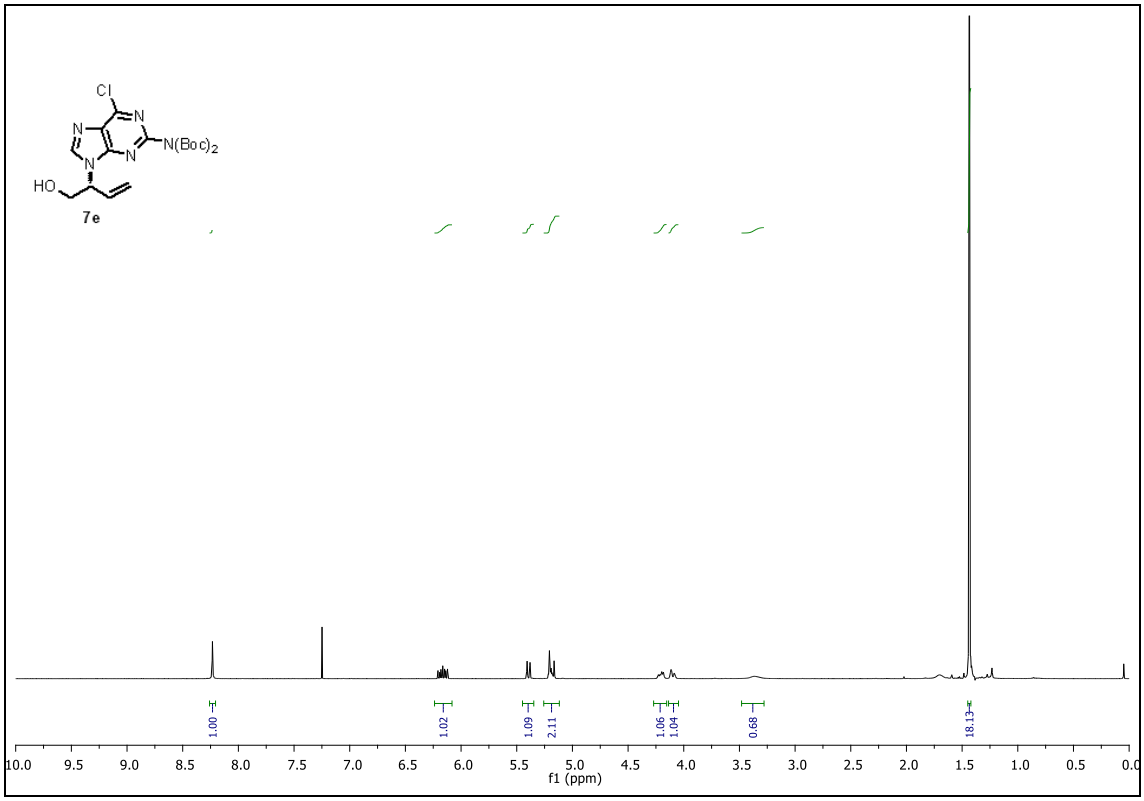
^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm) of (*R*)-1-(1-hydroxybut-3-en-2-yl)-1*H*-benzo[d]imidazole (ent-7d)



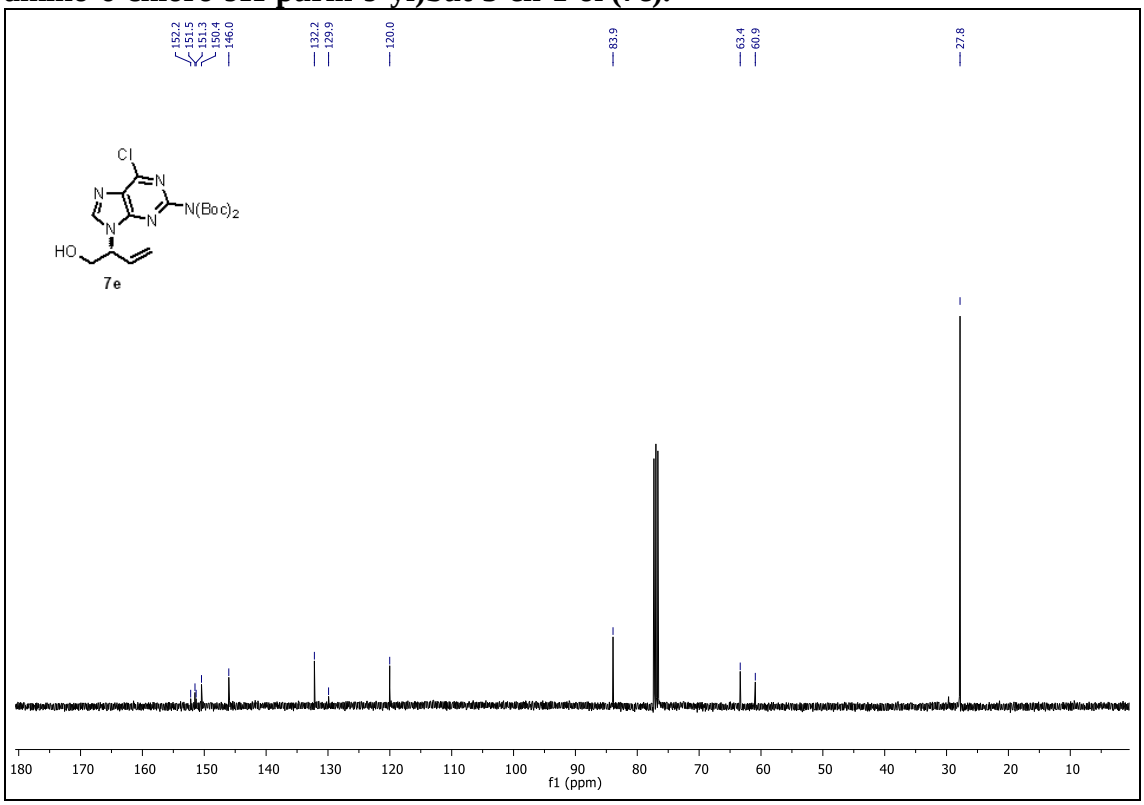
^{13}C NMR ($CDCl_3$, 100.6 MHz, δ in ppm) of (*R*)-1-(1-hydroxybut-3-en-2-yl)-1*H*-benzo[d]imidazole (ent-7d).



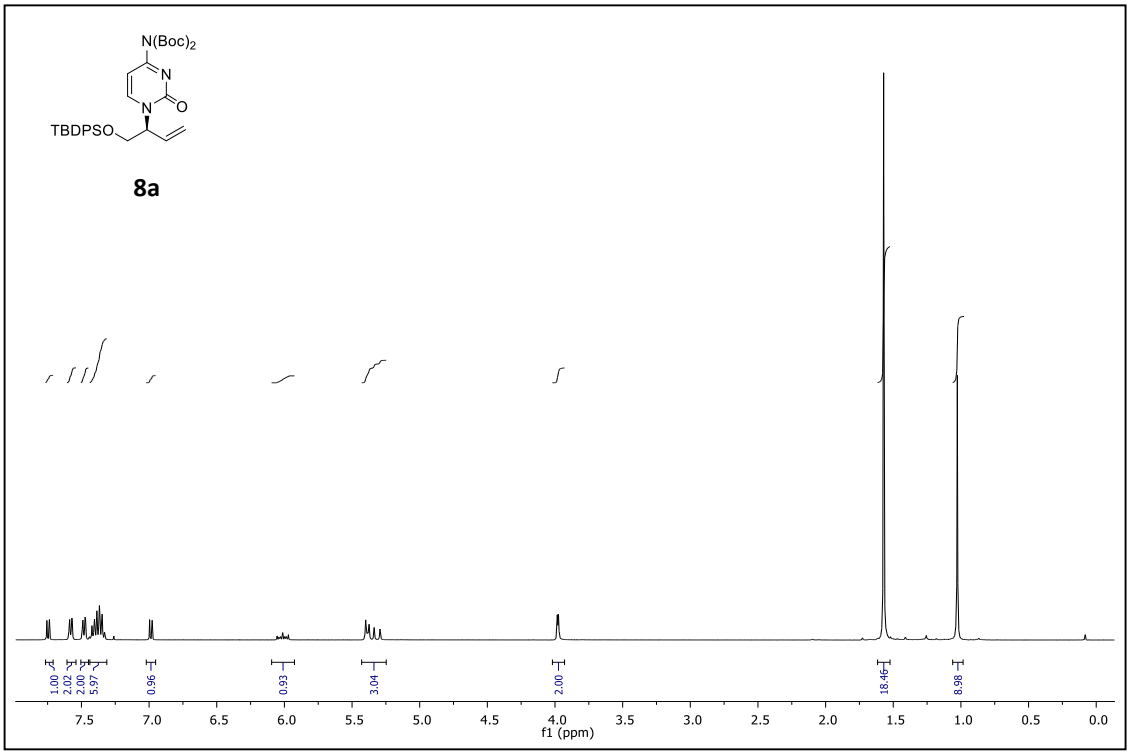
^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm) of *(S)*-*N*,*N*-Bis(*tert*-butoxycarbonyl)-2-(2-amino-6-chloro-9H-purin-9-yl)but-3-en-1-ol (7e).



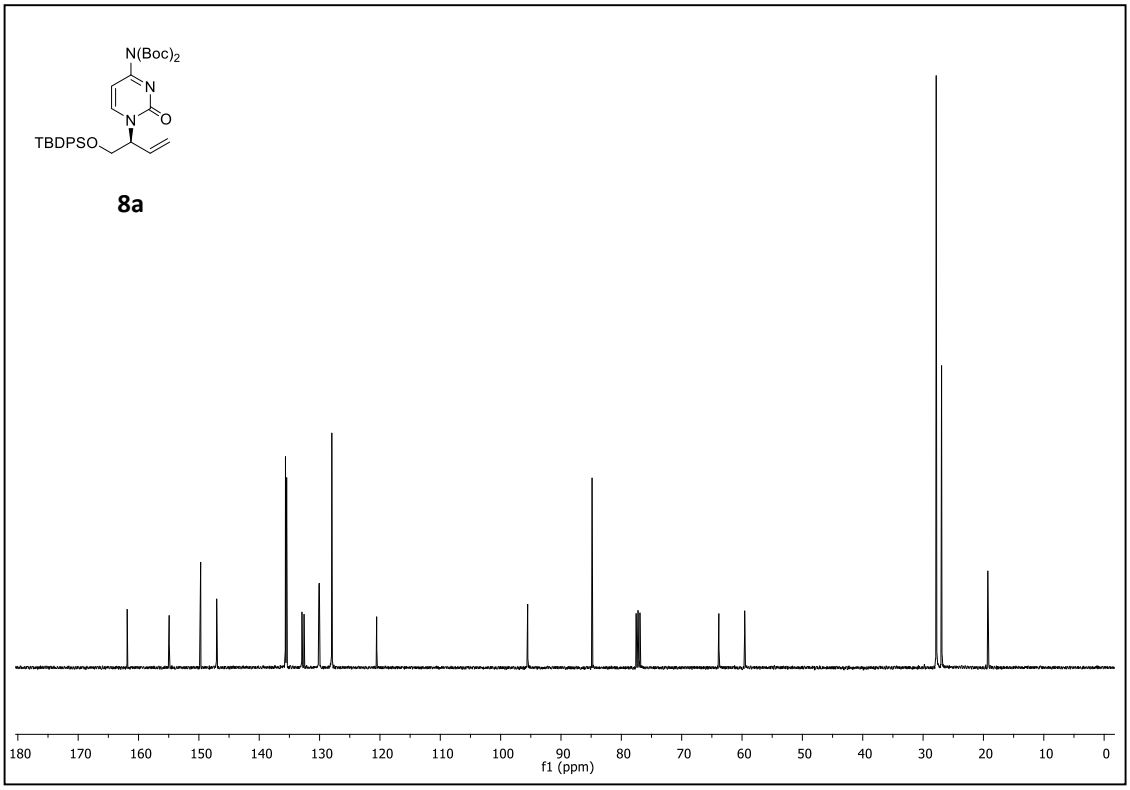
^{13}C NMR ($CDCl_3$, 100.6 MHz, δ in ppm) of *(S)*-*N*,*N*-Bis(*tert*-butoxycarbonyl)-2-(2-amino-6-chloro-9H-purin-9-yl)but-3-en-1-ol (7e).



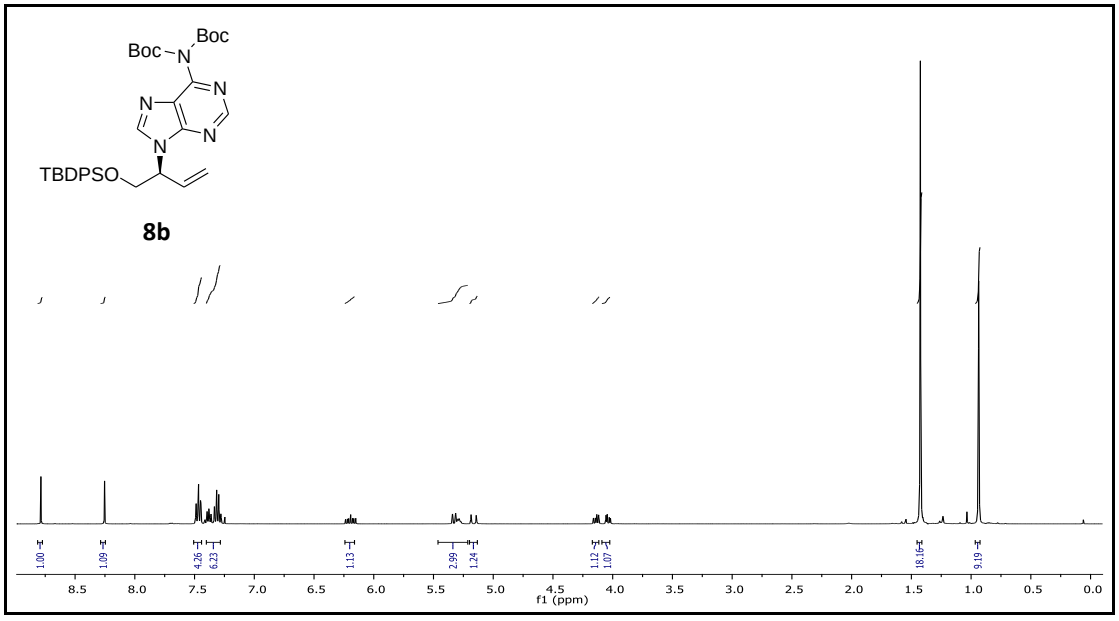
^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm) of (*S*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-1-[1-(*tert*-butyldiphenylsilyloxy)but-3-en-2-yl]cytosine (8a).



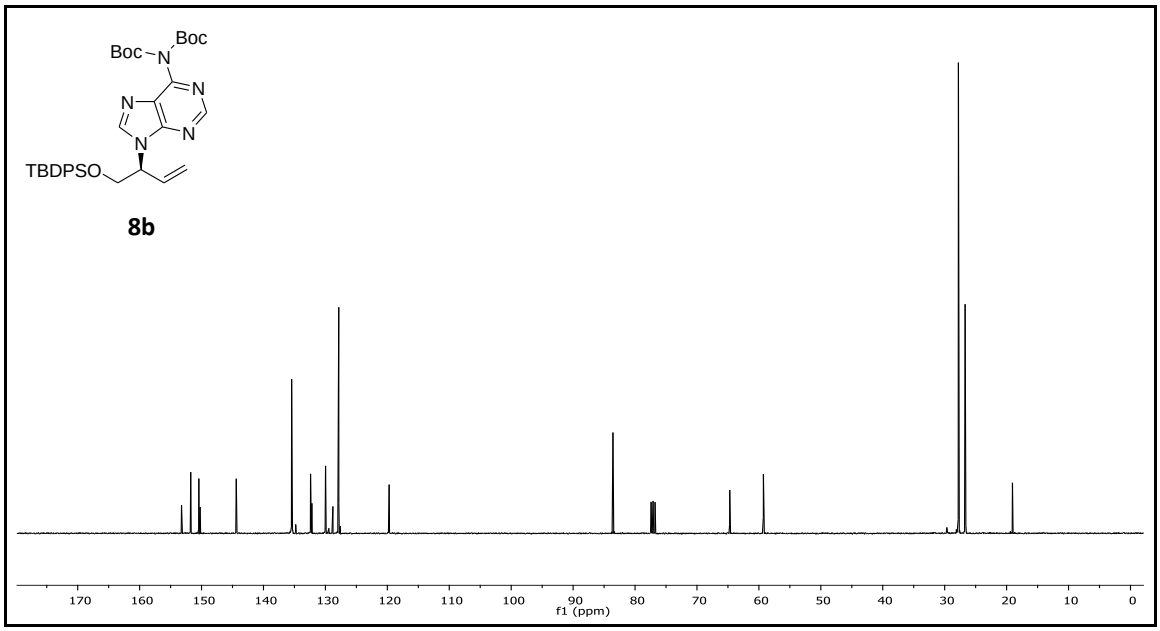
^{13}C NMR ($CDCl_3$, 100.6 MHz, δ in ppm) of (*S*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-1-[1-(*tert*-butyldiphenylsilyloxy)but-3-en-2-yl]cytosine (8a)



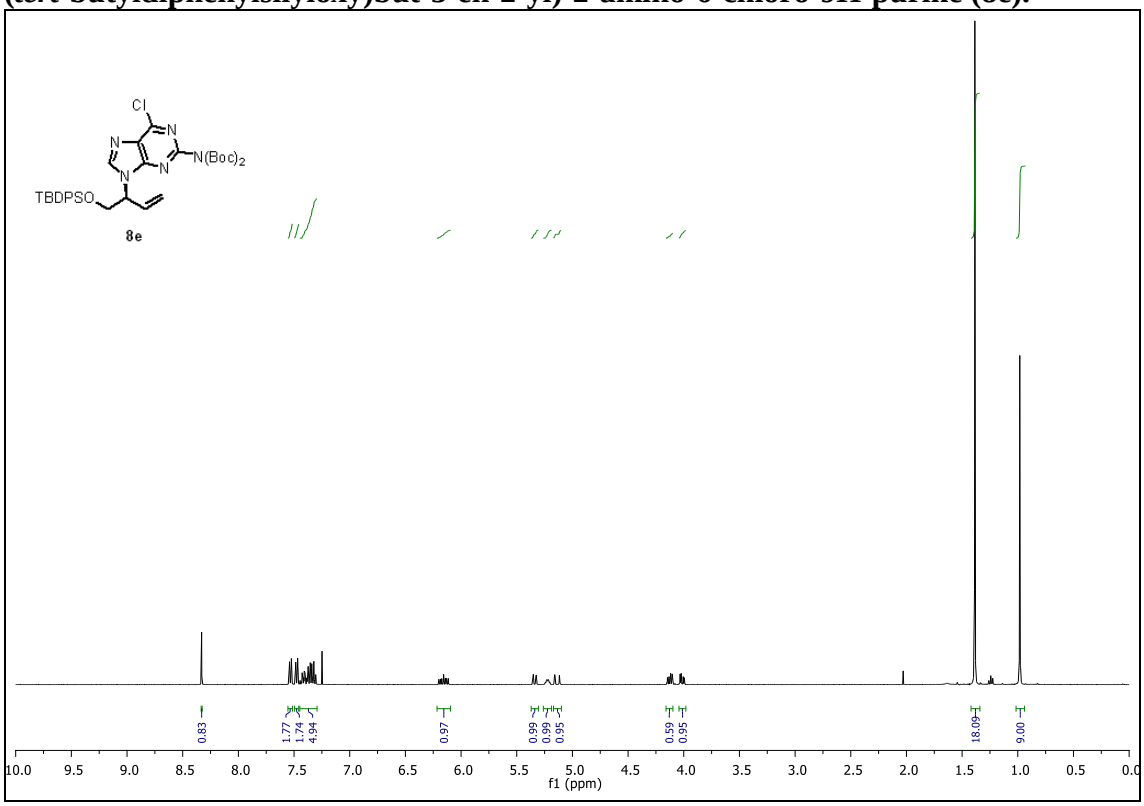
^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm) of (*S*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-9-[1-(tert-butyldiphenylsilyloxy)but-3-en-2-yl]adenine (8b)



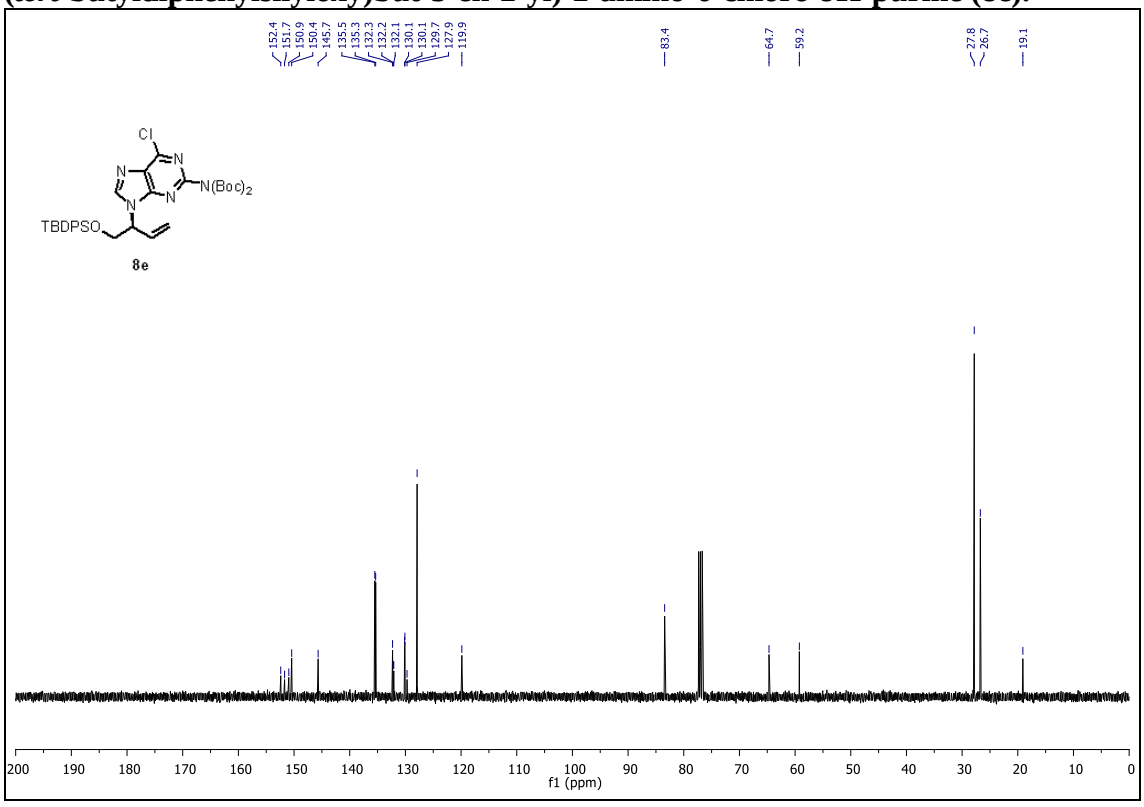
^{13}C NMR ($CDCl_3$, 100.6 MHz, δ in ppm) of (*S*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-9-[1-(tert-butyldiphenylsilyloxy)but-3-en-2-yl]adenine (8b)



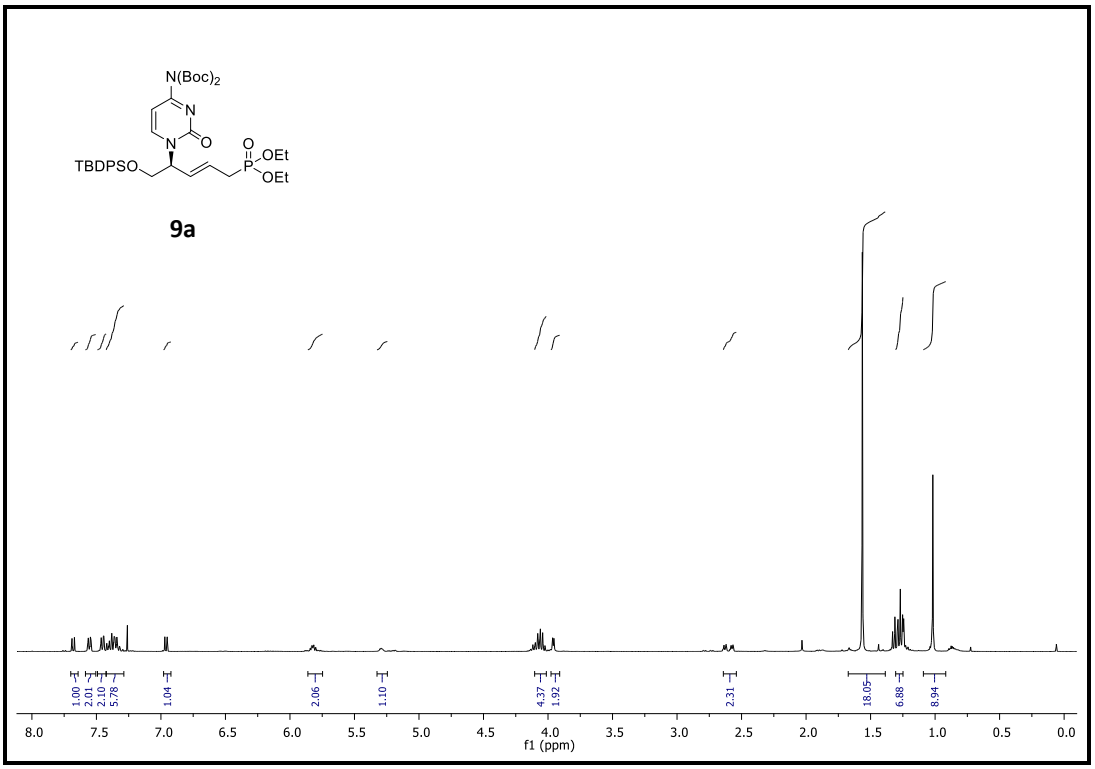
^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm) of (*S*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-9-(1-(*tert*-butyldiphenylsilyloxy)but-3-en-2-yl)-2-amino-6-chloro-9H-purine (8e).



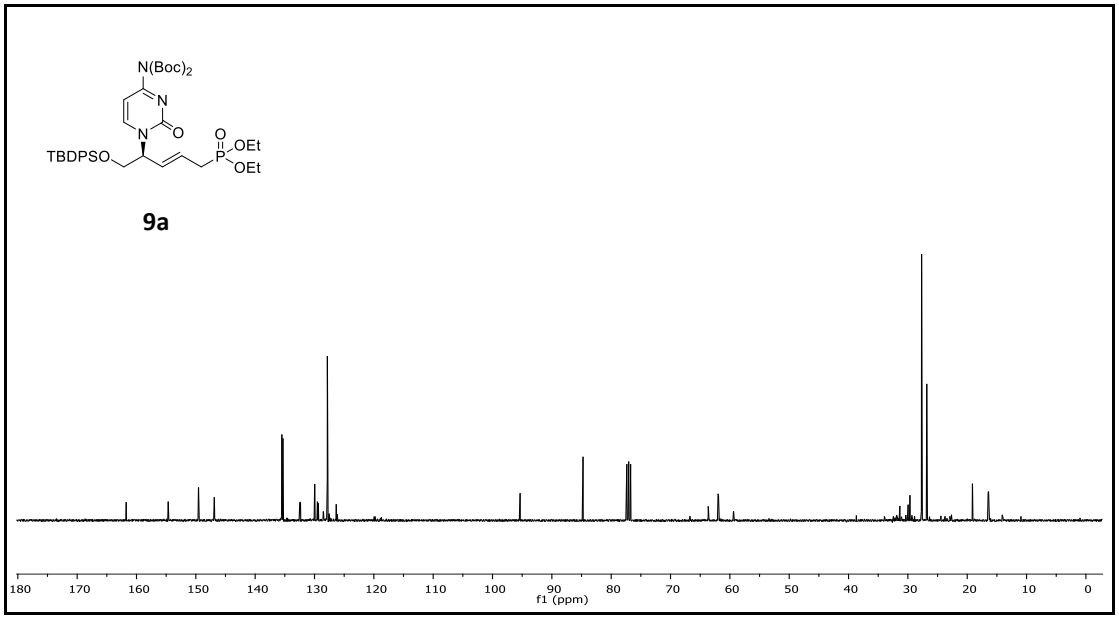
^{13}C NMR ($CDCl_3$, 100.6 MHz, δ in ppm) of (*S*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-9-(1-(*tert*-butyldiphenylsilyloxy)but-3-en-2-yl)-2-amino-6-chloro-9H-purine (8e).



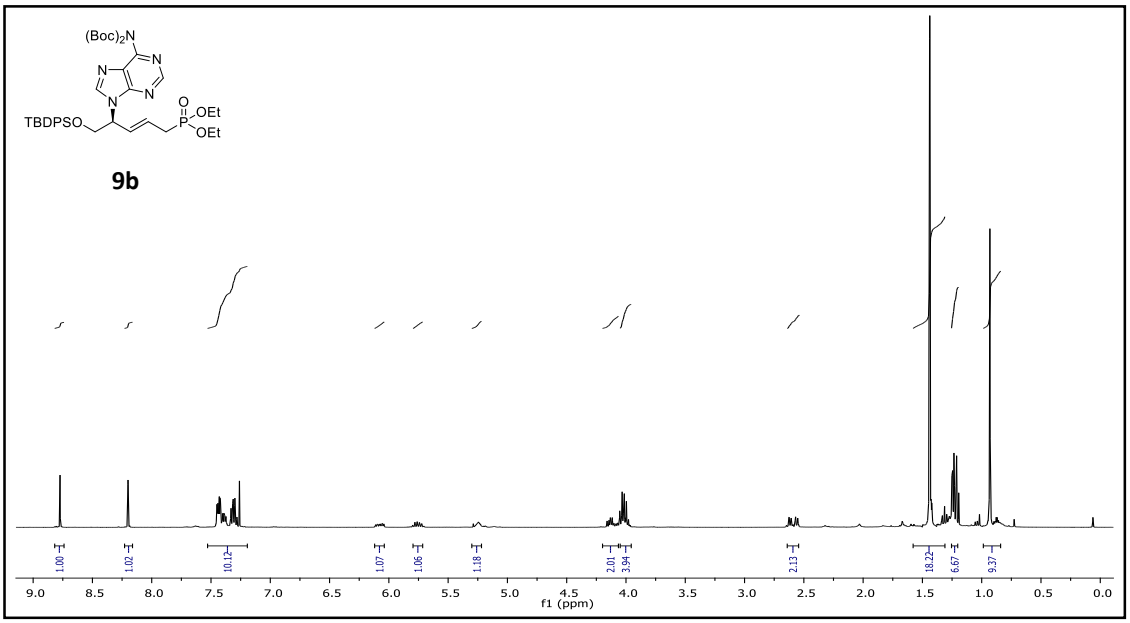
^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm) of Diethyl (2*E*,4*S*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-1-[1-(*tert*-butyldiphenylsilyloxy)-5-phosphonopent-3-en-2-yl]cytosine (9a).



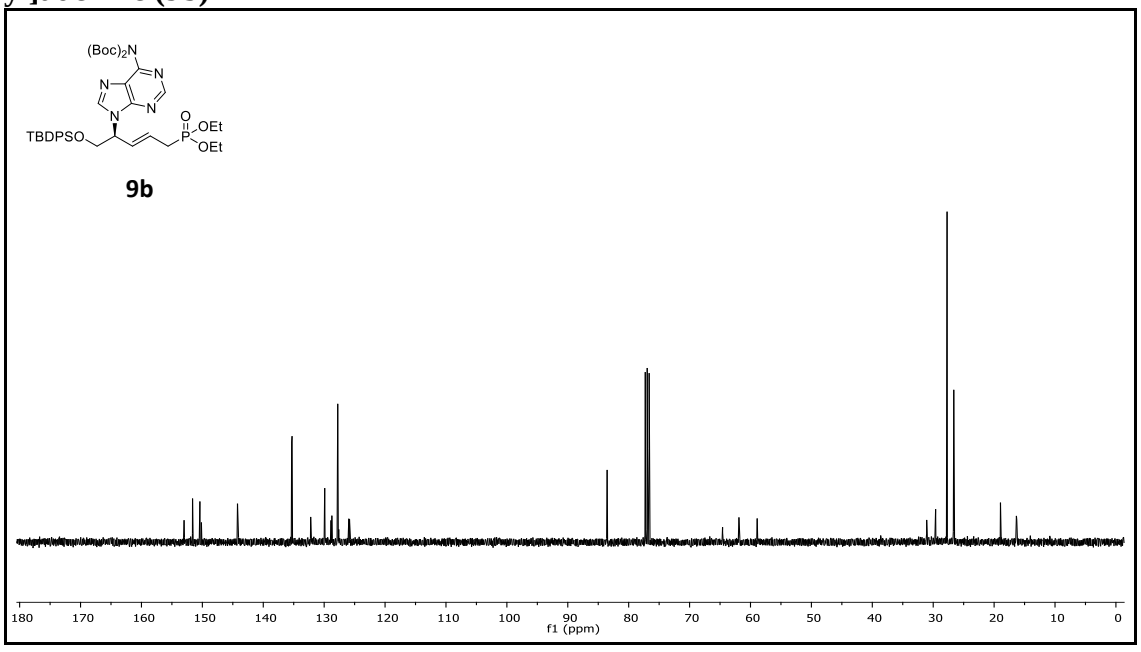
^{13}C NMR ($CDCl_3$, 100.6 MHz, δ in ppm) of Diethyl (2*E*,4*S*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-1-[1-(*tert*-butyldiphenylsilyloxy)-5-phosphonopent-3-en-2-yl]cytosine (9a).



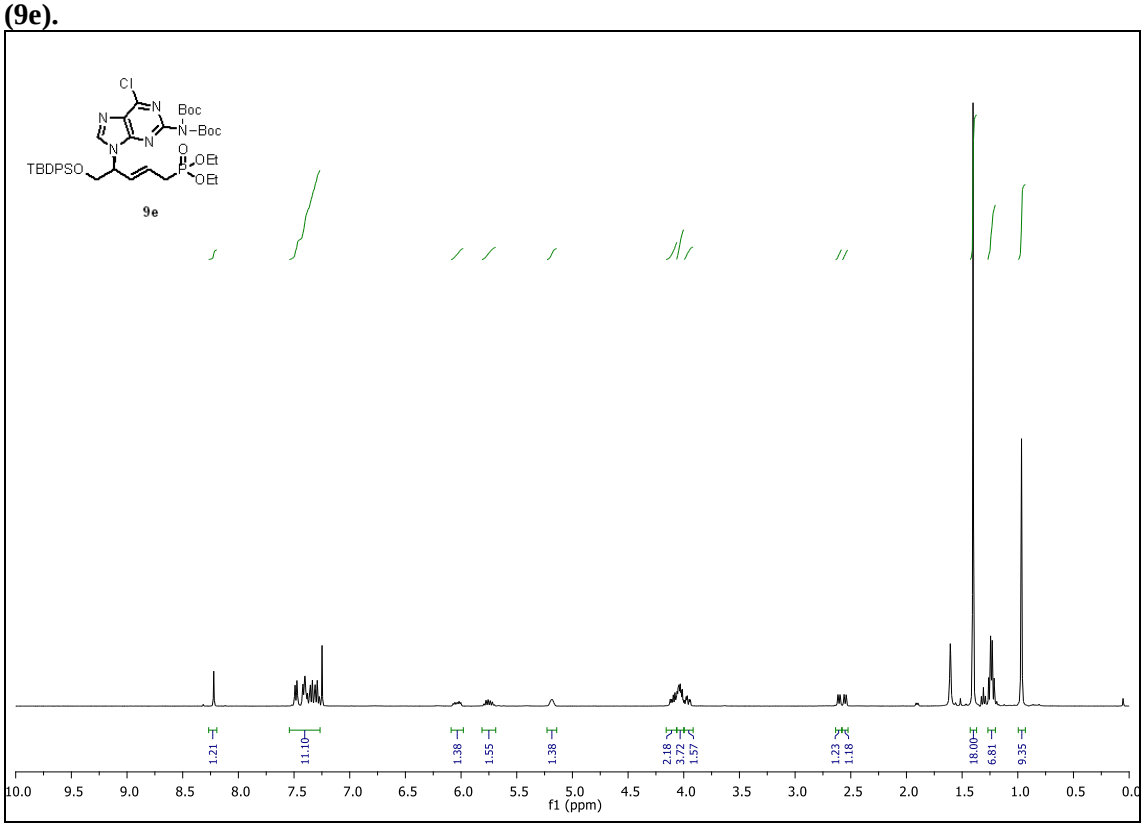
^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm) of Diethyl (2*E*,4*S*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-1-[1-(*tert*-butyldiphenylsilyloxy)-5-phosphonopent-3-en-2-yl]adenine (9b)



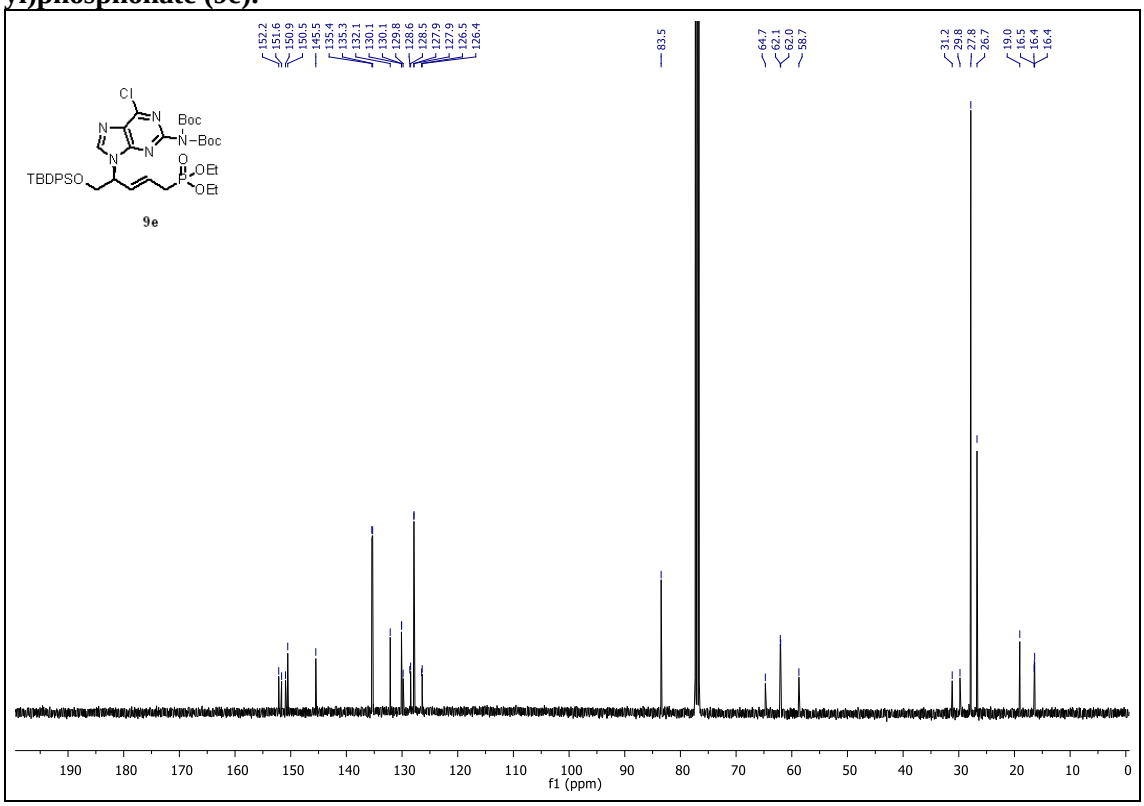
^{13}C NMR ($CDCl_3$, 100.6 MHz, δ in ppm) of Diethyl (2*E*,4*S*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-1-[1-(*tert*-butyldiphenylsilyloxy)-5-phosphonopent-3-en-2-yl]adenine (9b)



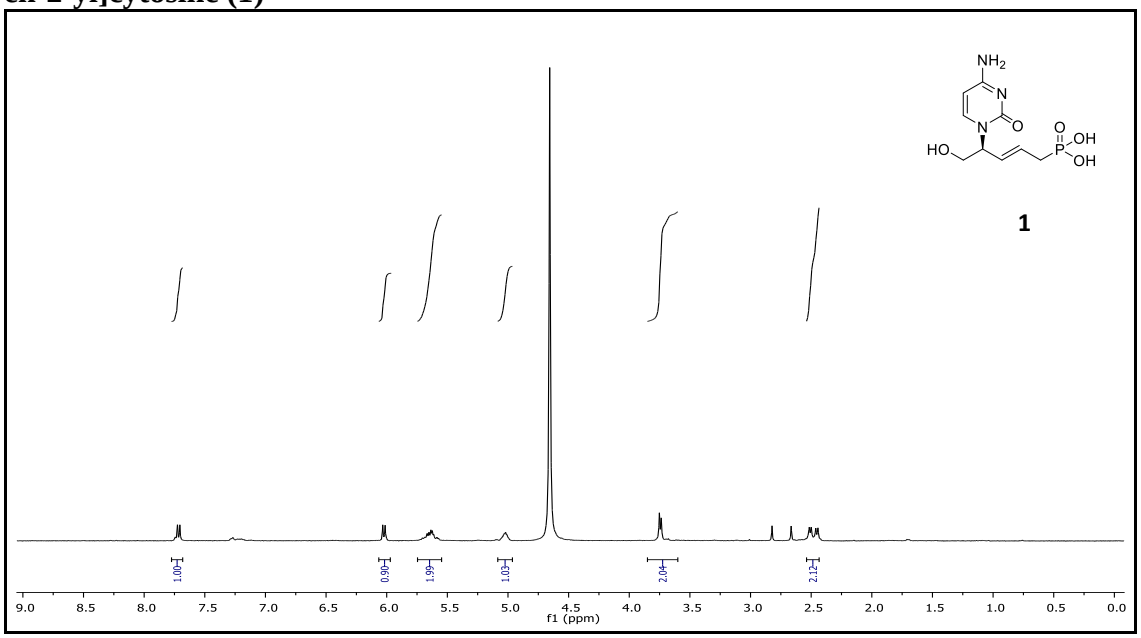
^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm) of Diethyl (*S*,*E*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-(4-(2-amino-6-chloro-9H-purin-9-yl)-5-((*tert*-butyldiphenylsilyl)oxy)pent-2-en-1-yl)phosphonate (9e).



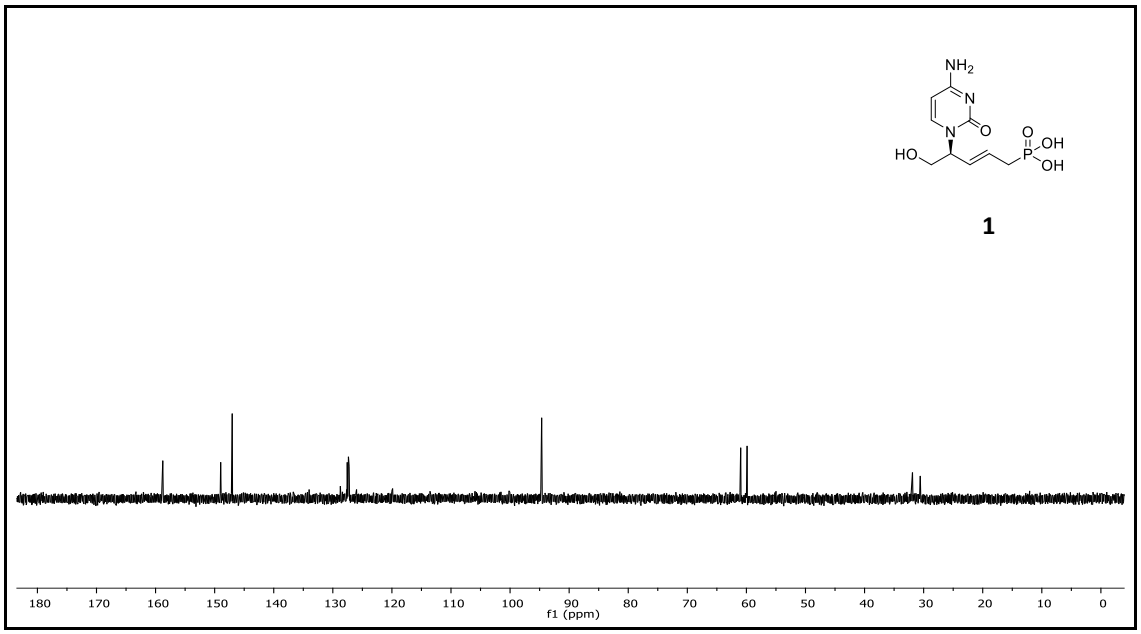
^{13}C NMR ($CDCl_3$, 100.6 MHz, δ in ppm) of Diethyl (*S*,*E*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-(4-(2-amino-6-chloro-9H-purin-9-yl)-5-((*tert*-butyldiphenylsilyl)oxy)pent-2-en-1-yl)phosphonate (9e).



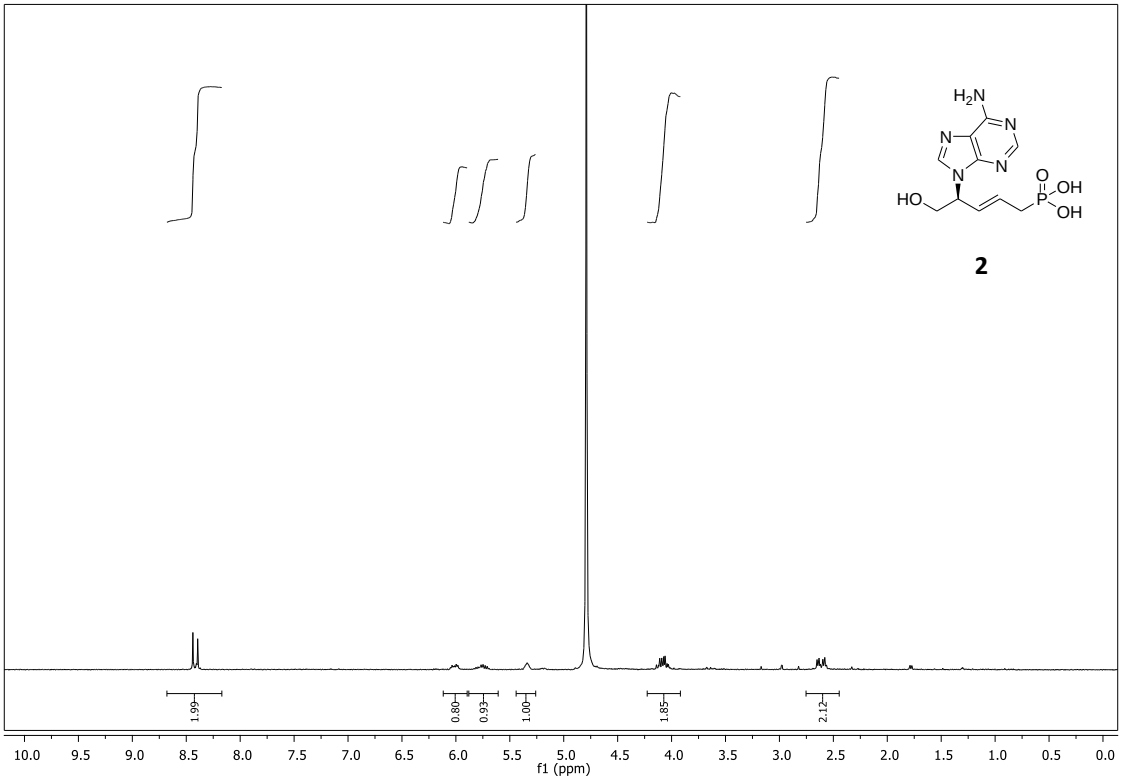
^{1}H NMR (D_2O, 400 MHz, δ in ppm) of (2*E*,4*S*)-1-[5-phosphono-1-hydroxypent-3-en-2-yl]cytosine (1)



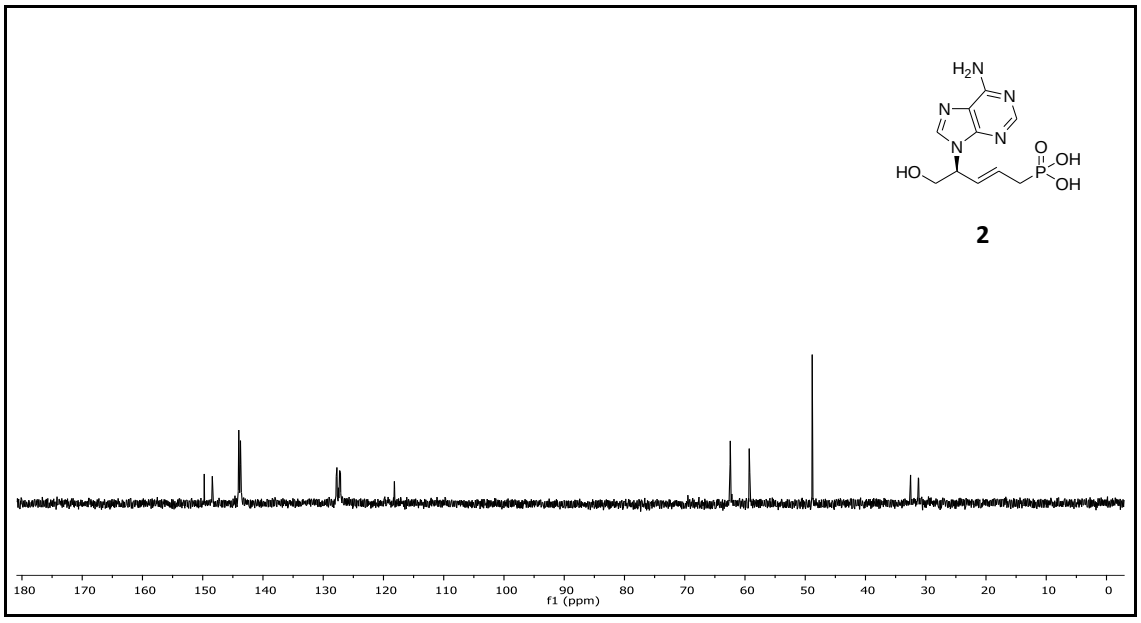
^{13}C NMR (D_2O, 100.6 MHz, δ in ppm) of (2*E*,4*S*)-1-[5-phosphono-1-hydroxypent-3-en-2-yl]cytosine (1)



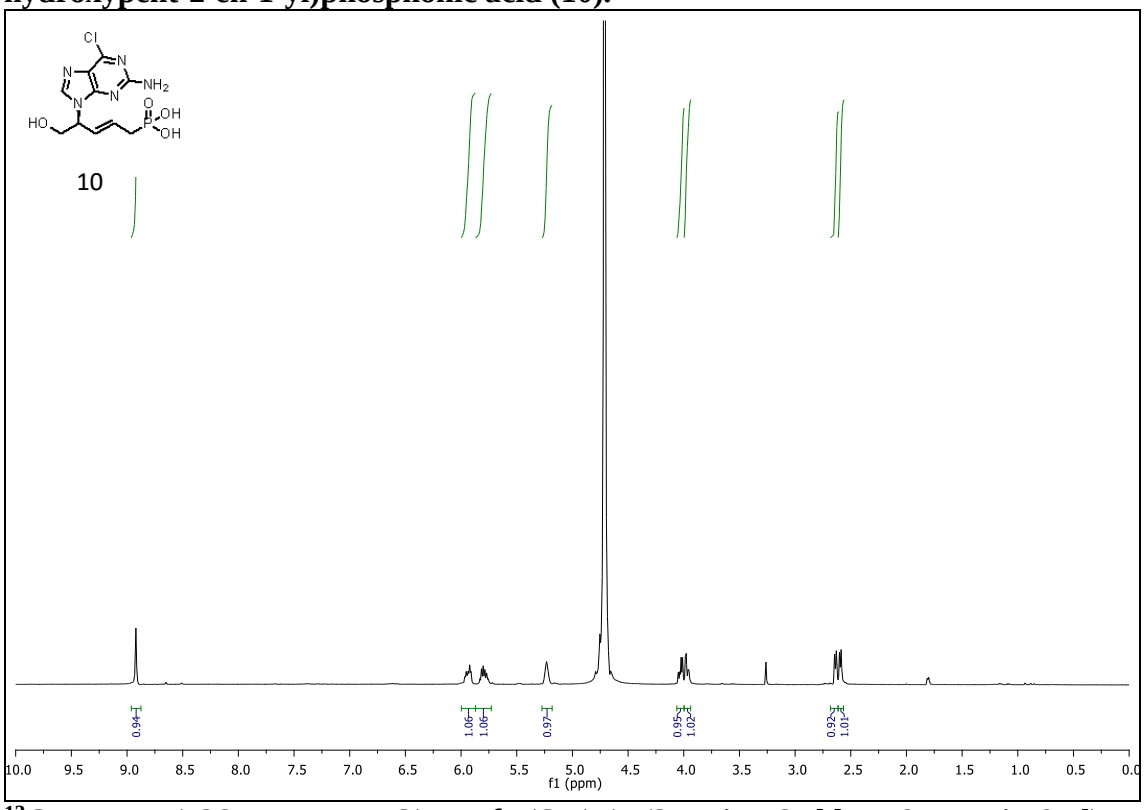
^{1}H NMR (D_2O, 400 MHz, δ in ppm) of (2*E*,4*S*)-1-[5-phosphono-1-hydroxypent-3-en-2-yl]adenine (2)



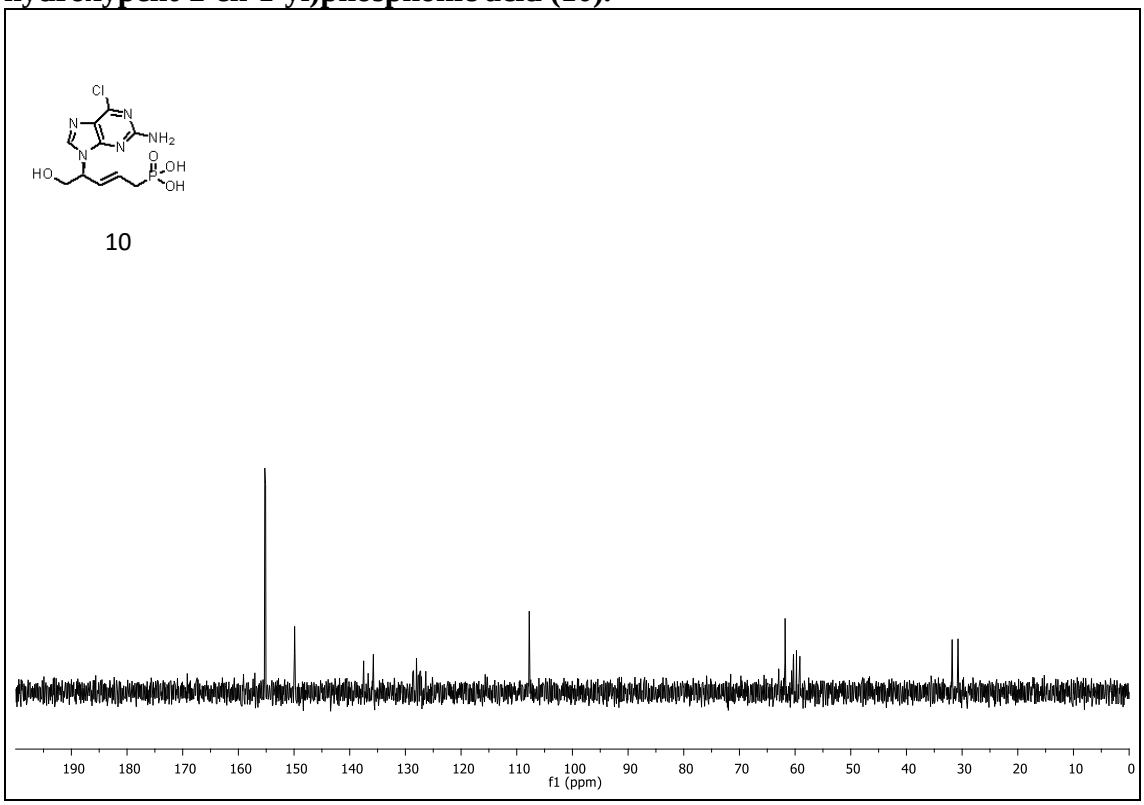
^{13}C NMR (D_2O, 100.6 MHz, δ in ppm) of (2*E*,4*S*)-1-[5-phosphono-1-hydroxypent-3-en-2-yl]adenine (2)



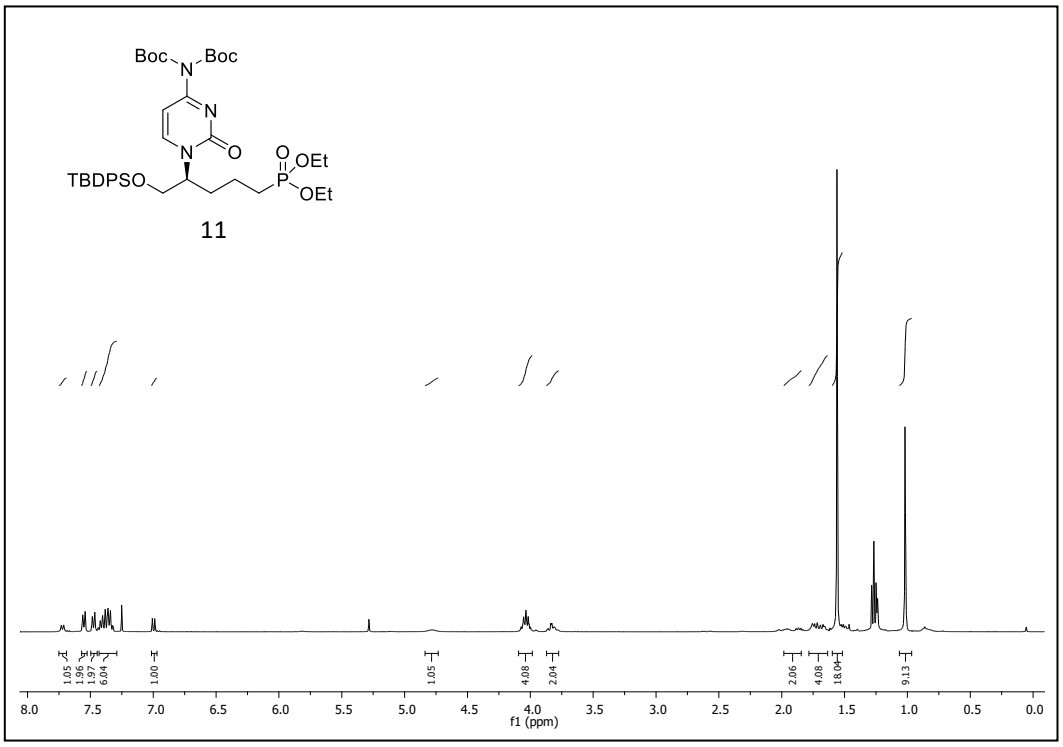
^{1}H NMR (500 MHz, D_2O) of (*S*,*E*)-(4-(2-amino-6-chloro-9H-purin-9-yl)-5-hydroxypent-2-en-1-yl)phosphonic acid (10).



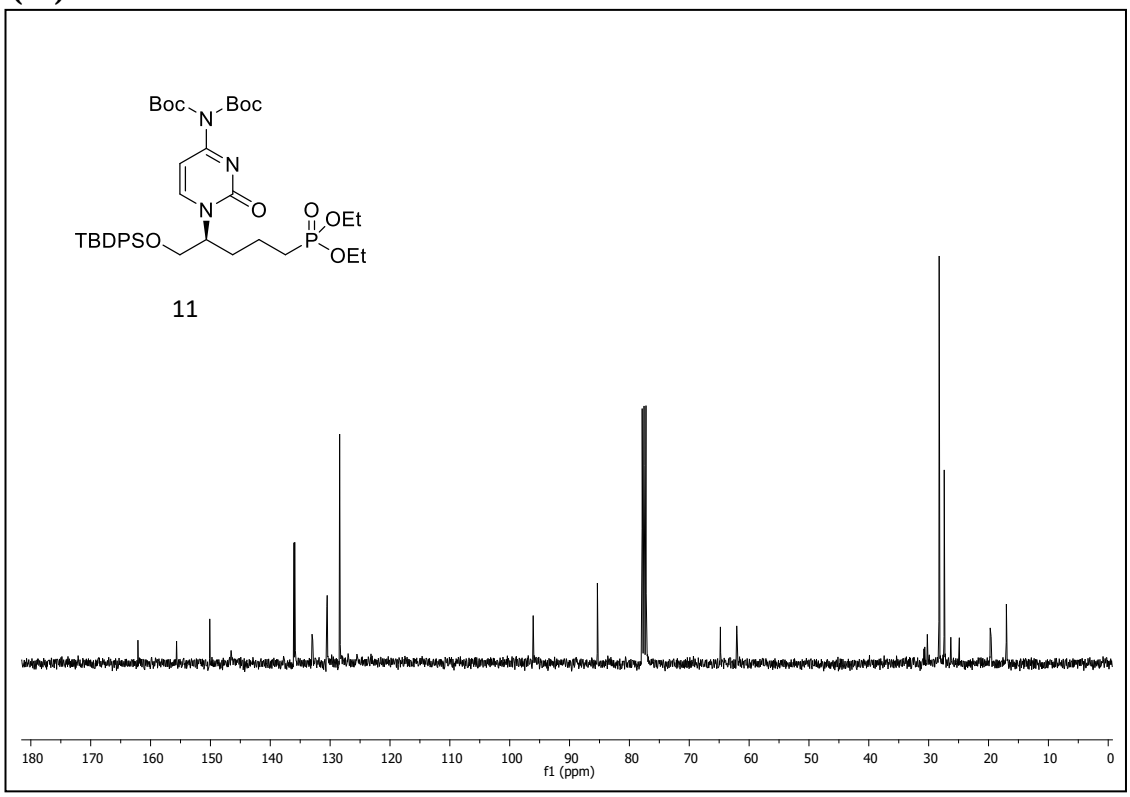
^{13}C NMR (126 MHz, D_2O) of (*S*,*E*)-(4-(2-amino-6-chloro-9H-purin-9-yl)-5-hydroxypent-2-en-1-yl)phosphonic acid (10).



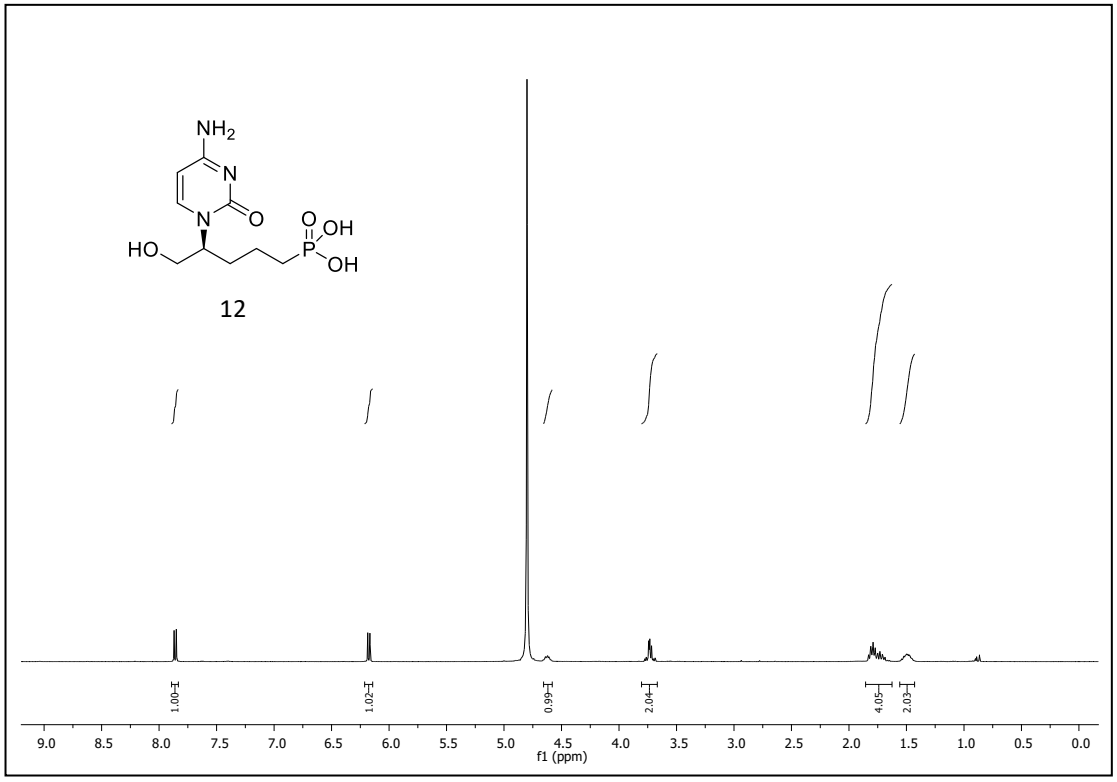
^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm) of Diethyl (*S*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-1-[1-(*tert*-butyldiphenylsilyloxy)-5-phosphonopent-2-yl]cytosine (11)



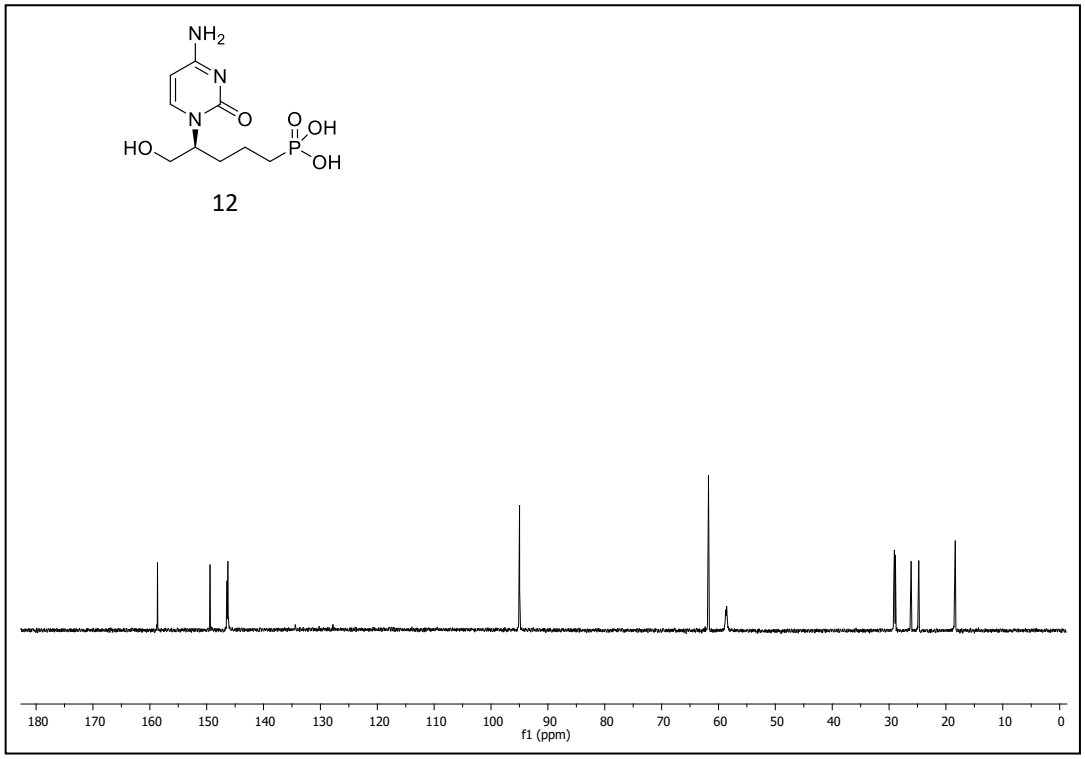
^{13}C NMR ($CDCl_3$, 100.6 MHz, δ in ppm) of Diethyl (*S*)-*N*,*N*-Bis(*tert*-butoxycarbonyl)-1-[1-(*tert*-butyldiphenylsilyloxy)-5-phosphonopent-2-yl]cytosine (11)



^{1}H NMR (D_2O, 400 MHz, δ in ppm) of (*S*)-1-[5-phosphono-1-hydroxypent-2-yl]cytosine (12)

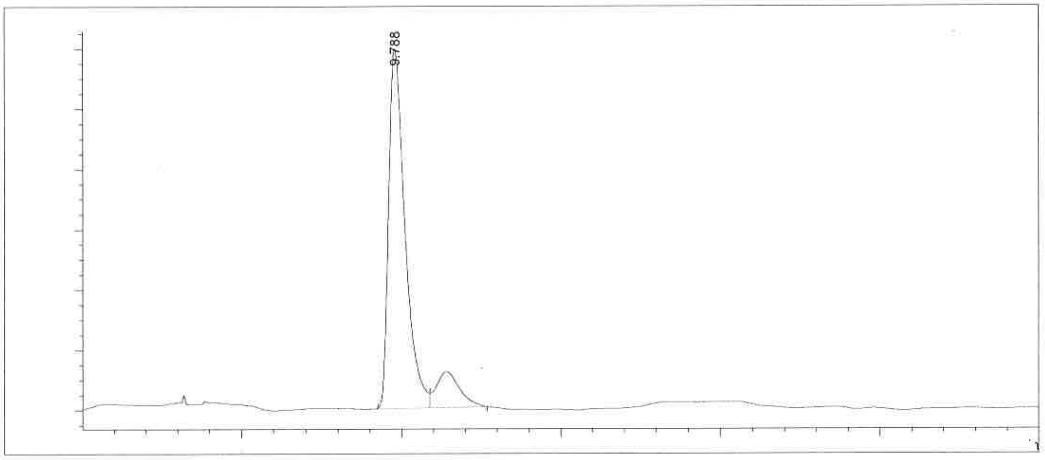


^{13}C NMR (D_2O, 100.6 MHz, δ in ppm) of (*S*)-1-[5-phosphono-1-hydroxypent-2-yl]cytosine (12)



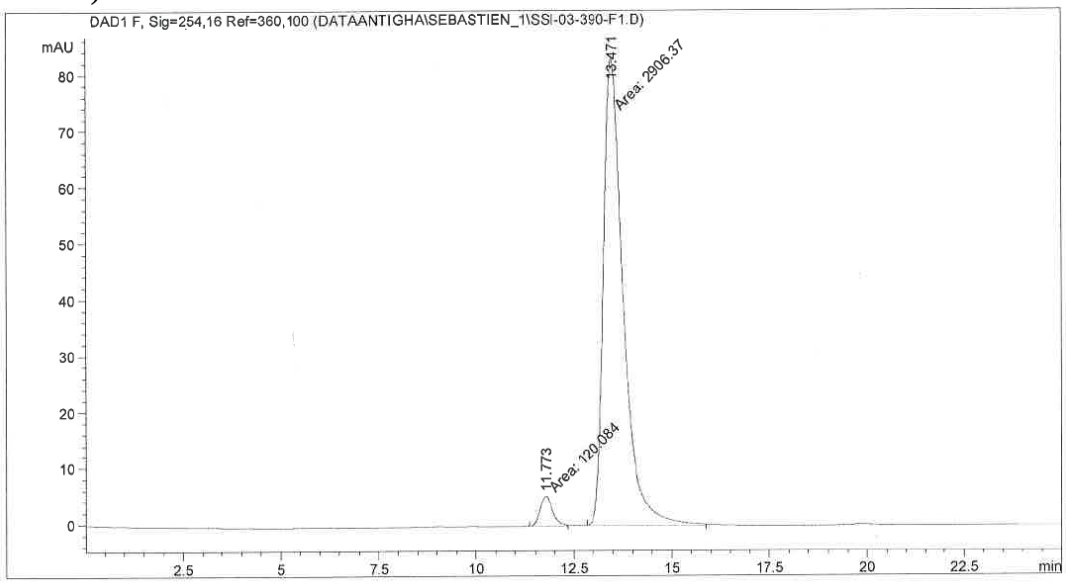
HPLC TRACES

ent-7a: Daicel Chiralcel OD-H, *n-hexane-^{i}PrOH, 90:10*, flow = 0.5 mL/min, detection, uv 210 nm; retention times (min), 9.79, 11.42, t_R(R) = 9.79 min and t_R(S) = 11.42 min): **75 %*ee***



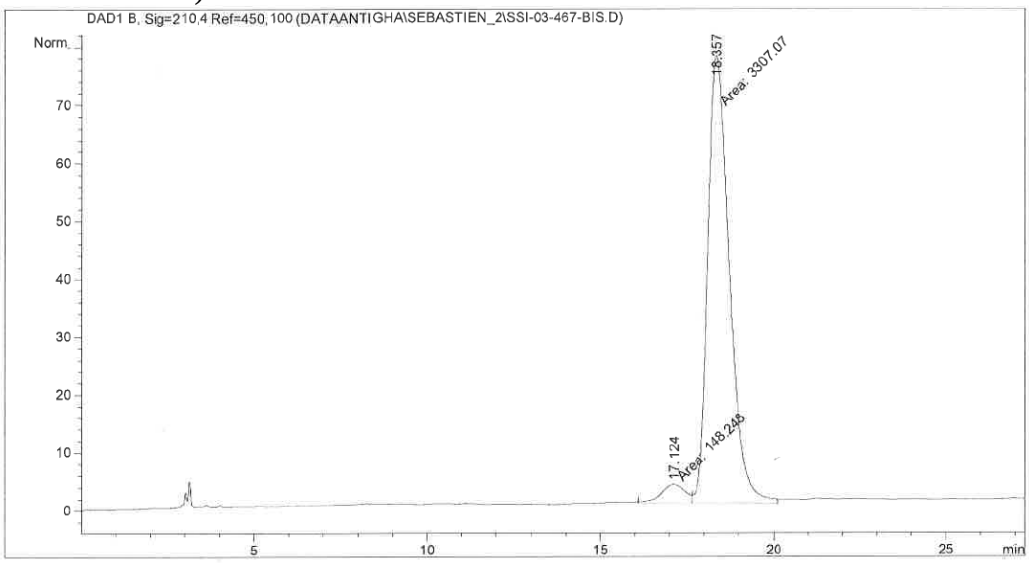
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.788	BB	0.5376	4273.54395	119.39807	87.3571
2	11.415	BB	0.7522	618.49707	12.02264	12.6429

7b: Daicel Chiralcel OD-H, *n-hexane-^{i}PrOH* 85:15, flow = 0.5 mL/min, detection, uv 254 nm; retention times (min), 11.77, 13.47, t_R(R) = 11.77 min and t_R(S) = 13.47 min): **92 %*ee***



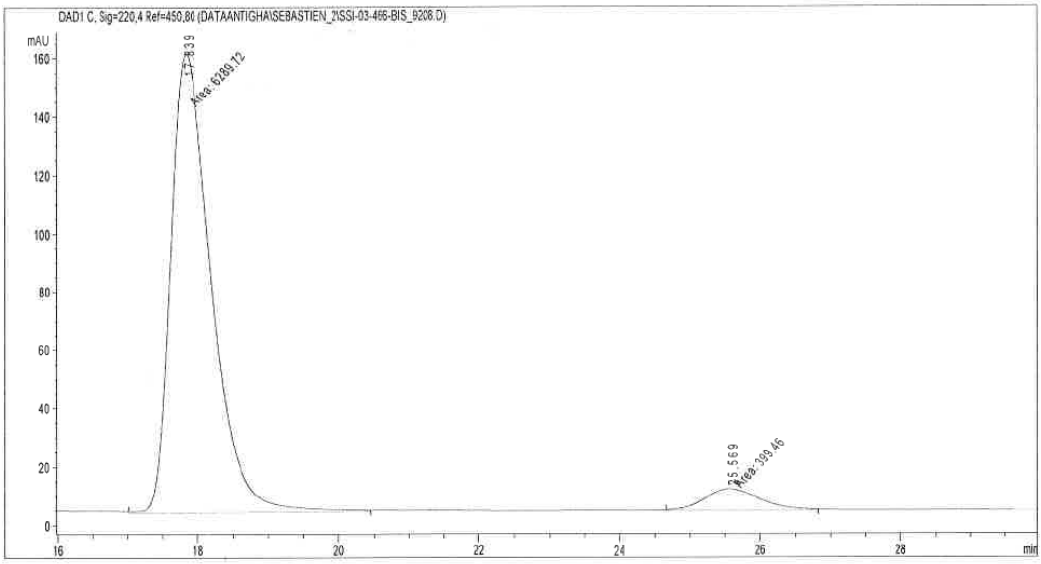
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.773	MM	0.3749	120.08413	5.33867	3.9678
2	13.471	MM	0.5834	2906.37036	83.02957	96.0322

ent-7c: Daicel Chiralcel OD-H, *n-hexane-^{i}PrOH, 90:10*, flow = 1 mL/min, detection, uv 210 nm; retention times (min), 17.12, 18.36, t_R(R) = 17.12 min and t_R(S) = 18.36 min): **91.4 %*ee***



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.124	MF	0.7821	148.24796	3.15906	4.2904
2	18.357	FM	0.7150	3307.07349	77.08272	95.7096

ent-7d: Daicel Chiralcel OD-H, *n-hexane-^{i}PrOH, 92:08,* flow = 1.0 mL/min, detection, uv 220 nm; retention times (min), 17.84, 25.57, t_R(R) = 17.84 min and t_R(S) = 25.57 min): **88 %*ee***



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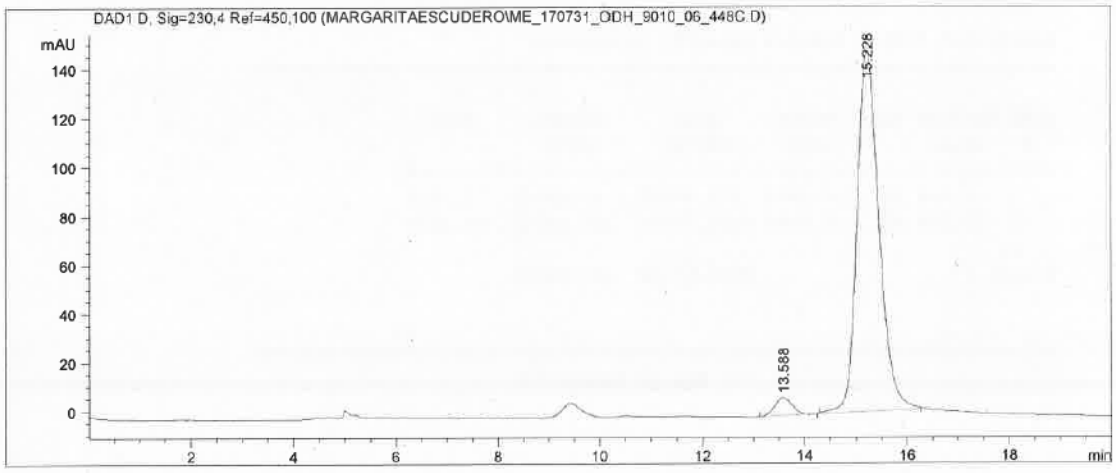
1	17.839 MM	MM	0.6607	6289.72	156.45424	94.0283
2	25.569 MM	MM	0.9269	399.46	7.58116	5.9717

7e: Daicel Chiralcel OD-H, *n-hexane-^{i}PrOH* 90:10, flow = 0.6 mL/min, detection, uv 230 nm; retention times (min), 13.5, 15.2, t_R(R) = 13.5 min and t_R(S) = 15.2 min): **92 %*ee***



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.588	BB	0.3636	172.97897	7.26869	3.7616
2	15.228	BB	0.4599	4425.59814	147.54933	96.2384