# NUCLEOSIDE PHOSPHORAMIDATE PRODRUGS

The essential material for this application, including the background of the invention, the disclosure of the invention, including Preparations and Examples, is incorporated by reference from pending and commonly owned U.S. Provisional application No. 60/909,315, filed March 30, 2007, as well as references cited therein, under the provisions of MPEP 608.01(p).

EXAMPLES

Example numbers **13-55** are prepared using similar procedures described for examples **5-8**, as disclosed in U.S. Provisional application No. 60/909,315. The identification and NMR/MS details are shown below:
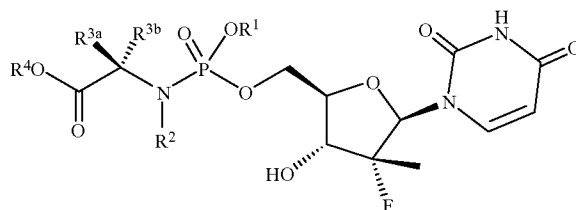
Example	R^1	R^2	R^{3a}	R^{3b}	R^4
13	Ph	H	H	Me	Et
14	1-Napth	H	H	Me	Bn
15	Ph	H	H	H	Me
16	2,4-Cl-Ph	H	H	Me	Me
17	1-Napth	H	H	Me	Me
18	Ph	*	H	*	Me
19	Ph	H	H	Me	n-Bu
20	Ph	H	H	Me	Bn
21	4-F-Ph	H	H	Me	Me
22	4-Cl-Ph	H	H	Me	Me
23	3,4-Cl-Ph	H	H	Me	Me
24	Ph	H	H	Me	2-Bu
25	Ph	H	H	Me	i-Pr
26	4-MeO-Ph	H	H	Me	n-Bu
27	4-F-Ph	H	H	Me	Et
28	4-F-Ph	H	H	Me	i-Pr
29	4-F-Ph	H	H	Me	Bn
30	4-MeO-Ph	H	H	Me	i-Pr
31	2-Cl-Ph	H	H	Me	Bn
32	2,4-Cl-Ph	H	H	Me	n-Bu
33	4-Me-Ph	H	H	Me	i-Pr
34	4-F-Ph	H	H	Me	n-Bu
35	3,4-diCl-Ph	H	H	Me	Et
36	2-Cl-Ph	H	H	Me	i-Pr
37	4-MeO-Ph	H	H	Me	Bn
38	Ph	H	H	Me	n-Pen

Example	R^1	R^2	R^{3a}	R^{3b}	R^4
39	4-Cl-Ph	H	H	Me	i-Pr
40	4-Cl-Ph	H	H	Me	n-Bu
41	4-Cl-Ph	H	H	Me	Et
42	4-Me-Ph	H	H	Me	n-Bu
43	4-Me-Phe	H	H	Me	Bn
44	Ph	H	H	Et	Me
45	Ph	H	H	Me	4-F-Bn
46	4-Cl-Ph	H	H	Me	n-Bu
47	Ph	H	H	Me	3-Me-1-Bu
48	3,4-diCl-Ph	H	H	Me	Bn
49	Ph	H	H	Me	c-Hex
50	Ph	H	Me	H	n-Bu
51	Ph	H	Me	H	i-Pr
52	Ph	H	Me	H	Bn
53	2-Cl-Ph	H	H	Me	n-Bu
54	4-Br-Ph	H	H	Me	i-Pr

*R^2 and R^{3b} together are –(CH$_2$)$_3$– as derived from L-proline

Example	NMR/MS
13	1H NMR (DMSO-d6) δ 1.12-1.16 (m, 3H), 1.20-1.28(m,6H), 3.70-3.90 (m, 2H), 4.00-4.08 (m, 3H), 4.18-4.45 (m, 2H), 5.52-5.58 (m, 1H), 5.85-5.98 (m, 1H), 6.00-6.20 (m, 2H), 7.16-7.23 (m, 3H), 7.37-7.40 (m, 2H) , 7.54-7.60 (m, 1H), 11.54 (s.1H) ; MS, m/e 516.1 (M+1)+
14	1H NMR (DMSO-d6) δ 1.18-1.30 (m, 6H), 3.78-4.10 (m, 3H), 4.38-4.49 (m, 2H), 4.99-5.11 (m, 2H), 5.28-5.40 (m, 1H), 5.85-6.10 (m, 2H), 6.30-6.41 (m, 1H), 7.28-7.32 (m, 5H), 7.41-7.60 (m, 5H), 7.73-7.76(m, 1H) , 7.94-8.11(m, 1H) , 8.13-8.15(m, 1H) , 11.50 (s.1H) ; MS, m/e 628.4 (M+1)+
15	1H NMR (DMSO-d6) δ 1.22 (d, J=22.4 Hz, 3H), 3.59(s, 3H), 3.63-3.69 (m, 2H), 3.74-3.8(m, 1H), 4.02(d, J=11.2 Hz, 1H), 4.23-4.28(m, 1H), 4.40-4.43 (m, 1H), 5.57-5.60 (m, 1H), 5.89(d, J=6.8 Hz, 1H), 6.00-6.06(m, 2H), 7.15-7.23 (m, 3H), 7.35-7.39 (m, 2H),7.52(d, J=8 Hz, 1H), 11.52(s, 1H) ; MS, m/e 487.97 (M+1)+
16	1H NMR (DMSO-d6) δ 1.22-1.28 (m, 6H), 3.57-3.60 (m, 3H), 3.84-3.92 (m, 2H), 4.00-4.04 (m, 1H), 4.31-4.44 (m, 2H), 5.54-5.61 (m, 1H), 5.85-6.10 (m, 2H), 6.32-6.43 (m, 1H), 7.44-7.54 (m, 3H), 7.72-7.75 (m, 1H), 11.54 (s.1H) ; MS, m/e 570.2 (M+1)+
17	1H NMR (DMSO-d6) δ 1.15-1.27 (m, 6H), 3.51-3.55 (d, 3H), 3.85-3.96 (m, 2H), 4.00-4.10(m, 1H), 4.30-4.46 (m, 2H), 5.31-5.39 (m, 1H), 5.89-6.05 (m, 2H), 6.22-6.34 (m, 1H), 7.44-7.60 (m, 5H), 7.73-7.77 (m, 1H), 7.93-7.96 (m, 1H), 8.12-8.14 (m, 1H),11.50(s.1H) ; MS, m/e 552.1 (M+1)+
18	1H NMR (DMSO-d6) δ 1.19 (d, J=22.8 Hz, 3H), 1.69-1.84 (m, 3H), 1.99-2.04 (m, 1H), 3.16-3.21 (m, 2H), 3.58 (s, 3H), 3.68-3.8 (m, 1H), 4.00 (m, 1H), 4.01-4.13 (m, 1H), 4.22-4.25 (m, 1 H), 4.5 (d, J = 11.2 Hz, 1H), 5.54 (d, J = 8.0 Hz, 1H), 5.86 (s, 1H), 5.6 (d, J = 19.6 Hz, 1H), 7.15-7.2 (m, 3H), 7.34 (t, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 1H), 11.38 (s, 1H) ; MS, m/e 527.93(M+1)+

Example	NMR/MS
19	1H NMR (DMSO-d6) δ 0.80-0.90 (m, 3H), 1.20-1.35 (m, 8H), 1.48-1.55 (m, 2H), 3.78-3.88 (m, 2H), 3.95-4.08 (m, 3H), 4.22-4.45 (m, 2H), 5.55-5.57(t, 1H), 5.85-6.18 (m, 3H), 7.14-7.23 (m, 3H), 7.35-7.40 (m, 2H), 7.51-7.60 (d, 1H), 11.50 (s.1H) ; MS, m/e 544.2 (M+1)+
20	1H NMR (DMSO-d6) δ 1.20-1.30 (m, 6H), 3.72-4.05 (m, 3H), 4.23-4.27 (m, 1H), 4.32-4.45 (m, 1H), 5.07-5.10(t, 2H), 5.52-5.56(t , 1H), 5.86-6.10 (m, 2H), 6.13-6.21(m,1H), 7.15-7.21 (m, 3H), 7.29-7.40 (m, 7H), 7.51-7.56 (d, 1H), 11.50 (s.1H) ; MS, m/e 578.2 (M+1)+
21	1H NMR (DMSO-d6) δ 1.28-1.34 (m, 6H), 3.65(d, J= 4 Hz, 3H), 3.85-3.96 (m, 2H), 4.06-4.12 (m, 1H), 4.30-4.34 (m,1H), 4.40-4.47 (m, 1H), 5.62-5.67 (m, 1H), 5.94-6.01(m, 1H), 6.09 (d, J=18.8 Hz, 1H), 6.17-6.26 (m, 1H), 7.27-7.33(m, 4H), 7.62 (d, J = 7.6 Hz, 1H), 11.61 (s, 1H) ; MS, m/e 519.94(M+1)+
22	1H NMR (DMSO-d6) δ 1.22-1.28 (m, 6H), 3.58 (d, 2H), 3.70-3.95(m,2H), 3.95-4.08 (m,1H), 4.23-4.45 (m, 2H), 5.55-5.61(t , 1H), 5.85-6.10 (m, 2H), 6.15-6.23(m,1H), 7.20-7.26 (m, 2H), 7.43-7.46 (m, 2H), 7.54-7.57 (d, 1H), 11.50 (s.1H) ; MS, m/e 536.1 (M+1)+
23	1H NMR (DMSO-d6) δ 1.13 (m, 6H), 3.49 (s, 3H), 3.61-3.85 (m, 2H), 3.90-3.93 (m, 1H), 4.16-4.22 (m, 1H), 4.27-4.31 (m, 1H), 5.47-5.52 (m, 1H), 5.82 (d, J = 11.6 Hz, 1H), 5.93(d, J = 19.2 Hz, 1H), 6.15-6.25 (m, 1H), 7.13 (t, J = 9.6 Hz, 1H), 7.43 (d, J = 12Hz, 2H), 7.57 (d, J = 6.0 Hz, 1H), 11.43(s, 1H) ; MS, m/e 569.85 (M+1)+
24	1H NMR (DMSO-d6) δ 0.83 (d, J = 6.8 Hz, 6H), 1.20-1.26 (m, 6H), 1.79-1.86 (m, 1H), 3.73-3.90 (m, 4H), 4.01 (t, J = 11.2 Hz, 1H), 4.21-4.28 (m, 1H), 4.33-4.42 (m, 1H), 5.54 (t, J = 7.6 Hz, 1H), 5.85-5.92 (m, 1H), 5.99-6.13 (m, 2H), 7.19 (t, J = 8 Hz, 3H), 7.36 (t, J = 7.6 Hz, 2H), 7.53 (d, J = 7.6 Hz, 1H), 11.52 (s, 1H) ; MS, m/e 544.00 (M+1)+
25	1H NMR (DMSO-d6) δ 1.13-1.28 (m, 12H), 3.74-3.81 (m, 2H), 3.95-4.08 (m,1H), 4.20-4.45 (m, 2H), 4.83-4.87 (m, 1H), 5.52-5.58 (m, 1H), 5.84-6.15 (m, 3H), 7.17-7.23 (m, 3H), 7.35-7.39 (m, 2H), 7.54-7.57 (m, 1H), 11.50 (s.1H) ; MS, m/e 530.2 (M+1)+
26	1HNMR (400MHz, DMSO): δ =0.78-0.82 (m, 3H), 1.29-1.47 (m, 8H), 1.49-1.54 (m, 2H), 3.66-3.87 (m, 5H), 3.96-4.02 (m, 3H), 4.21-4.39 (m, 2H), 5.57 (t, J= 12.0Hz, 1H), 5.84-6.05 (m, 3H), 6.90 (dd, J1 =8.0Hz, J2=4.0Hz, 2H), 7.09-7.14 (dd, J1=16.0Hz, J2=4.0Hz, 2H), 7.55 (d, J =8.0Hz, 1H), 11.48-11.62 (s, 1H)
27	1H NMR (DMSO-d6) δ 1.12-1.28 (m, 9H), 3.72-3.94(m,2H) ,3.98-4.10 (m,3H), 4.21-4.42(m,2H), 5.55-5.61 (t, 1H), 5.85-6.20 (m, 3H), 7.18-7.25 (m,4H), 7.55-7.58 (d, 1H), 11.50 (s.1H) ; MS, m/e 533.90 (M+1)+
28	1H NMR (DMSO-d6) δ 1.13-1.30 (m, 12H), 3.74-3.85(m,2H) ,3.98-4.06 (m,1H), 4.23-4.41(m,2H), 4.83-4.87 (m, 1H), 5.55-5.61 (t, 1H), 5.85-6.12 (m, 3H), 7.18-7.24 (m,4H), 7.55-7.58 (d, 1H), 11.50 (s.1H) ; MS, m/e 547.91 (M+1)+
29	1H NMR (DMSO-d6) δ 1.10-1.23 (m, 6H), 3.65-3.89(m,3H) ,4.10-4.30 (m,2H), 4.96-5.00(m,2H), 5.46-5.50 (t, 1H), 5.75-5.96 (m, 2H), 6.04-6.12(m,1H), 7.05-7.11 (m,4H), 7.20-7.24 (d, 5H), 7.42-7.45(d,1H), 11.50 (s.1H) ; MS, m/e 595.94 (M+1)+

Example	NMR/MS
30	1HNMR (400MHz, DMSO): δ=1.15-1.27 (m, 12H), 3.71-3.89 (m, 5H), 3.98-4.02 (m, 1H), 4.22-4.25 (m, 1H), 4.33-4.39 (m, 1H), 4.84-4.87 (m, 1H), 5.57 (t, J= 12.0Hz, 1H), 5.91-6.03 (m, 3H), 6.90 (d, J= 8.0Hz, 2H), 7.09-7.14 (m, 2H), 7.55 (d, J= 8.0Hz, 1H), 11.51 (s, 1H)
31	1H NMR (DMSO-d6) δ 1.23 (m, 6 H), 3.93-4.00 (m, 3 H), 4.27-4.40 (m, 2H), 5.0(t, J= 7.2 Hz, 2 H), 5.53 (m ,1 H), 5.80-6.0(m , 2 H), 6.30(m, 1H), 7.15 (d, J= 2.4 Hz, 1 H), 7.27 (m, 6 H), 7.51 (m, 3 H), 11.5 (s, 1 H) ; MS, m/e 579.87(M+1)+ / 596.78 (M+18)+
32	1H NMR (DMSO-d6) δ=0.82 (m, 3 H),1.23 (m, 8 H) , 1.47 (m, 2 H), 3.86 (m, 2 H), 3.84 (m, 3 H),4.27-4.43 (m, 2H), 5.5 (m , 1 H), 6.02 (m ,2 H), 6.35(m, 1H), 7.44 (m, 3 H), 7.77 (m, 1 H), 11.5 (s, 1 H) ; MS, m/e 611.87(M+1)+
33	1H NMR (DMSO-d6) δ 1.14-1.27 (m, 12H), 2.17-2.26 (m, 3H), 3.73-3.82 (m, 1H), 3.99-4.02 (m, 1H), 4.23-4.26 (m, 1H), 4.37-4.40 (m, 1H), 4.82-4.88 (m, 1H), 5.52-5.58 (m, 1H), 5.85-6.07 (m, 3H), 7.01-7.20 (m, 4H), 7.55 (d, J = 16Hz, 1H), 11.51 (s, 1H) ; MS, m/e 543.98 (M+1)+; 1108.86 (2M+23)+
34	1H NMR (DMSO-d6) δ 0.82-0.89 (m,3H), 1.20-1.31 (m, 8H), 1.48-1.53 (m,2H), 3.77-3.90 (m,2H) ,3.95-4.10 (m,3H), 4.21-4.45(m,2H), 5.56-5.61 (t, 1H), 5.83-6.20 (m, 3H), 7.18-7.25 (m,4H), 7.55-7.58 (d, 1H), 11.50 (s.1H) ; MS, m/e 584.1 (M+23)+
35	1H NMR (DMSO-d6) δ1.12-1.31 (m, 9H), 3.77-3.92 (m,2H), 3.95-4.08 (m,3H), 4.21-4.45(m,2H), 5.56-5.62 (t, 1H), 5.80-6.11 (m, 2H), 6.18-6.33(m,1H), 7.18-7.25 (m,1H), 7.49-7.56 (d, 2H), 7.62-7.67(m,1H), 11.50 (s.1H) ; MS, m/e 606.1 (M+23)+
36	1HNMR (400MHz, DMSO): δ =1.12-1.16 (m, 6H), 1.21-1.27 (m, 6H), 3.79-3.85 (m, 2H), 4.00-4.07 (m, 1H), 4.28-4.32 (m, 1H), 4.38-4.43 (m, 1H), 4.83-4.87 (m, 1H), 5.56 (dd, J1=16.0Hz, J2=8.0Hz, 1H), 5.85-6.12 (m, 2H), 6.20-6.33 (m, 1H), 7.19-7.22 (m, 1H), 7.33 (t, J= 16.0Hz, 1H), 7.48-7.55 (m, 3H), 11.55 (s, 1H)
37	1HNMR(400MHz,DMSO): δ=1.19-1.26 (m, 6H), 3.69-3.70 (s, 3H), 3.87 (m, 2H), 3.99 (m, 1H), 4.20-4.21 (m, 1H), 4.35 (m, 1H), 5.07-5.09 (m, 2H), 5.54 (t, J = 16.0Hz, 1H), 5.85-5.92 (m, 1H), 6.04-6.10 (m, 2H), 6.86 (d, J= 8.0Hz, 2H), 7.09 (dd, J1=16.0Hz, J2=4.0Hz, 2H), 7.30-7.34 (m, 5H), 7.53 (s, 1H), 11.52 (s, 1H)
38	1H NMR (DMSO-d6) δ 0.79-0.81 (m, 3H), 1.17-1.23 (m, 10H), 3.74-3.81 (m, 2H), 3.94-3.96 (m, 3H), 4.19-4.36 (m, 2H), 5.49-5.54 (m, 1H), 5.87-6.08 (m,3H), 7.14-7.33 (m, 3H), 7.31-7.35 (m, 2H), 7.51 (d, J = 8Hz, 1H), 11.51 (s, 1H) ; MS, m/e 557.9 (M+1)+; 1136.88 (2M+23)+
39	1H NMR (DMSO-d6) δ 1.04-1.19 (m, 12H), 3.76-3.80 (m , 2H), 3.98-4.08 (m, 1H), 4.42-4.42 (m, 2H), 4.82-4.85 (m, 1H), 5.55-5.60 (m, 1H), 5.80-6.20 (m,3H),7.20-7.25(m, 2H), 7.43 (d, J = 8.8Hz, 1H), 7.54 (d, J = 8Hz, 1H), 11.51 (s, 1H) ; MS, m/e 563.88 (M+1)+; 1148.73 (2M+23)+

Example	NMR/MS
40	1H NMR (DMSO-d6) δ 0.85 (t, J = 7.2 Hz, 3H), 1.22-1.33 (m, 8H),1.45-1.53 (m, 2H), 3.80-3.87 (m, 2H), 3.96-4.04 (m, 3H), 4.24-4.27 (m, 1H), 4.35-4.39 (m, 1H), 5.56-5.61 (m, 1H), 5.82-6.11 (m, 2H), 6.15-6.18 (m, 1H), 7.20-7.56 (m, 4H), 7.51-7.57 (m.1H) , 11.54 (s, 1H); MS, m/e577.95(M+1)+
41	1H NMR (DMSO-d6) δ 1.14 (t, J = 7.0Hz, 3H), 1.20-1.28 (m, 6H),3.77-3.88 (m, 2H), 3.99-4.07 (m, 3H), 4.24-4.28 (m, 1H), 4.34-4.43 (m, 1H), 5.56-5.61 (m, 1H), 5.86-6.13 (m, 2H), 6.15-6.24 (m, 1H), 7.20-7.26 (m, 2H), 7.44 (d, J = 7.6Hz, 2H) , 7.55 (d, J = 7.6Hz, 1H), 11.55 (s, 1H); MS, m/e549.11(M+1)+
42	1H NMR (DMSO-d6) δ 0.79-0.83 (m, 3H), 1.17-1.28 (m, 8H), 1.45-1.47 (m, 2H), 2.22 (d, J = 2.8Hz, 1H), 3.70-3.90 (m, 2H), 3.95-3.98 (m, 3H), 4.10-4.40 (m, 2H), 5.51 (t, 1H), 5.80-5.90 (m, 1H), 5.95-6.05 (m, 2H), 7.02-7.06 (m, 2H), 7.51 (t, J = 4.2Hz , 4H), 7.51 (d, 1H), 11.51 (s, 1H) ; MS, m/e 557.99(M+1)+; 1136.84(2M+23)+
43	1H NMR (DMSO-d6) δ 1.16-1.24 (m, 6H), 2.22 (s , 3H), 3.65-4.03 (m,3H), 4.11-4.38 (m, 2H), 5.04-5.05 (m, 2H), 5.48-5.50 (m, 1H), 5.77-5.87 (m,1H),5.90-6.11 (m, 2H), 6.98-7.10 (m, 4H), 7.28-7.32 (m, 5H), 7.50 (t ,1H), 11.48 (s, 1H) ; MS, m/e 592.00 (M+1)+.
44	1H NMR (DMSO-d6) δ 0.70-0.80 (m, 3H), 1.11-1.26 (m, 3H), 1.42-1.61 (m, 2H), 3.50-3.54 (m, 3H), 3.58-3.80 (m, 2H), 3.91-4.02 (m, 1H), 4.12-4.38 (m, 2H), 5.47-5.52 (m,1H),5.90-6.03 (m, 2H), 7.08-7.16 (m, 3H), 7.26-7.35 (m, 2H),7.48 (t,1H),11.45 (s, 1H) ; MS, m/e 515.95 (M+1)+; 1052.82 (2M+23)+
45	1HNMR (400MHz, DMSO): δ 1.20-1.26 (m, 6H), 3.80-3.93 (m, 2H), 3.98 (s, 1H), 4.25-4.26 (m, 1H), 4.36-4.37 (m, 1H), 5.07 (s, 2H), 5.52-5.55 (m, 1H), 5.86-5.87(m, 1H), 5.98-6.04 (m, 1H), 6.14-6.17 (m, 1H), 7.15-7.20 (m, 5H), 7.36 (dd, J = 20.0, 8.0 Hz, 4H), 7.54 (s, 1H), 11.55 (s, 1H)
46	1HNMR (400MHz, DMSO): δ 1.21-1.28 (m, 6H), 3.71-3.88 (m, 1H), 3.91-3.98 (m, 1H), 4.00-4.01 (m, 1H), 4.23-4.27 (m, 1H), 4.35-4.38 (m, 1H), 5.08 (d, J = 4.0Hz, 2H), 5.57 (dd, J = 12.0, 8.0 Hz, 1H), 5.91 (d, J = 8.0 Hz, 1H), 6.01 (d, J = 8.0 Hz, 1H), 6.22-6.24 (m, 1H), 7.17-7.23 (m, 2H), 7.31-7.40 (m, 7H), 7.53 (s, 1H), 11.50 (s, 1H)
47	1H NMR (DMSO-d_6) δ 0.80-0.82 (m, 6H), 1.18-1.40 (m, 8H), 1.50-1.58 (m, 1H), 3.71-3.82 (m, 3H), 3.97-3.4.01 (m, 3H), 4.21-4.40 (m, 2H), 5.30(t, J = 8.6 Hz, 1H), 5.81-6.10 (m, 3H), 7.15-7.20 (m, 3H), 7.32-7.36 (m, 2H), 7.48 (d, J = 8.4 Hz, 1H), 11.38 (s, 1H) ; MS, m/e 557.98 (M+1)+; 1136.88 (2M+23)+
48	1H NMR (DMSO-d_6) δ 1.05-1.37 (m, 6H), 3.71-3.82 (m, 1H), 3.87-4.02 (m, 2H), 4.28-4.29 (m, 1H),4.36-4.38 (m, 1H),5.04 (d, J = 5.2Hz, 2H), 5.55-5.64 (m, 1H), 5.85-5.94 (m, 1H), 6.00-6.05 (m, 1H), 6.29-6.40 (m, 1H),7.17-7.24 (m, 1H), 7.30-7.41 (m, 5H), 7.45-7.58 (m, 2H), 7.61 (d, J = 4.0Hz, 1H), 11.53 (s, 1H); MS, m/e545.80(M+1)+;

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