

(51) International Patent Classification⁶ : C07D 421/04, 473/30, A61K 31/505, 31/52	A1	(11) International Publication Number: WO 98/41522 (43) International Publication Date: 24 September 1998 (24.09.98)
(21) International Application Number: PCT/US98/05517 (22) International Filing Date: 19 March 1998 (19.03.98) (30) Priority Data: 60/041,265 19 March 1997 (19.03.97) US (71) Applicants (for all designated States except US): EMORY UNIVERSITY [US/US]; 2009 Ridgewood Drive, Atlanta, GA 30322 (US). THE UNIVERSITY OF GEORGIA RESEARCH FOUNDATION, INC. [US/US]; Boyd Graduate Studies Research Center, Athens, GA 30602-7411 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): SCHINAZI, Raymond, F. [US/US]; 1524 Regency Walk Drive, Decatur, GA 30033 (US). CHU, Chung, K. [US/US]; 115 Cedar Springs Place, Athens, GA 30605 (US). DU, Jinfa [US/US]; 111 College Station Road, K-207, Athens, GA 30605 (US). (74) Agent: KNOWLES, Sherry, M.; King & Spalding, 191 Peachtree Street, Atlanta, GA 30303-1763 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>

The reaction scheme illustrates the synthesis of nucleoside phosphonates 14a-f and 15a-f. It begins with the reaction of $\text{InCH}_2\text{COOR}_2$ (1) with K_2CNVEOH to form intermediate 2, $\text{NCS-CH}_2\text{COOR}_2$. Intermediate 2 is then reacted with $\text{NaBH}_4/\text{BOA}(\text{AcOH})$ to yield 3, $(\text{SeCH}_2\text{COOR}_2)_2$. Compound 3 is treated with Ag_2AOH to produce 4, $(\text{SeCH}_2\text{COOR}_2)_2$. Compound 4 is then reacted with NaOCH_2CHO and $\text{H}_2\text{PO}_4/\text{toluene}$ to form intermediate 5, a cyclic phosphonate. Intermediate 5 is then reacted with Ag_2O to produce 6, a cyclic phosphonate. Compound 6 is then reacted with $\text{Silylated Base}^a/\text{THFOTNCS}_2\text{Cl}_2$ to yield 7, a cyclic phosphonate. Compound 7 is then reacted with MeOH/MeOH to produce 8, a cyclic phosphonate. Compound 8 is then reacted with MeOH/MeOH to produce 9, a cyclic phosphonate. Compound 9 is then reacted with MeOH/MeOH to produce 10, a cyclic phosphonate. Compound 10 is then reacted with MeOH/MeOH to produce 11, a cyclic phosphonate. Compound 11 is then reacted with MeOH/MeOH to produce 12, a cyclic phosphonate. Compound 12 is then reacted with MeOH/MeOH to produce 13, a cyclic phosphonate. Compound 13 is then reacted with MeOH/MeOH to produce 14a-f, a cyclic phosphonate. Compound 14a-f is then reacted with MeOH/MeOH to produce 15a-f, a cyclic phosphonate.

Chemical structures of the four nucleoside analogs are shown below:

- (+)-β-Se-ddC
- (-)-β-Se-ddC
- (+)-β-Se-FddC
- (-)-β-Se-FddC

A method and composition for the treatment of HIV infection, HBV infection, or abnormal cellular proliferation in humans and other host animals is disclosed that includes the administration of an effective amount of a 1,3-oxaselenolane nucleoside or a pharmaceutically acceptable salt thereof, optionally in a pharmaceutically acceptable carrier.