

D-1,3-Dioxolane 및 D-1,3-Oxathiolane 피리미딘 뉴클레오사이드의 합성

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Synthesis of D-1,3-Dioxolane and D-1,3-Oxathiolane Pyrimidine Nucleosides

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Abstract—We synthesized D-1,3-dioxolanyl acetate from D-mannose using Frazer-Reide reaction and D-1,3-oxathiolanyl acetate from either D-mannose or D-galactose in good yields. These acetates were conjugated with various disilylated pyrimidine base using trimethylsilyl trifluoromethane sulfonate as a Lewis acid catalyst to obtain 32 different D-nucleosides.

Keywords □ *Anti-viral agent*, D-1,3-oxathiolanyl acetate, D-1,3-dioxolanyl acetate, D-1,3-oxathiolanyl pyrimidine nucleoside, D-1,3-dioxolanyl pyrimidine nucleoside

(±)-BCH-189¹⁾, (±)-dioxane-T²⁾, 6-(phenylthio)-acyclo-nucleoside(HEPT)³⁾ 및 4'-azido thymidine⁴⁾과 같은 비자연형의 뉴클레오사이드류가 낮은 부작용과 항 HIV효과가 높다는 사실이 보고된후 이들의 유도체의 합성연구가 활발히 이루어지고 있다. 저자 등은 이미 이들 중에서 (±)-BCH-189와 (±)-dioxolane-T의 당부분을 기존의 방법^{5,6)}을 개선하여 합성⁷⁾하였다. 본 연구에서는 합성된 D-1,3-dioxolanyl acetate 및 D-1,3-oxathiolanyl acetate와 각종 비자연형의 염기류를 축합하여 얻어진 뉴클레오사이드류(Scheme I, II, III)의 항 바이러스작용을 검색하므로써 새로운 항 바이러스제의 개발을 시도하고자 하였다.

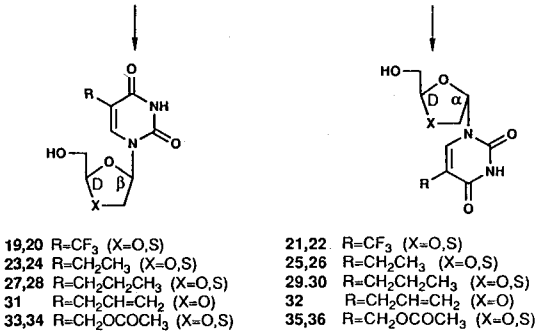
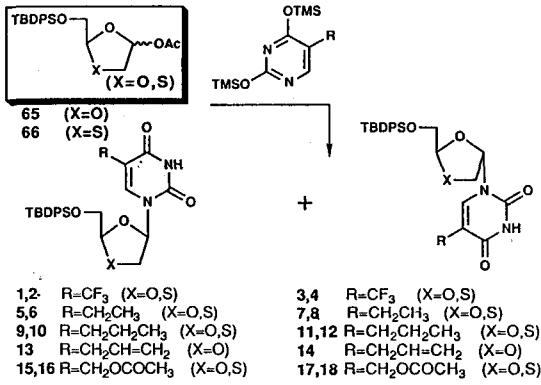
실 험

사용한 시약들은 Aldrich Chem Co. 및 Sigma Chem Co.의 것을 사용하였고 모든 유기용매는 정제하여 사용하였다. Column chromatography는 Kiesel

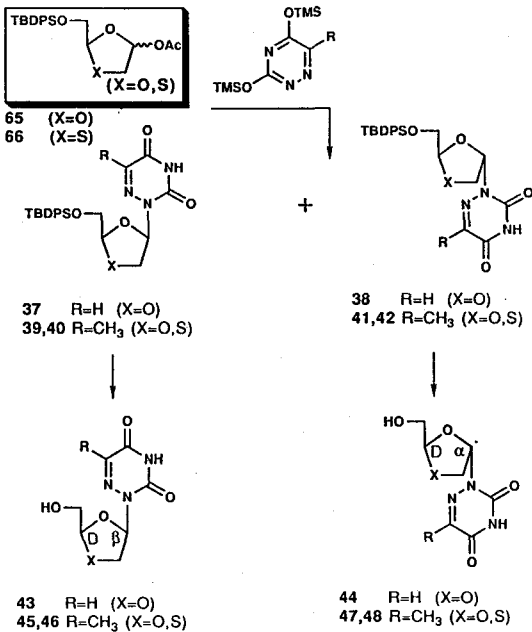
gel 60, 70~230 mesh를 사용 하였으며 TLC는 Kiesel gel 60F₂₅₆를 사용 하였다. 융점은 Buchi 535 melting point apparatus를 이용하여 측정하였고 온도 보정은 하지 않았다. NMR-스펙트럼은 TMS를 내부 표준물질로 하여 Bruker wp 80sy spectrophotometer와 Jeol Gcx 400 FT NMR spectrophotometer를 사용하여 얻었으며 선광도는 JASCO DIP-360 Digital polarimeter를 사용하여 그 값을 얻었다.

보호된 뉴클레오사이드의 일반 합성법—건조한 염기(3.82 mmol)와 ammonium sulfate(축매량)을 무수 hexamethyldisilazane(10 ml)에 현탁시키고, 일야 환류시켰다. 투명한 반응액을 상온까지 냉각하고 무수 상태를 유지하면서 용매를 감압 농축하여 무색투명한 오일상의 disilylation된 염기를 얻었다. 이 오일상의 잔사에 무수 1,2-dichloroethane(5 ml)을 가하여 녹이고 같은 용매(5 ml)에 용해된 1,3-dioxolane acetate 혹은 1,3-oxathiolane acetate(1.91 mmol)용액을 가한 후 0°C까지 냉각한 다음 trimethylsilyl trifluoromethane sulfonate(3.82 mmol)을 천천히 가하고

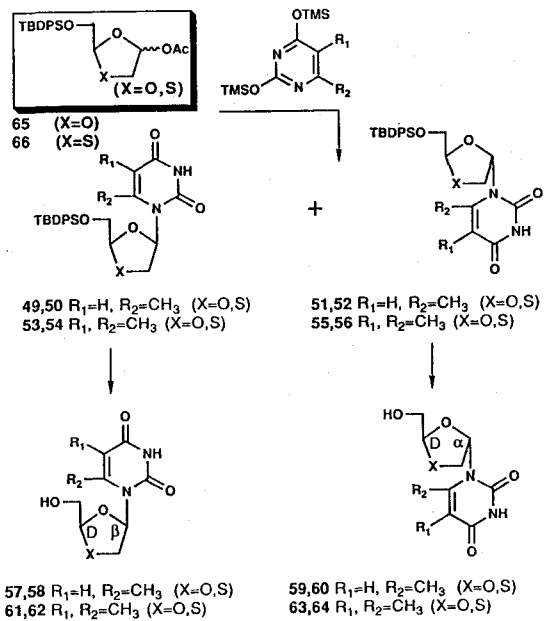
*본 논문에 관한 문의는 이 저자에게로



Scheme I



Scheme II



Scheme III

실온에서 2시간 동안 교반하였다. TLC로 반응 종결을 확인한 후 포화 NaHCO₃ 용액(10 ml)를 가하고 30분 간 더 교반하였다. 생성된 고체를 celite로 여과하여 제거하고 여액을 methylene chloride로 추출 후 포화 NaHCO₃ 용액, brine순으로 세척하고, 무수 MgSO₄로 건조시켰다. 다시 celite로 여과한 후 여액을 감압 농축하여 잔사를 실리카겔 column chromatography (n-hexane : ethyl acetate = 2 : 1)로 정제하여 보호된 D-dioxolanyl nucleoside 및 oxathiolanyl nucleoside를 얻었다. 그러나, D-Oxathiolane nucleoside의 경우에는 anomeric mixture의 분리를 탈 보호한 후 행하였다.

(2R,4R)-1-[2-[(*tert*-Butyldiphenylsilyl)oxymethyl]-1,3-dioxolan-4yl]-5-trifluoromethyl uracil (1) and (2R,4S)-1-2-[(*tert*-butyldiphenylsilyl)oxy methyl-1,3-dioxolan-4yl]-5-trifluoromethyl uracil (3) - 오일상의 화합물 1 및 3을 수율 36.4% 및 35.4%로 얻었다. ¹H NMR(CDCl₃, 400 MHz) δ 1.054(s, 9H, t-Bu), 3.491(s, 2H, H-5'), 3.916(dd, 1H, Hb-2'), 4.227(dd, 1H, Ha-2'), 5.151(t, 1H, H-4'), 6.201(dd, 1H, H-1'), 7.456(m, 10H, Ar), 8.609(s, 1H, H-6) and 3; δ 1.053(s, 9H, t-Bu), 3.743~3.814(m, 2H, H-5'), 4.077(dd, 1H, Hb-2'), 4.436(dd, 1H, Ha-2'), 5.565(t, 1H, H-4'), 6.193(dd, 1H, H-1'), 7.449~7.986(m, 10H, Ar),

8.655(s, 1H, H-6)

(2S,5R)-1-[2-[(*tert*-Butyldiphenylsilyl)]oxymethyl-1,3-oxathiolan-5-yl]-5-trifluoromethyl uracil (2) and (2S,5R)-1-[2-[(*tert*-butyldiphenylsilyl)oxy methyl]-1,3-oxathiolan-5-yl]-5-trifluoromethyl uracil (4)—Anomeric mixture로서 무색 오일상의 2와 4(69.7%)을 얻었다.

(2R,4R)-1-[2-[(*tert*-Butyldiphenylsilyl)]oxymethyl]-1,3-dioxolan-4yl]-5-ethyl uracil (5) and (2R,4S)-1-[2-[(*tert*-butyldiphenylsilyl)oxy methyl]-1,3-dioxolan-4yl]-5-ethyl uracil (7)—오일상의 화합물 5 및 7을 수율 31% 및 37%로 얻었다. 5; ¹H NMR (CDCl₃, 400 MHz) δ 1.052(s, 9H, t-Bu), 1.069(t, 3H, -CH₂CH₃), 2.274(dd, 2H, -CH₂CH₃), 3.678(s, 1H, 2H, H-5'), 4.101(dd, 1H, Hb-2'), 4.231(dd, 1H, Ha-2'), 5.581(t, 1H, H-4'), 6.201(dd, 1H, H-1'), 7.104~7.674 (m, 10H, Ar), 7.803(s, 1H, H-6') and 7; δ 1.064(s, 9H, t-Bu), 1.071(t, 3H, -CH₂CH₃), 2.302(dd, 2H, -CH₂CH₃), 3.599~3.642(m, 2H, H-5'), 4.224(dd, 1H, Hb-2'), 4.209(dd, 1H, Ha-2'), 5.603(t, 1H, H-4'), 6.303(dd, 1H, H-1'), 7.224~7.723(m, 10H, Ar), 7.883(s, 1H, H-6)

(2S,5R)-1-[2-[(*tert*-Butyldiphenylsilyl)oxymethyl]-1,3-oxathiolan-5-yl]-5-ethyluracil (6) and (2S,5S)-1-[2-[(*tert*-butyldiphenylsilyl)oxymethyl]-1,3-oxathiolan-5-yl]-5-ethyl uracil (8)—Anomeric mixture로서 무색 오일상의 6, 8(64%)를 얻었다.

(2R,4R)-1-[2-[(*tert*-Butyldiphenylsilyl)oxymethyl]-1,3-dioxolan-4yl]-5-propyl uracil (9) and (2R,4S)-1-[2-[(*tert*-butyldiphenylsilyl)oxymethyl]-1,3-dioxolan-4yl]-5-propyl uracil (11)—오일상의 화합물 9 및 11을 수율 38% 및 38%로 얻었다. 9; ¹H NMR (CDCl₃, 400 MHz) δ 0.780(t, 3H, -CH₂CH₂CH₃), 1.052(s, 9H, t-Bu), 1.27~1.66(m, 2H, -CH₂CH₂CH₃), 2.038(t, 2H, -CH₂CH₂CH₃), 3.469(s, 2H, H-5'), 3.866(1H, Hb-2'), 4.129(dd, 1H, Ha-2'), 5.088(t, 1H, H-4'), 6.328(t, 1H, H-1'), 7.397~7.954(m, 10H, Ar), 8.201(s, 1H, H-6) and 11; δ 0.927(t, 3H, -CH₂CH₂CH₃), 1.014(s, 9H, t-Bu), 1.527~2.012(m, 2H, -CH₂CH₂CH₃), 2.040(t, 2H, -CH₂CH₂CH₃), 3.471(s, 2H, H-5'), 3.867(dd, 1H, Hb-2'), 4.129(dd, 1H, Ha-2'), 5.088(t, 1H, H-4'), 6.328(dd, 1H, H-1'), 7.397~7.987

(m, 10H, Ar), 8.416(s, 1H, H-6)

(2S,5R)-1-[2-[(*tert*-Butyldiphenylsilyl)oxymethyl]-1,3-oxathiolan-5-yl]-5-propyluracil (10) and (2S,5S)-1-[2-[(*tert*-butyldiphenylsilyl)oxymethyl]-1,3-oxathiolan-5-yl]-5-propyl uracil (12)—Anomeric mixture로서 무색 오일상의 10, 12(63.7%)를 얻었다.

(2R,4R)-1-[2-[(*tert*-Butyldiphenylsilyl)]oxymethyl-1,3-dioxolan-4yl]-5-[2-(propylene)] uracil (13) and (2R,4S)-1-[2-[(*tert*-butyldiphenylsilyl)oxy methyl-1,3-dioxolan-4yl]-5-[2-(propylene)] uracil (14)—오일상의 화합물 13 및 14을 수율 31% 및 41%로 얻었다. 13; ¹H NMR(CDCl₃, 400 MHz) δ 1.069(s, 9H, t-Bu), 2.868(dd, 2H, CH₂CH=CH₂), 3.491(s, 2H, H-5'), 3.879(dd, 1H, Hb-2'), 4.146(dd, 1H, Ha-2'), 4.919~5.456(m, 2H, -CH₂CHCH₂), 5.119(t, 1H, H-4'), 5.610~6.261(m, 1H, -CH₂CH=CH₂), 6.333(t, 1H, H-1'), 7.411(m, 10H, Ar), 8.277(s, 1H, H-6) and 14; δ 1.071(s, 9H, t-Bu), 3.085(m, 2H, -CH₂CH=CH₂), 3.491~3.534(m, 2H, H-5'), 4.035(dd, 1H, Hb-2'), 4.361(dd, 1H, Ha-2'), 5.158~5.683(m, 2H, CH₂CH=CH₂), 5.515(t, 1H, H-H-4'), 5.842~6.483(m, 1H, CH₂CH=CH₂), 6.302(dd, 1H, H-1'), 7.421(m, 10H, Ar), 8.215(s, 1H, H-6)

(2S,5R)-1-[2-[(*tert*-Butyldiphenylsilyl)oxymethyl]-1,3-oxathiolan-5-yl]-5-acetoxymethyl uracil (16) and (2S,5S)-1-[2-[(*tert*-butyldiphenylsilyl)oxymethyl]-1,3-oxathiolan-5-yl]-5-acetoxymethyl uracil (18)—Anomeric mixture로서 무색 오일상의 16, 18(69.4%)를 얻었다.

(2R,4R)-1-[2-[(*tert*-Butyldiphenylsilyl)oxymethyl]-1,3-dioxolan-4yl]-5-acetoxymethyl uracil (15) and (2R,4S)-1-[2-[(*tert*-butyldiphenylsilyl)oxy methyl]-1,3-dioxolan-4yl]-5-acetoxymethyl uracil (17)—오일상의 화합물 15 및 17을 수율 37% 및 36%로 얻었다. 15; ¹H NMR(CDCl₃, 400 MHz) δ 1.102(s, 9H, t-Bu), 1.921(s, 3H, CH₂OCOCH₃), 3.495(s, 2H, CH₂OCOCH₃) 3.945(s, 2H, H-5'), 4.179(dd, 1H, Hb-2'), 4.589(dd, 1H, Ha-2'), 5.1113(t, 1H, H-4'), 6.293(dd, 1H, H-1'), 7.442~8.176(m, 10H, Ar), 8.305(s, 1H, H-6) and 17; δ 1.071(s, 9H, t-Bu), 2.055(s, 3H, CH₂OCOCH₃), 3.486(s, 2H, CH₂OCOCH₃), 3.719~3.793(m, 2H, H-5'), 4.059(dd, 1H, Hb-2'), 4.439(dd, 1H,

Table I—¹H NMR Spectra(a=CDCl₃, b=DMSO-d₆, c=Methanol-d₄, d=Acetone-d₆)

Compound	H-1'	Ha-2'	Hb-2'	H-4'	Ha-5'	Hb-5'	other signals
19 c	6.205(dd, J _{1',2a1} =3.2, J _{1',2b} =3.2)	4.279(dd, J _{2a,1'} =3.2, J _{2a,2b} =10.4)	4.770(dd, J _{2b,1'} =5.2, J _{4',5b'} =1.6)	4.970(t, J _{4',5a'} =1.6, J _{5a,5b'} =9.6)	3.810(dd, J _{5a,4'} =1.6, J _{5b',5a'} =9.6)	3.767(d, J _{5b',4'} =1.6,	8.825(s,H-6)
	6.194(dd, J _{1',2a} =2.0, J _{1',2b} =4.8)	3.454(dd, J _{2a,1'} =4.8, J _{2a,2b} =8.0)	3.214(dd, J _{2b,1'} =2.0, J _{2b,2a'} =8.0)	5.184(t, J _{4',5a'} =2.8, J _{4',5b'} =2.8)	3.954(dd, J _{5a,4'} =2.8, J _{5a',5b'} =13.2)	3.771(d, J _{5b',5a'} =13.2)	8.90(s,H-6)
20 a	6.092(dd, J _{1',2a} =3.2, J _{1',2b} =5.2)	4.412(dd, J _{2a,1'} =5.2, J _{2a,2b} =9.6)	4.114(dd, J _{2a,1'} =3.2, J _{2b,2a'} =9.6)	5.444(t, J _{4',5a'} =1.6, J _{4',5b'} =3.2)	3.807(dd, J _{5a,4'} =1.6, J _{5a',5b'} =12.2)	3.769(dd, J _{5b',5a'} =12.2)	
	6.362(dd, J _{1',2a} =1.6, J _{1',2b} =4.8)	3.192(dd, J _{2a,1'} =1.6, J _{2a,2b} =12.4)	2.752(dd, J _{2b,1'} =4.8, J _{2b,2a'} =12.4)	5.522(t, J _{4',5a'} =4.4, J _{4',5b'} =4.4)	3.532(m, J _{5a,4'} =4.4)	3.532(m, J _{5b',4'} =4.4)	7.98(s,H-6)
21 c	6.333(dd, J _{1',2a} =1.6, J _{1',2b} =6.0)	4.290(dd, J _{2a,1'} =1.6, J _{2a,2b} =10.0)	4.171(dd, J _{2b,1'} =6.0, J _{4',5b'} =2.0)	5.009(t, J _{4',5a'} =2.0, J _{5a,5b'} =10.8)	3.823(dd, J _{5a,4'} =2.0, J _{5a',5a'} =10.8)	3.805(dd, J _{5a,4'} =2.0, J _{5b',5a'} =10.8)	1.070(t,-CH ₂ CH ₃) 2.261(q,-CH ₂ CH ₃)
	6.336(dd, J _{1',2a} =4.8, J _{1',2b} =5.6)	3.596(dd, J _{2a,1'} =4.8, J _{2a,2b} =12.8)	3.277(dd, J _{2b,1'} =5.6, J _{2b,2a'} =12.8)	5.305(t, J _{4',5a'} =4.4, J _{4',5b'} =4.4)	3.916(dm, J _{5a,4'} =4.4)	3.917(m, J _{5b',4'} =4.4)	1.097(t,-CH ₂ CH ₃) 7.827(s,H-6)
22 a	6.288(dd, J _{1',2a} =3.2, J _{1',2b} =5.6)	4.406(dd, J _{2a,1'} =5.6, J _{2a,2b} =9.2)	4.132(dd, J _{2a,1'} =2, J _{2b,2a'} =9.2)	5.539(t, J _{4',5a'} =3.6, J _{4',5b'} =3.6)	3.609(dd, J _{5a,4'} =3.6, J _{5a',5b'} =12.4)	3.571(dd, J _{5b',4'} =3.6, J _{5b',5a'} =12.4)	1.078(t,-CH ₂ CH ₃) 2.305(q,-CH ₂ CH ₃)
	6.510(dd, J _{1',2a} =3.2, J _{1',2b} =6.0)	3.590(dd, J _{2a,1'} =3.2, J _{2a,2b} =12.4)	4.279(dd, J _{2b,1'} =6.0, J _{2b,2a'} =12.4)	5.609(dd, J _{4',5a'} =4.4, J _{4',5b'} =5.6)	3.699(m, J _{5a,4'} =4.4)	3.699(m, J _{5b',4'} =5.6)	1.083(t,-CH ₂ CH ₃) 2.305(q,-CH ₂ CH ₃) 7.374(s,H-6)
23 c	6.328(dd, J _{1',2a} =1.6, J _{1',2b} =6.0)	4.281(dd, J _{2a,1'} =1.6, J _{2a,2b} =10.0)	4.175(dd, J _{2b,1'} =6.0, J _{2b,2a'} =10.0)	5.007(t, J _{4',5a'} =2.4, J _{4',5b'} =2.4)	3.819(dd, J _{5a,4'} =2.4, J _{5a',5b'} =4.2)	3.797(dd, J _{5a,4'} =2.4, J _{5b',5a'} =4.2)	0.883(t,-CH ₂ CH ₂ CH ₃) 1.497(m,-CH ₂ CH ₂ CH ₃) 2.212(t,-CH ₂ CH ₂ CH ₃)
	6.291(t, J _{1',2a} =5.6, J _{1',2b} =5.6)	3.392(dd, J _{2a,1'} =5.6, J _{2a,2b} =11.6)	3.05(dd, J _{2b,1'} =5.6, J _{2b,2a'} =11.6)	5.243(t, J _{4',5a'} =2.8, J _{4',5b'} =4.4)	3.962(dd, J _{5a,4'} =2.8, J _{5a',5b'} =12.4)	3.811(dd, J _{5b',4'} =4.4, J _{5b',5a'} =12.4)	0.869(t,-CH ₂ CH ₂ CH ₃) 1.458(m,-CH ₂ CH ₂ CH ₃) 2.229(t,-CH ₂ CH ₂ CH ₃) 7.486(s,H-6)
24 a	6.289(dd, J _{1',2a} =2.8, J _{1',2b} =5.6)	4.397(dd, J _{2a,1'} =5.6, J _{2a,2b} =9.6)	4.123(dd, J _{2a,1'} =2.8, J _{2b,2a'} =9.6)	5.535(t, J _{4',5a'} =3.2, J _{4',5b'} =3.2)	3.602(dd, J _{5a,4'} =3.2, J _{5a',5b'} =6.4)	3.571(dd, J _{5b',4'} =3.2, J _{5b',5a'} =6.4)	0.884(t,-CH ₂ CH ₂ CH ₃) 1.502(m,-CH ₂ CH ₂ CH ₃) 2.263(t,-CH ₂ CH ₂ CH ₃) 7.386(s,H-6)
	6.492(dd, J _{1',2a} =2.8, J _{1',2b} =5.6)	3.502(dd, J _{2a,1'} =5.6, J _{2a,2b} =12.8)	3.041(dd, J _{2b,1'} =2.8, J _{2b,2a'} =12.8)	5.536(t, J _{4',5a'} =4.8, J _{4',5b'} =4.8)	3.603(m, J _{5a,4'} =4.8)	3.573(m, J _{5b',4'} =4.8)	0.860(t,-CH ₂ CH ₂ CH ₃) 1.457(m,-CH ₂ CH ₂ CH ₃) 2.222(t,-CH ₂ CH ₂ CH ₃) 7.219(s,H-6)
25 c	6.190(dd, J _{1',2a} =2.8, J _{1',2b} =5.6)	4.353(dd, J _{2a,1'} =5.6, J _{2a,2b} =9.6)	4.039(dd, J _{2b,1'} =2.8, J _{2b,2a'} =9.6)	5.419(t, J _{4',5a'} =3.2, J _{4',5b'} =3.2)	3.573(dd, J _{5a,4'} =3.2, J _{5a',5b'} =12.0)	3.009(m,-CH ₂ CH=CH ₂), J _{5b',4'} =3.2, J _{5b',5a'} =12.0)	5.009-5.096(m,-CH ₂ CH=CH ₂), 5.805-5.872(m,-CH ₂ CH=CH ₂), 7.339(s,H-6)
	6.265(dd, J _{1',2a} =2.8, J _{1',2b} =5.2)	4.192(dd, J _{2a,1'} =2.8, J _{2a,2b} =9.6)	4.092(dd, J _{2b,1'} =5.2, J _{2b,2a'} =9.6)	4.942(t, J _{4',5a'} =3.6, J _{4',5b'} =3.6)	3.740(dd, J _{5a,4'} =3.6, J _{5a',5b'} =12.4)	3.740(dd, J _{5b',4'} =3.6, J _{5b',5a'} =12.4)	2.985(m,-CH ₂ CH=CH ₂), 5.086(m,-CH ₂ CH=CH ₂), 5.835(M,-CH ₂ CH=CH ₂), 7.778(s,H-6)

Table I. Continued

	6.135(dd,	4.13(dd,	3.950(dd,	4.854(t,	3.668(dd,	3.631(dd,	1.880(s,-CH ₂ OCOCH ₃)
33	J _{1,2a} '=0.8,	J _{2a,1} '=0.8,	J _{2b,1} '=4.4,	J _{4,5a} '=5.2,	J _{5a,4} '=5.2,	J _{5b,4} '=5.2,	3.328(s,-CH ₂ OCOCH ₃)
c	J _{1,2b} '=4.4	J _{2a,2b} '=10.4)	J _{2b,2a} '=10.4)	J _{4,5b} '=5.2)	J _{5a,5b} '=10.4)	J _{5b,5a} '=10.4	8.071(s,H-6)
	6.324(dd,	3.434(dd,	3.104(dd,	5.284(t,	3.577(m,	3.534(m,	2.060(s,-CH ₂ OCOCH ₃)
34	J _{1,2a} '=5.6,	J _{2a,1} '=5.6,	J _{2b,1} '=7.6,	J _{4,5a} '=4.0,	J _{5a,4} '=4.0)	J _{5b,4} '=4.0)	4.870(s,-CH ₂ OCOCH ₃)
a	J _{1,2b} '=7.6)	J _{2a,2b} '=12.0)	J _{2b,2a} '=12.0)	J _{4,5b} '=4.0)			8.290(s,H-6)
	6.061(dd,	4.269(dd,	3.956(dd,	5.351(t,	3.480(dd,	3.425(dd,	1.853(s,-CH ₂ OCOCH ₃)
35	J _{1,2a} '=2.8,	J _{2a,1} '=5.2,	J _{2b,1} '=2.8,	J _{4,5a} '=3.2,	J _{5a,4} '=3.2,	J _{5b,4} '=3.2,	3.432(s,-CH ₂ OCOCH ₃)
c	J _{1,2b} '=5.2)	J _{2a,2b} '=9.6)	J _{2b,2a} '=9.6)	J _{4,5b} '=3.2)	J _{5a,5b} '=9.2)	J _{5b,5a} '=9.2)	7.643(s,H-6)
	6.519(dd,	3.549(dd,	3.149(dd,	5.539(t,	3.749(m,	3.749(m,	1.853(s,-CH ₂ OCOCH ₃)
36	J _{1,2a} '=2.8,	J _{2a,1} '=2.8,	J _{2b,1} '=5.6,	J _{4,5a} '=5.6,	J _{5a,4} '=5.6)	J _{5b,4} '=5.6)	3.432(s,-CH ₂ OCOCH ₃)
a	J _{1,2b} '=5.6)	J _{2a,2b} '=12.0)	J _{2b,2a} '=12.0)	J _{4,5b} '=5.6)			8.850(s,H-6)
	6.378(dd,	4.186(dd,	4.000(dd,	4.955(t,	3.465(dd,	3.414(dd,	7.313(s,H-6)
43	J _{1,2a} '=2.8,	J _{2a,1} '=2.8,	J _{2b,1} '=6.4,	J _{4,5a} '=4.4,	J _{5b,4} '=4.4,		
a	J _{1,2b} '=6.4)	J _{2a,2b} '=9.2)	J _{2b,2a} '=9.2)	J _{5a,5b} '=11.6)	J _{5b,5a} '=11.6)		
	6.395(dd,	4.248(dd,	4.119(dd,	5.222(t,	3.438(dd,	3.402(dd,	7.568(s,H-6)
44	J _{1,2a} '=4.0	J _{2a,1} '=6.4,	J _{2b,1} '=4.0,	J _{4,5a} '=3.6,	J _{5b,4} '=3.6,		
a	J _{1,2b} '=6.4)	J _{2a,2b} '=8.8)	J _{2b,2a} '=8.8)	J _{4,5b} '=3.6)	J _{5a,5b} '=11.2)		
	6.370(dd,	4.329(dd,	4.044(dd,	5.033(t,	3.602(d,	3.768(d,	
45	J _{1,2a} '=2.4,	J _{2a,1} '=2.4,	J _{2b,1} '=6.4,	J _{4,5a} '=4.0,	J _{5a,4} '=4.0,	J _{5b,4} '=4,	2.115(s,-CH ₃)
c	J _{1,2b} '=6.4)	J _{2a,2b} '=9.2)	J _{2b,2a} '=9.2)	J _{4,5b} '=4.0)	J _{5a,5b} '=9.2)	J _{5b,5a} '=9.2)	
	6.333(dd,	3.503(dd,	3.203(dd,	5.313(t,	4.143(dd,	3.933(dd,	7.273(s,H-6)
46	J _{1,2a} '=4.0,	J _{2a,1} '=5.2,	J _{2b,1} '=4.0,	J _{4,5a} '=2.8,	J _{5a,4} '=2.8,	J _{5b,4} '=2.8,	1.274(s,-CH ₃)
a	J _{1,2b} '=5.2)	J _{2a,2b} '=12.0)	J _{2b,2a} '=12.0)	J _{4,5b} '=2.8)	J _{5a,5b} '=12.8)		
	6.423(dd,	4.240(dd,	4.194(dd,	5.297(t,	3.506(dd,	3.772(dd,	
47	J _{1,2a} '=4.4,	J _{2a,1} '=6.4,	J _{2b,1} '=4.4,	J _{4,5a} '=3.2,	J _{5a,4} '=3.2,	J _{5b,4} '=3.2,	2.105(s,-CH ₃)
c	J _{1,2b} '=6.4)	J _{2a,2b} '=9.6)	J _{2b,2a} '=9.6)	J _{4,5b} '=3.2)	J _{5a,5b} '=10.6)	J _{5b,5a} '=10.6)	
	6.197(t,	3.457(dd,	3.217(dd,	5.187(t,	3.957(dd,	3.757(dd,	7.125(s,H-6)
48	J _{1,2a} '=7.2,	J _{2a,1} '=7.2,	J _{2ab,1} '=7.2,	J _{4,5a} '=2.8,	J _{5a,4} '=2.8,	J _{5b,4} '=2.8,	1.176(s,-CH ₃)
a	J _{1,2b} '=7.2)	J _{2a,2b} '=12.8)	J _{2b,2a} '=12.8)	J _{4,5b} '=2.8)	J _{5a,5b} '=13.2)	J _{5b,5a} '=13.2)	
	6.310(dd,	4.126dd,	3.913(t,	3.831(t,	3.826(dd,	3.807(dd,	
57	J _{1,2a} '=2.4,	J _{2a,1} '=2.4,	J _{2b,1} '=8.8,	J _{4,5a} '=3.2	J _{5a,4} '=3.2	J _{5b,4} '=2.8,	2.196(s,-CH ₃)
c	J _{1,2b} '=8.4)	J _{2a,2b} '=8.4)	J _{2b,2a} '=8.4)	J _{4,5b} '=2.8)	J _{5a,5b} '=9.8)	J _{5b,5a} '=9.8)	
	6.316(dd,	3.516(dd,	3.246(dd,	5.146(t,	3.736(m,	3.736(m,	2.376(s,-CH ₃)
58	J _{1,2a} '=6.8,	J _{2a,1} '=8.4,	J _{2b,1} '=6.8,	J _{4,5a} '=4.8,	J _{5a,4} '=4.8)	J _{5b,4} '=4.8)	
a	J _{1,2b} '=8.4)	J _{2a,2b} '=12.0)	J _{2b,2a} '=12.0)	J _{4,5b} '=4.8			
	6.356(t,	3.378(dd,	3.218(dd,	5.568(t,	3.668(m,	3.668(m,	2.249(s,-CH ₃)
59	J _{1,2a} '=6.8,	J _{2a,1} '=6.8,	J _{2b,1} '=6.8,	J _{4,5a} '=2.8,	J _{5a,4} '=2.8	J _{5b,4} '=2.8)	
a	J _{1,2b} '=7.4)	J _{2a,2b} '=11.0)	J _{2b,2a} '=11.0)	J _{4,5b} '=2.8			
	6.347(t,	3.367(dd,	3.207(dd,	5.557(t,	3.657(m,	3.657(m,	2.237(s,-CH ₃)
60	J _{1,2a} '=7.2,	J _{2a,1} '=7.2,	J _{2b,1} '=7.2,	J _{4,5a} '=2.6,	J _{5a,4} '=2.6	J _{5b,4} '=2.6)	
a	J _{1,2b} '=7.2)	J _{2a,2b} '=10.8)	J _{2b,2a} '=10.8)	J _{4,5b} '=2.6			
	6.308(dd,	4.124(dd,	3.911(t,	4.829(t,	3.824(dd,	3.805(dd,	1.711(s,-CH ₃)
61	J _{1,2a} '=2.0,	J _{2a,1} '=2.0,	J _{2b,1} '=8.4,	J _{4,5a} '=2.8,	J _{5a,4} '=2.8,	J _{5b,4} '=2.8,	2.196(s,-CH ₃)
c	J _{1,2b} '=8.4)	J _{2a,2b} '=8.4)	J _{2b,2a} '=8.4)	J _{4,5b} '=2.8)	J _{5a,5b} '=9.8)	J _{5b,5a} '=9.8)	
	6.332(dd,	3.652(dd,	3.1729dd,	5.282(t,	3.782(m,	3.782(m,	9.292(br s,NH)
62	J _{1,2a} '=3.2,	J _{2a,1} '=3.2,	J _{2b,1} '=6.0,	J _{4,5a} '=3.2,	J _{5a,4} '=3.2)	J _{5b,4} '=3.2)	2.372(s,-CH ₃)
a	J _{1,2b} '=6.0)	J _{2a,2b} '=10.4)	J _{2b,2a} '=10.4)	J _{4,5b} '=3.2)			1.952(s,-CH ₃)

Table I. Continued

	6.018(t,	4.198(t,	4.125(t,	5.353(t,	3.417(dd,	3.329(dd,	1.671(s,-CH ₃)
63	J _{1',2a'} =6.8,	J _{2a',1'} =6.8,	J _{2b',1'} =6.8,	J _{4',5a'} =2.4,	J _{5a',4'} =2.4,	J _{5b',4'} =2.4,	2.130(s,-CH ₃)
c	J _{1',2b'} (=6.8)	J _{2a',2b'} (=6.8)	J _{2b',2a'} (=6.8)	J _{4',5b'} =2.4)	J _{5a',5b'} =8.4)	J _{5b',5a'} =8.4)	
	6.564(t,	3.574(dd,	3.374(dd,	5.664(t,	3.784(m,	3.784(m,	9.294(br s,-NH)
64	J _{1',2a'} =7.6,	J _{2a',1'} =7.6,	J _{2b',1'} =7.6,	J _{4',5a'} =4.8,	J _{5a',4'} =4.8)	J _{5b',4'} =4.8)	3.436(s,-CH ₃)
a	J _{1',2b'} (=7.6)	J _{2a',2b'} (=10.8)	J _{4',5b'} (=4.8)				1.99(s,CH ₃)

Table II—Melting Points and Optical Rotations

Compound	mp,(°C)	[α] _D , deg
19	202-206	16.87(C=1.07, MeOH)
20	111-119	-47.26(C=1.65, MeOH)
21	foam	-33.1(C=1.11, MeOH)
22	110-115	15.67(C=0.55, MeOH)
23	143-147	-12.45(C=1.123, MeOH)
24	foam	-51.85(C=1.12, MeOH)
25	foam	6.42(C=1.21, MeOH)
26	foam	61.79(C=1.15, MeOH)
27	149-152	-10.87(C=1.352, MeOH)
28	foam	-41.27(C=1.40, MeOH)
29	foam	6.1(C=1.230, MeOH)
30	87-90	67.47(C=1.18, MeOH)
31	153-157	-19.24(C=1.00, MeOH)
32	foam	1.14(C=1.05, MeOH)
33	foam	-8.8(C=1.12, MeOH)
34	103-111	-62.29(C=1.15, MeOH)
35	foam	-1.9(C=1.23, MeOH)
36	foam	49.59(C=1.12, MeOH)
43	foam	56.28(C=1.00, MeOH)
44	foam	-51.89(C=1.00, MeOH)
45	foam	-55.55(C=1.25, MeOH)
46	foam	84.69(C=1.95, MeOH)
47	foam	37.12(C=1.25, MeOH)
48	foam	-20.16(C=1.55, MeOH)
57	140-143	19.7(C=1.5, MeOH)
58	foam	-84.63(C=1.26, MeOH)
59	132-136	-32.17(C=2.0, MeOH)
60	foam	104.8(C=1.13, MeOH)
61	184-186	-11.09(C=1.26, MeOH)
62	foam	-35.13(C=1.4, MeOH)
63	172-174	-8.63(C=1.1, MeOH)
64	foam	34.19(C=1.05, MeOH)

Ha-2'), 5.586(t, 1H, H-H-4'), 6.273(dd, 1H, H-1'), 7.451~7.998(m, 10H, Ar), 9.003(s, 1H, H-6)

탈보호된 D-1,3-dioxolane 및 D-1,3-oxathiolane류의 일반합성법

보호된 D-1,3-dioxolane 혹은 D-1,3-oxathiolane류 크레오사이드(0.31 mmol)을 무수 THF (5 ml)에 용해하고 1.0M *tetra-n*-butylammonium fluoride in THF (0.5 ml, 0.5 mmol)을 부가하여 무수를 유지하면서 실온에서 1시간 교반하였다. TLC로 반응종결을 확인한 후에 용매를 감압증발, 잔사를 실리카겔 column chromatography로 정제 하여 탈보호된 D-1,3-dioxolane 및 D-1,3-oxathiolane류 크레오사이드류를 얻었다. 이들 뉴크레오사이드들의 NMR-스펙트럼 및 physical constant 는 Table I 및 II에 나타내었다.

(+)-(2R,4R)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-5-trifluoromethyl uracil (19)—Silica gel column chromatography(n-hexane : ethyl acetate = 1 : 3)로 정제 분리하여 무색 고체의 19 (93%)을 얻었다.

(-)-(2R,4S)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-5-trifluoromethyl uracil (21)—Silica gel column chromatography (n-hexane : ethyl acetate = 1 : 3)로 정제분리하여 foam 상의 21 (92%)을 얻었다.

(+)-(2S,5R)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-5-trifluoromethyl uracil (20) and (-)-(2S,5R)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-5-trifluoromethyl uracil (22)—Silica gel column chromatography (n-hexane : ethyl acetate = 1 : 3)로 정제 분리하여 무색 고체 20(47.4%), 22(48.6%)을 얻었다.

(-)-(2R,4R)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-5-ethyl uracil (23)—Silica gel column chromatography (n-hexane : ethyl acetate = 1 : 2)로 정제 분리하여 무색 고체 23 (95%)을 얻었다.

(+)-(2S,5R)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-5-ethyluracil (24) and (-)-(2S,5S)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-5-ethyluracil (26)—Silica gel column chromatography (n-hexane

: ethyl acetate=1:3)로 정제 분리하여 foam상의 24(49%)과 26(48.6%)를 얻었다.

(+)-(2R,4S)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-5-ethyl uracil (25)—Silica gel column chromatography (n-hexane : ethyl acetate=1:2)로 정제 분리하여 foam 상의 25 (96%)을 얻었다.

(+)-(2S,5R)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-5-propyluracil (28) and (-)-(2S,5S)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-5-propyl uracil (30)—Silica gel column chromatography (n-hexane : ethyl acetate=1:3)로 정제 분리하여 foam 상의 28 (46%)과 무색 고체 30(44.7%)을 얻었다.

(+)-(2R,4R)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-5-propyl uracil (27)—Silica gel column chromatography (n-hexane : ethyl acetate=1:3)로 정제 분리하여 무색 고체 27 (96%)을 얻었다.

(+)-(2R,4S)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-5-propyl uracil (29)—Silica gel column chromatography (n-hexane : ethyl acetate=1:3)로 정제 분리하여 foam상의 29 (95%)을 얻었다.

(-)-(2R,4R)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-5-(2-propylene)uracil (31)—Silica gel column chromatography (n-hexane : ethyl acetate=1:3)로 정제 분리하여 무색 고체 31 (85%)을 얻었다.

(+)-(2R,4S)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-5-(2-propylene) uracil (32)—Silica gel column chromatography (n-hexane : ethyl acetate=1:3)로 정제 분리하여 foam상의 32 (85%)을 얻었다.

(-)-(2R,4R)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-5-acetoxymethyl uracil (33)—Silica gel column chromatography (n-hexane : ethyl acetate=1:3)로 정제 분리하여 foam상의 33 (92%)을 얻었다.

(-)-(2R,4R)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-5-acetoxymethyl uracil (35)—Silica gel column chromatography (n-hexane : ethyl acetate=1:3)로 정제 분리하여 foam상의 35 (88%)을 얻었다.

(+)-(2S,5R)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-5-acetoxymethyl uracil (34) and (-)-(2S,5S)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-5-acetoxymethyl uracil (36)—Silica gel column chro-

matography (n-hexane : ethyl acetate=1:2)로 정제 분리하여 무색 고체 34(46.6%)와 foam상의 36 (47.4%)를 얻었다.

(2R,4R)-1-[2-(*tert*-Butyldiphenylsilyl)oxymethyl-1,3]-dioxolan-4yl]-6-azauracil (37) and (2R,4S)-1-[2-[*tert*-butyldiphenylsilyl)oxymethyl]-1,3-dioxolan-4yl]-6-azauracil (38)—오일상의 화합물 37 및 38을 수율 25.4% 및 19%로 얻었다. 37; ¹H NMR (CDCl₃, 400 MHz) δ 1.065 (s, 9H, t-Bu), 3.722~3.918 (m, 2H, H-5'), 4.276(dd, 1H, Hb-2'), 4.352(dd, 1H, Ha-2'), 5.501(t, 1H, H-4'), 6.567(dd, 1H, H-1'), 7.419~7.947(m, 10H, Ar), 9.061(s, H-5) and 38; δ 1.054 (s, 9H, t-Bu), 3.753(s, 2H, H-5'), 4.122(dd, 1H, Hb-2'), 4.335(dd, 1H, Ha-2'), 5.242(t, 1H, H-H-4'), 6.477 (dd, 1H, H-1'), 7.382~7.846(m, 10H, Ar), 9.015(s, 1H, H-5)

(2R,4R)-1-[2-(*tert*-Butyldiphenylsilyl)oxymethyl]-1,3-dioxolan-4yl]-6-azathymine (39) and (2R,4S)-1-[2-[*tert*-butyldiphenylsilyl)oxymethyl]-1,3-dioxolan-4yl]-6-azathymine (41)—오일상의 화합물 39 및 41을 수율 25.2% 및 41%로 얻었다. 39; ¹H NMR (CDCl₃, 400 MHz) δ 1.109(s, 9H, t-Bu), 2.247(s, 3H, CH₃), 3.824~4.010(m, 2H, H-5'), 4.119(dd, 1H, Hb-2'), 4.218(dd, 1H, Ha-2'), 5.573(t, 1H, H-4'), 6.497(t, 1H, H-1'), 7.530(m, 10H, Ar), 8.920(br s, 1H, NH) and 41; δ 1.207(s, 9H, t-Bu), 2.132(s, 3H, CH₃), 3.809 (s, 2H, H-5'), 4.203(dd, 1H, Hb-2'), 4.303(dd, 1H, Ha-2'), 5.276(t, 1H, H-H-4'), 6.455(t, 1H, H-1'), 7.428~7.935(m, 10H, Ar), 8.604(br s, 1H, NH)

(2S,5R)-1-[2-[*tert*-Butyldiphenylsilyl)oxymethyl]-1,3-oxathiolan-5-yl]-6-azathymine(40) and (2S,5S)-1-[2-[*tert*-butyldiphenylsilyl)oxymethyl]-1,3-oxathiolan-5-yl]-6-azathymine (42)—Anomeric mixture로서 foam 상의 40, 42(62.3%)를 얻었다.

(+)-(2R,4R)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-6-aza uracil (43)—Silica gel column chromatography (n-hexane : ethyl acetate=1:3)로 정제 분리하여 foam상의 43(95%)을 얻었다.

(-)-(2R,4S)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-6-aza uracil (44)—Silica gel column chromatography(n-hexane : ethyl acetate=1:3)로 정제 분리하여 foam상의 44(92%)을 얻었다.

(-)-(2S,4S)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-6-aza thymine (45) — Silica gel column chromatography (n-hexane : ethyl acetate = 1 : 3)로 정제 분리하여 foam상의 45(93%)을 얻었다.

(+)-(2R,4S)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-6-aza thymine (47) — Silica gel column chromatography(n-hexane : ethyl acetate = 1 : 3)로 정제 분리하여 foam상의 47(94%)을 얻었다.

(+)-(2S,5R)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-6-azathymine (46) and (-)-(2S,5S)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-6-azathymine (48) — Silica gel column chromatography(n-hexane : ethyl acetate = 1 : 2)로 정제 분리하여 foam상의 46(25.7 mg, 47.7%)와 48(25 mg, 46.4%)를 얻었다.

(2R,4R)-1-[2-[(*tert*-Butyldiphenylsilyl)oxymethyl]-1,3-dioxolan-4yl]-6-methyl uracil (49) and (2R,4S)-1-[2-[(*tert*-butyldiphenylsilyl)oxymethyl]-1,3-dioxolan-4yl]-6-methyl uracil (51) — Anomeric mixture로서 무색 oil상의 49와 51(82%)을 얻었다.

(2S,5R)-1-[2-[(*tert*-Butyldiphenylsilyl)oxymethyl]-1,3-oxathiolan-5-yl]-6-methyluracil (50) and (2S,5S)-1-[2-[(*tert*-butyldiphenylsilyl)oxymethyl]-1,3-oxathiolan-5-yl]-6-methyluracil (52) — Anomeric mixture로서 무색 oil상의 50, 52(55%)를 얻었다.

(2R,4R)-1-[2-[(*tert*-Butyldiphenylsilyl)oxymethyl]-1,3-dioxolan-4yl]-5,6-dimethyl uracil (53) and (2R,4S)-1-[2-[(*tert*-butyldiphenylsilyl)oxymethyl]-1,3-dioxolan-4yl]-5,6-dimethyl uracil (55) — 오일상의 화합물 53 및 55을 수율 26% 및 29%로 얻었다. 53; ¹H NMR(CDCl₃, 400 MHz) δ 1.111(s, 9H, t-Bu), 1.693(s, 3H, 5-CH₃), 2.178(s, 3H, 6-CH₃), 3.542~3.612(m, 2H, H-5'), 3.800(dd, 1H, Hb-2'), 4.98(dd, 1H, Ha-2'), 4.797(t, 1H, H-4'), 6.219(dd, 1H, H-1'), 7.733~8.376(m, 10H, Ar) and 55; δ 1.088(s, 9H, t-Bu), 1.550(s, 3H, 5-CH₃), 2.188(s, 3H, 6-CH₃), 3.314~3.406(m, 2H, H-5'), 4.051(dd, 1H, Hb-2'), 4.137(dd, 1H, Ha-2'), 5.290(t, 1H, H-4'), 6.014(dd, 1H, H-1'), 7.797~8.412(m, 10H, Ar)

(2S,5R)-1-[2-[(*tert*-Butyldiphenylsilyl)oxymethyl]-1,3-oxathiolan-5-yl]-5,6-dimethyluracil (54) and (2S,5S)-1-[2-[(*tert*-butyldiphenylsilyl)oxymethyl]-1,3-oxathiolan-5-yl]-5,6-dimethyluracil (56) —

Anomeric mixture로서 무색 oil상의 54, 56(59.4%)을 얻었다.

(2R,4R)-and(2R,4S)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-6-methyl uracil (57, 59) — Silica gel column chromatography (n-hexane : ethyl acetate = 1 : 5)로 정제 분리하여 57(93%), 59(89%)을 얻었다.

(+)-(2S,5R)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-6-methyl uracil(58) and (-)-(2S,5S)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-6-methyl uracil (60) — Silica gel column chromatography(n-hexane : ethyl acetate = 1 : 5)로 정제 분리하여 foam상의 58(48.2%)와 60(47.4%)를 얻었다.

(-)-(2R,4R)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-5,6-dimethyl uracil (61) — Silica gel column chromatography (n-hexane : ethyl acetate = 1 : 5)로 정제 분리하여 무색 고체 61(60%)을 얻었다.

(+)-(2R,4S)-1-[2-(Hydroxymethyl)-1,3-dioxolan-4-yl]-5,6-dimethyl uracil (63) — Silica gel column chromatography (n-hexane : ethyl acetate = 1 : 5)로 정제 분리하여 무색 고체 63(97%)을 얻었다.

(+)-(2S,5R)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-5,6-dimethyl uracil (62) and (-)-(2S,5S)-1-[2-(Hydroxymethyl)-1,3-oxathiolan-5-yl]-5,6-dimethyl uracil (64) — Silica gel column chromatography (n-hexane : ethyl acetate = 1 : 4)로 정제 분리하여 foam상의 62(48.7%)와 64(48.6%)를 얻었다 (Table I, Table II).

결과 및 고찰

본 저자 등이 개선된 방법⁷⁾으로 합성한 D-1,3-dioxolanyl acetate (65)와 D-1,3-oxathiolanyl acetate (66)를 여러 종류의 염기(9종), 5-alkyluracil 및 6-azauracil, 6-azathymine 그리고 5,6-dialkyluracil을 HMDS(hexamethyldisilazane) 용매에서 ammonium sulfate을 산 촉매로 하여 disilylation한 후 Vuerb-ruggen 조건¹⁰⁾에서 축합하여 D-1,3-dioxolane의 뉴크레오사이드 및 D-1,3-oxathiolane 뉴크레오사이드류를 얻은 후 tetrabutylammonium fluoride로 탈보호하여 D-form의 뉴크레오사이드류 32종을 합성하였다. 이들의 anomeric mixture는 column chroma-

tography로 정제 분리하였으며 일반적인 물성의 경향은 D-1,3-dioxolane 뉴클레오사이드류는 대부분이 탈보호하기 전이 극성차가 더 컸으며 이것은 D-1,3-oxathiolane 뉴클레오사이드류와 반대의 경향을 나타내었다. 이렇게 하여 분리 정제된 anomer의 구조 결정은 ¹H NMR 패턴에서 쉽게 확인할 수 있다.¹²⁾ 첫째로 anomeric proton은 β-형의 nucleoside류가 α-형의 nucleoside류 보다 고자장에 나타나며 이는 기존에 잘 알려진 β-뉴클레오사이드의 chemical shift의 패턴과 일치하였다. 두번째로 4'-proton에 있어서는 염기와 cis관계의 α-형의 chemical shift는 저자장에 나타났으며 이는 염기의 anisotropy effect 때문이라고 사료된다. 세번째로는 2'위치의 diastereotopic proton들의 α-형 및 β-형의 ¹H NMR 패턴에서도 쉽게 구별이 가능하였다.

항바이러스 작용 검색 결과 HIV(Human Immunodeficiency Virus)에 대해서는 현저한 효능을 가진 것이 없었으며, 수종의 DNA virus에 대한 activity는 화합물 46이 Human Cytomegalovirus에 대해 비교적 양호한 결과를 나타내었으며 재검토를 수행중이다.

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