38. Regioselective Transformations of 2′,3′-Seconucleosides into Anhydro Structures and Chiral Crown Ethers[1])

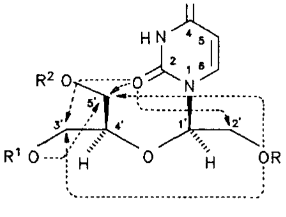
by **Vinko Škarić***, **Vesna Čaplar**, **Đurđica Škarić**, and **Mladen Žinić**

Laboratory of Stereochemistry and Natural Products, Ruđer Bošković Institute, 41001 Zagreb, Croatia

(21.X.91)

Intramolecular cyclisation of properly protected and activated derivatives of 2′,3′-secouridine (= 1-{2-hydroxy-1-[2-hydroxy-1-(hydroxymethyl)ethoxy]-ethyl}uracil; **1**) provided access to the 2,2′-, 2,3′-, 2,5′-, 2′,5′-, 3′,5′-, and 2′,3′-anhydro-2′,3′-secouridines **5**, **16**, **17**, **26**, **28**, and **31**, respectively (*Schemes 1–3*). Reaction of 2′,5′-anhydro-3′-*O*-(methylsulfonyl)- (**25**) and 2′,3′-anhydro-5′-*O*-(methylsulfonyl)-2′,3′-secouridine (**32**) with CH_2Cl_2 in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene generated the N(3)-methylene-bridged bis-uridine structure **37** and **36**, respectively (*Scheme 3*). Novel chiral 18-crown-6 ethers **40** and **44**, containing a hydroxymethyl and a uracil-1-yl or adenin-9-yl as the pendant groups in a 1,3-*cis* relationship, were synthesized from 5′-*O*-(triphenylmethyl)-2′,3′-secouridine (**2**) and 5′-*O*,N^6-bis(triphenylmethyl)-2′,3′-secoadenosine (**41**) on reaction with 3,6,9-trioxaundecane-1,11-diyl bis(4-toluenesulfonate) and detritylation of the thus obtained (triphenylmethoxy) methyl compound **39** and **43**, respectively (*Scheme 4*).

Introduction. – Ring-opening of the aglycones [2] [3] or furanosyl parts of the natural nucleosides aimed at obtaining a number of pharmacologically interesting substances. Our interest for the aliphatic analogues of nucleosides [4–6] as well as for acyclovir [7] and ganciclovir-like [8] compounds, having the ring-opened furanosyl part of nucleosides, led us to the most versatile 2′,3′-seconucleosides. To our surprise, such ring-opened polyhydroxy compounds and their intramolecular transformations have not yet been studied sufficiently. Therefore, we considered all possible modes of intramolecular interactions of properly activated and configurationally defined derivatives of 2′,3′-secouridine (**1**, $R = R^1 = R^2 = H$), as outlined in the formula by the dotted lines, and we thus obtained isomeric 2,2′-, 2,5′-, 2,3′-, 2′,3′-, 2′,5′-, and 3,5′- anhydro structures of the oxazol, dioxazepine, 1,4-dioxane, and oxetane type[2]).



1 R,R¹, or R² = H,Ms,Ac, or Tr[2])

---

[1]) Preliminary communication: [1].

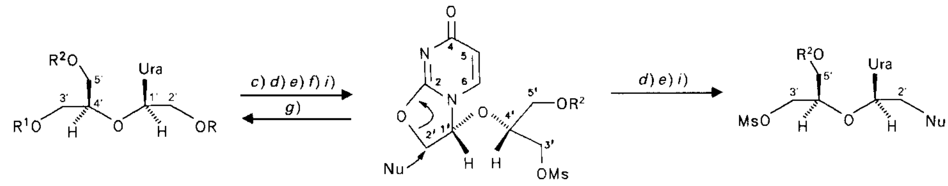
[2]) Nucleoside numbering is used for the 2′,3′-seconucleosides and their anhydro structures, systematic names are given in the *Exper. Part*.

We also investigated the use of properly protected 2′,3′-secouridine and 2′,3′-secoadenosine in the syntheses of the novel chiral lariat [18]crown ethers [1]. Thus, the chiral macrocycles containing functionalized aliphatic chains and *cis*-situated complementary uracil-1-yl or adenin-9-yl groups as the pendant groups were successfully prepared. *Stoddart* and coworkers [9] [10] synthesized chiral crown ethers by insertion of D-mannitol segments or related compounds. *Lehn* and *Sirlin* [11] prepared a chiral macrocyclic catalyst bearing cysteinyl residues. *Lehn* and coworkers [12] also inserted tartaric acid into the structural framework of noncarbohydrate targets yielding *cis*- or *trans*-dicarboxylato-substituted [18]crown-6 ethers.

So far, only a limited number of nucleophilic substitutions of CH_2Cl_2 are known. We now observed that 2′,3′- and 2′,5′-anhydro-2′,3′-secouridine can react with CH_2Cl_2 in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to give the corresponding N(3)-methylene-bridged bis-uridine structures.

Results and Discussion. – We firstly reconsidered the synthesis of the scarcely described 5′-*O*-(triphenylmethyl)-2′,3′-secouridine (**2**) by $NaIO_4$ oxidation [13] of 5′-*O*-(triphenylmethyl)uridine [14], followed by $NaBH_4$ reduction [13] of the intermediate 2′,3′-dialdehyde. The optical rotation and NMR data of **2** and of its 2′,3′-di-*O*-acetyl (**3**) [15] [16] and 2′,3′-di-*O*-mesyl derivative **4** [17] (*Scheme 1*) are reported in the *Exper. Part* and in *Tables 1* and *2*, respectively.

Scheme 1



b) **2** R = R¹ = H, R² = Tr
3 R = R¹ = Ac, R² = Tr a)
4 R = R¹ = Ms, R² = Tr
h) **10** R = H, R¹ = Ms, R² = Tr
11 R = Ac, R¹ = Ms, R² = Tr a)
12 R = R¹ = Ms, R² = H

5 R² = H
9 R² = Tr

Nu = Cl⁻ or MeO
Ura = uracil-1-yl

a) **6** Nu = Cl, R² = H
7 Nu = Cl, R² = Ac
8 Nu = Cl, R² = Tr
13 Nu = MeO, R² = H

a) Ac_2O, py. *b*) MsCl, py. *c*) 1.6N aq. HCl, dioxane at r.t. *d*) At 60°. *e*) 2N aq. HCl, DMF. *f*) DBU, CH_2Cl_2. *g*) 1N aq. NaOH, dioxane. *h*) MeOH, *Amberlyst 15*. *i*) MeOH/MeCN 2:1,80°.

2,2′-Anhydro Structures. The reaction of **4** with 1.6N aq. HCl in dioxane at r.t. resulted in the formation of 2,2′-anhydro-3′-*O*-(methylsulfonyl)-2′,3′-secouridine (**5**) in high yields. However, when **4** was heated with 1.6N aq. HCl in dioxane at elevated temperature, 2′-chloro-2′-deoxy-3′-*O*-(methylsulfonyl)-2′,3′-secouridine (**6**) was isolated and characterized as the 5′-*O*-acetyl derivative **7** (*Scheme 1*). Analogously, treatment of **4** with 2N aq. HCl in DMF [17] proceeded at room temperature to 2′-chloro-2′-deoxy-3′-*O*-(methylsulfonyl)-5′-*O*-(triphenylmethyl)-2′,3′-secouridine (**8**; 88% yield), formed on nucleophilic substitution by Cl^- at C(2′) of the intermediate 2,2′-anhydro-3′-*O*-(methylsulfonyl)-5′-*O*-(triphenylmethyl)-2′,3′-secouridine (**9**) which unexpectedly had retained the 5′-*O*-(triphenylmethyl) protection. The 5′-*O*-(triphenylmethyl) compound **9** [17] was prepared independently by treatment of **4** with DBU in CH_2Cl_2 and submitted to 2N aq. HCl in DMF to yield **8**.

Table 1. *^{1}H-NMR Data* (δ in ppm, J in Hz, internal standard TMS) *of the 2′,3′-Secouridines and Their Anhydro Structures*[a])[b])[c])

	Solvent	H–N(3)[d]) (br. *s*)	H–C(6) (*d*)	H–C(1′) (*t*)	H–C(5) (*d*)	2 H–C(2′) (*d*)[e])	2 H–C(3′) (*d*)[e])	H–C(4′) (*m*)[e])	2 H–C(5′) (*d*)[e])
1	CD_3OD		7.76 (J = 8.1)	5.95 (J = 6.1)	5.76 (J = 8.1)		3.81–3.60 (*m*)		
2	$(CD_3)_2SO$	11.06	7.53 (J = 8.2)	5.51 (J = 5.3)	5.46 (J = 8.2)		3.62–3.44 (*m*)		3.05 (J = 5.3)
3	$(CD_3)_2SO$	11.44	7.67 (J = 8.2)	6.00 (J = 5.6)	5.55 (J = 8.2)	4.47–4.09 (*m*)		3.79	3.06 (J = 5.0)
4	$(CD_3)_2SO$		7.70 (J = 8.2)	6.04 (J = 5.3)	5.57 (J = 8.2)	4.45–4.33 (*m*)		3.9	4.45–4.33 (*m*)
5	$(CD_3)_2SO$		8.06 (J = 7.9)	6.2 (*dd*, J = 5.6, 2.3)	5.99 (J = 7.9)	4.93 (*d*, J = 10.3, 5.6), 4.63 (*d*, J = 10.3, 2.3)	4.38 (J = 4.4)	4.37	3.66 (J = 4.4)
6	CD_3CN		7.60 (J = 8.2)	6.09 (J = 5.9)	5.75 (J = 8.2)	4.37 (J = 5.0)	3.86 (J = 5.6)	3.9	3.58 (J = 5.0)
8	$(CD_3)_2SO$		7.65	6.14	5.60	4.47	3.96	4.00	3.30
9	$(CD_3)_2SO$		7.86 (J = 7.6)	6.11 (*dd*, J = 5.6, 2.1)	5.80 (J = 7.6)	4.86 (*d*, J = 10.3, 5.6), 4.56 (*d*, J = 10.3, 2.3)	4.40 (J = 2.6)	4.31	3.21 (J = 2.6)
10	CD_3CN	10.06	7.48 (J = 8.2)	5.89 (J = 5.6)	5.59 (J = 8.2)	4.41 (*dd*, J = 4.4, 2.6)	3.92–3.49 (*m*)		3.24 (J = 5.3)
11	$CDCl_3$	9.40	7.43 (J = 8.2)	6.08 (J = 5.3)	5.62 (J = 8.2)	4.51–4.00 (*m*)		3.68	3.25 (J = 5.3)
12	CD_3CN	9.72	7.64 (J = 7.9)	6.14 (J = 5.3)	5.77 (J = 7.9)	4.43 (J = 5.3)	4.39 (J = 9.1)	3.94	3.59 (J = 5.6)
13[f])	CD_3CN	9.54	7.56 (J = 8.2)	6.05 (J = 5.6)	5.72 (J = 8.2)	4.35 (J = 5.9)	3.65 (J = 5.6)	3.88 (*sext.*, J = 5.0)	3.55 (J = 5.0)
14	$(CD_3)_2CO$	10.24	7.72 (J = 8.2)	6.16 (J = 5.6)	5.74 (J = 8.2)		4.61–4.03 (*m*)		
15	$(CD_3)_2CO$	10.07	7.68 (J = 8.2)	6.20 (J = 5.6)	5.72 (J = 8.2)		4.54–4.13 (*m*)		
18	$(CD_3)_2CO$	10.18	7.73 (J = 8.1)	6.15 (J = 5.6)	5.70 (J = 8.1)		4.61–3.88 (*m*)		3.65 (J = 3.5)
19	CD_3CN	9.23	7.60 (J = 8.2)	5.91 (J = 5.3)	5.71 (J = 8.2)	4.36 (J = 5.0)	3.73 (J = 4.7)	3.85 (*sext.*, J = 5.9)	3.36 (J = 5.3)

Table 1 (cont.)

	Solvent	H–N(3)[d]) (br. *s*)	H–C(6) (*d*)	H–C(1′) (*t*)	H–C(5) (*d*)	2 H–C(2′) (*d*)[e])	2 H–C(3′) (*d*)[e])	H–C(4′) (*m*)[e])	2 H–C(5′) (*d*)[e])
20	$(CD_3)_2CO$	10.09	7.71 (*J* = 8.1)	6.16 (*J* = 5.6)	5.66 (*J* = 8.1)	4.50–4.03 (*m*)		3.86	3.60 (*J* = 5.9)
21	$(CD_3)_2CO$		7.86 (*J* = 8.2)	6.31 (*J* = 5.9)	5.84 (*J* = 8.2)	4.53–3.81 (*m*)		3.49	4.53–3.81 (*m*)
22	$(CD_3)_2CO$	10.22	7.71 (*J* = 7.9)	6.13 (*J* = 5.9)	5.82 (*J* = 7.9)	4.58–4.08 (*m*)	3.52 (*J* = 4.7)	3.95–3.74	4.58–4.08 (*m*)
23	$(CD_3)_2CO$		7.71 (*J* = 8.1)	6.15 (*J* = 5.6)	5.72 (*J* = 8.1)		4.46–3.54 (*m*)		
24	$(CD_3)_2CO$		7.71 (*J* = 8.1)	6.16 (*J* = 5.6)	5.38 (*J* = 8.1)		4.52–4.11 (*m*)		
25	CD_3CN	9.62	8.07 (*J* = 8.2)	5.87 (*J* = 3.2)	6.70 (*J* = 8.2)	3.98 (*dd*, *J* = 9.7, 3.2)	3.68 (*dd*, *J* = 9.7, 7.6)	4.20	4.30 (*J* = 3.2)
26	$(CD_3)_2SO$		7.97 (*J* = 7.9)	5.72 (*J* = 3.8)	5.60 (*J* = 7.9)		3.91–3.65 (*m*)		3.47 (*J* = 3.81)
27[g])	$CDCl_3$		7.98 (*J* = 8.2)	6.00 (*J* = 3.5)	5.75 (*J* = 8.2)		4.54–3.29 (*m*)		
28	$(CD_3)_2CO$		7.65 (*J* = 8.2)	5.65 (*J* = 5.3)	5.65 (*J* = 8.2)	3.81 (*J* = 5.3)	4.87–3.42 (*m*)		
29	$(CD_3)_2CO$	10.10	7.66 (*J* = 8.2)	5.89 (*J* = 5.9)	5.68 (*J* = 7.9)		4.86–4.15 (*m*)		
30	$(CD_3)_2CO$	10.20	7.70 (*J* = 8.2)	5.97 (*J* = 5.3)	5.72 (*J* = 8.2)		4.96–3.84 (*m*)		
31	CD_3CN	9.16	7.60 (*J* = 7.9)	5.80 (*dd*, *J* = 10.0, 2.9)	5.72 (*J* = 7.9)	3.88 (*dd*, *J* = 10.8, 10.0)	3.51 (*dd*, *J* = 10.8, 2.9)	4.18 (*d*, *J* = 10.0, 7.0), 4.12 (*d*, *J* = 2.9, 0.9)	3.38 (*d*, *J* = 7.0, 4.5), 3.19 (*d*, *J* = 4.5, 0.9)
32	$(CD_3)_2CO$	10.17	7.73 (*J* = 8.2)	5.76 (*dd*, *J* = 10.0, 2.9)	5.32 (*J* = 8.2)		4.12–3.31 (*m*)		
33[h])	$(CD_3)_2CO$	10.22	8.11 (*J* = 8.2)	6.12 (*dd*, *J* = 10.0, 2.9)	5.93 (*J* = 8.2)	4.19–3.54 (*m*)		4.47	4.57 (*m*)
34[g])	$CDCl_3$	10.09	7.37 (*J* = 8.1)	5.81 (*J* = 2.9)	5.75 (*J* = 8.1)		4.4–3.10 (*m*)		
35[a])	$CDCl_3$	10.16	7.44 (*J* = 8.2)	5.94 (*dd*, *J* = 7.0, 2.9)	5.77 (*J* = 8.2)	4.08–3.91 (*m*)	3.58–3.17 (*m*)	4.39	4.32

[a]) Ph_3C: 7.4–7.29 for **2**–**4**, **8**–**11**, **35**. [b]) $MeSO_2$: 3.31–3.05 for **4**–**6**, **8**–**15**, **18**, **19**, **25**, **30**, **32**. [c]) MeCO: 2.20–1.98 for **3**, **11**, **14**, **15**, **18**, **20**–**24**, **29**. [d]) Disappearing in D_2O. [e]) Unless otherwise stated. [f]) MeO: 3.38 (*s*). [g]) PhCO: 8.04–8.02 and 7.52 (*m*). [h]) $MeC_6\mathit{H}_4$: 7.78 and 7.36 (2*d*, *J* = 8.2); $\mathit{Me}C_6H_4$: 2.45 (*s*).

Table 2. *^{13}C-NMR Data* (δ in ppm, internal standard TMS) *of the 2′,3′-Secouridines and Their Anhydro Structures*[a][b][c][d]

	Solvent	C(4) (*s*)	C(2) (*s*)	C(6) (*d*)	C(5) (*d*)	C(1′) (*d*)	C(4′) (*d*)	C(3′) (*t*)	C(2′) (*t*)	C(5′) (*t*)
1	CD_3OD	161.1	148.0	138.2	97.9	79.8	76.6	59.1[e]	58.0[e]	58.0[e]
2	$(CD_3)_2CO$	163.3	151.4	140.8	101.9	84.4	80.1	66.8[e]	64.1[e]	61.6
3	$(CD_3)_2SO$	162.9	150.1	140.2	102.4	80.2	76.0	62.8	62.8	62.8
4	$(CD_3)_2CO$	162.7	151.1	139.9	103.1	81.2	76.6	68.7[e]	68.1[e]	63.0
5	$(CD_3)_2SO$	171.4	160.3	137.3	108.7	87.0	78.4	69.7	73.6	60.3
6	CD_3CN	163.8	151.0	140.2	102.0	82.8	77.7	68.5	43.5	60.1
8	$(CD_3)_2CO$	162.8	151.3	139.6	102.9	83.0	76.6	68.6	43.6	63.0
9	$(CD_3)_2SO$	171.1	160.3	136.9	108.8	86.8	76.5	73.6	69.4	63.2
10	CD_3CN	164.9	152.4	141.9	103.3	84.9	77.0	70.0	63.7	62.8
11	$CDCl_3$	162.9	150.6	138.9	103.1	80.9	76.0	67.6	62.7	62.4
12	CD_3CN	164.2	150.9	140.6	102.0	80.9	77.6	68.4	67.8	59.9
13[f]	CD_3CN	165.8	152.6	142.5	103.1	82.9	78.2	69.9	72.6	61.3
14	$(CD_3)_2CO$	162.9	151.2	140.3	102.5	81.4	75.5	68.3	63.0[e]	62.9[e]
15	$(CD_3)_2CO$	163.0	151.4	140.1	102.8	81.0	74.9	62.9[e]	62.2[e]	68.7
18	$(CD_3)_2CO$	163.4	151.3	140.5	102.3	81.4	78.2	68.7	63.0	60.9
19	CD_3CN	166.3	153.6	143.4	103.8	85.7	79.0	70.8	63.8	62.4
20	$(CD_3)_2CO$	163.8	152.0	141.1	102.9	81.8	79.0	64.0	63.8	62.2
21	$(CD_3)_2CO$	163.0	151.4	140.6	102.7	80.6	76.8	65.0[e]	62.9[e]	64.4
22	$(CD_3)_2CO$	163.5	151.7	140.9	103.1	81.2	76.5	64.4	66.4[e]	63.4[e]
23	$(CD_3)_2CO$	163.2	151.5	140.6	102.4	81.6	79.0	64.2[e]	63.3[e]	61.2
24	$(CD_3)_2CO$	163.5	152.0	140.9	103.1	81.8	76.2	63.6[e]	64.2	63.2[e]
25	CD_3CN	165.6	152.3	143.9	102.4	76.6	69.5	67.0	67.0	69.2
26	$(CD_3)_2SO$	163.3	150.8	142.3	101.1	74.8	70.9	67.1[e]	66.3[e]	60.2
27	$CDCl_3$	163.1	150.5	141.1	102.1	75.2	68.7	67.4[e]	66.9[e]	62.8
28	CD_3OD	166.2	153.2	142.4	103.5	84.8	73.1	79.6	63.2	79.3
29	$(CD_3)_2CO$	163.3	152.0	139.9	102.8	80.6	71.9	77.7[e]	62.9	77.3[e]
30	$(CD_3)_2CO$	163.4	151.7	140.5	103.7	81.4	72.9	78.2[e]	68.2	77.9[e]
31	CD_3CN	164.4	151.1	141.2	103.2	79.1	76.8	68.2[e]	68.1[e]	64.2
32	$(CD_3)_2CO$	162.7	150.2	140.5	102.0	78.9	77.8	67.6[e]	67.2[e]	61.5
33[g]	$(CD_3)_2CO$	162.8	150.2	140.3	102.3	78.7	74.7	68.5[e]	67.3[e]	65.9
34	$CDCl_3$	163.3	150.0	139.5	102.9	78.7	78.6	67.9[e]	67.7[e]	66.2
35	$CDCl_3$	166.1	150.1	139.4	102.4	78.7	74.8	67.9[e]	66.9[e]	63.2

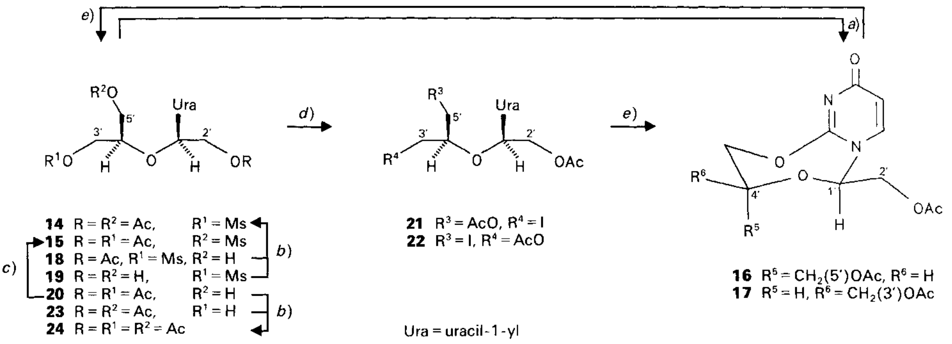
[a] *Ph*$_3$C at 145–127.1 and Ph$_3$*C* at 88.2–86.3 (*s*) for **2–4**, **8–11**, and **31**. [b] Ph*C*O at 166.1–165.9 (*s*) and *Ph*CO at 133.4–128.5 for **27** and **32**. [c] Me*C*O at 176.3–169.6 (*s*) and *Me*CO at 20.7–19.8 (*q*) for **3**, **11**, **14**, **15**, **18**, **20–24**, and **29**. [d] $MeSO_2$: 38.5–36.2 (*q*) for **4–6**, **8–15**, **18**, **19**, **25**, **30**, and **32**. [e] Interchangeable. [f] MeO: 59.8 (*q*). [g] *Me*C_6H_4 at 21.7 (*q*).

We next took advantage of the known behaviour of 2,2′-anhydropyrimidine nucleosides in alkaline media to obtain the configurationally defined 3′-*O*-(methylsulfonyl)-5′-*O*-(triphenylmethyl)-2′,3′-secouridine (**10**; 95%) from 2,2′-anhydro-2′,3′-secouridine **9** on treatment with 1N aq. NaOH in dioxane. Product **10** was characterized as 2′-*O*-acetyl derivative **11**.

The hitherto unknown 2′,3′-bis-*O*-(methylsulfonyl)-2′,3′-secouridine (**12**) was prepared by heating the 5′-*O*-(triphenylmethyl) compound **4** in MeOH and in the presence of the ion exchanger *Amberlyst 15*. Curiously, **12** was converted into 2′-*O*-methyl-3′-*O*-(methylsulfonyl)-2′,3′-secouridine (**13**; 54%) when heated in MeOH/MeCN 2:1 at 80°. This reaction proceeded most probably through MeO^- attack at C(2′) of the intermediate 2,2′-anhydro compound **5** (see *Exper. Part*).

2,3′- and 2,5′-Anhydro Structures. Attempted intramolecular cyclisation of 2′,5′-di-*O*-acetyl-3′-*O*-(methylsulfonyl)-2′,3′-secouridine (**14**) [17] and of the hitherto unknown 2′,3′-di-*O*-acetyl-5′-*O*-(methylsulfonyl)-2′,3′-secouridine (**15**; *Scheme 2*) into 2′,5′-di-*O*-acetyl-2,3′-anhydro- (**16**) and 2′,3′-di-*O*-acetyl-2,5′-anhydro-2′,3′-secouridine (**17**), respectively, by means of *t*-BuOK in DMF resulted in an unseparable mixture of products.

Scheme 2



14 R = R² = Ac, R¹ = Ms
15 R = R¹ = Ac, R² = Ms
18 R = Ac, R¹ = Ms, R² = H
19 R = R² = H, R¹ = Ms
20 R = R¹ = Ac, R² = H
23 R = R² = Ac, R¹ = H
24 R = R¹ = R² = Ac

21 R³ = AcO, R⁴ = I
22 R³ = I, R⁴ = AcO

Ura = uracil-1-yl

16 R⁵ = CH₂(5′)OAc, R⁶ = H
17 R⁵ = H, R⁶ = CH₂(3′)OAc

a) *t*-BuOK, DMF. *b*) Ac_2O, py. *c*) MsCl, py. *d*) NaI, MeCOEt. *e*) AgOAc, 50% MeOH.

The 2′,5′-di-*O*-acetyl compound **14** was prepared from 2′-*O*-acetyl-5′-*O*-(triphenylmethyl) compound **11** by treatment with *Amberlyst 15* in MeOH and acetylation of the thus obtained mixture of 2′-*O*-acetyl-3′-*O*-(methylsulfonyl)-2′,3′-secouridine (**18**) and 3′-*O*-(methylsulfonyl)-2′,3′-secouridine (**19**). It is worth noting that the latter can also be prepared from 2,2′-anhydro compound **9** in 63% yield if heated in 80% AcOH or from **4** in 80% yield if treated with *Amberlyst 15* in $MeCN/Me_2CO/H_2O$ 1:1:1. The 2′,3′-di-*O*-acetyl isomer **15** was prepared by detritylation of **3** in 80% AcOH and mesylation of the thus obtained 2′,3′-di-*O*-acetyl-2′,3′-secouridine (**20**; *Scheme 2*).

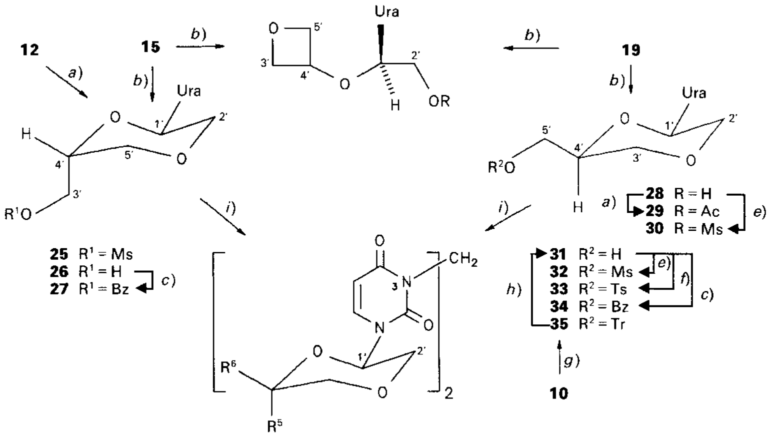
The earlier reported successful conversion of 5′-deoxy-5′-iodouridine into the corresponding 2,5′-anhydro structure [18] prompted us to synthesize 2′,5′-di-*O*-acetyl-3′-deoxy-3′-iodo-2′,3′-secouridine (**21**; 88.8%) from **14** and 2′,3′-di-*O*-acetyl-5′-deoxy-5′-iodo-2′,3′-secouridine (**22**; 92%) from **15** by reaction with NaI in MeCOEt (*Scheme 2*). The 3′- and 5′-iodo compounds **21** and **22**, however, on treatment with AgOAc in 50% MeOH [18], yielded a product mixture from which 2′,5′-di-*O*-acetyl- and 2′,3′-di-*O*-acetyl derivatives **23** and **20** [15], respectively, were isolated, indicating the intermediacy of the 2,3′-anhydro- and 2,5′-anhydro structures **16** and **17**, respectively (see *Exper. Part*). Acetylation of the di-*O*-acetyl compounds **20** and **23** afforded 2′,3′,5′-tri-*O*-acetyl-2′,3′-secouridine (**24**).

2′,5′-Anhydro Structures. On heating 2′,3′-di-*O*-mesyl compound **12** (*Scheme 1*) in MeCN, the novel 3′-*O*-(methylsulfonyl)-2′,3′-secouridine (**25**) was obtained in 81% yield by C(5′)—O⁻, C(2′) cyclisation (*Scheme 3*). The target 2′,5′-anhydro compound **26**, a *trans*-2,6-disubstituted 1,4-dioxane, was formed in 49% yield from 5′-*O*-mesyl compound **15** in the reaction with 1N aq. NaOH at 100° and characterized as 3′-*O*-benzoyl derivative **27**. In contrast to the C(5′)—O⁻, C(2′) cyclisation **12** → **25**, the transformation **15** → **26** proceeded by C(2′)—O⁻, C(5′) cyclisation.

3′,5′-Anhydro Structures. It turned out that the C(2′)—O$^-$, C(5) cyclisation **15**→**26** was accompanied by C(3′)—O$^-$, C(5) cyclisation yielding 3′,5′-anhydro-2′,3′-secouridine (**28**; 46.5%). The latter was characterized as the 2′-*O*-acetyl and 2′-*O*-mesyl derivatives **29** and **30**, respectively.

2′,3′-Anhydro Structures. To induce the regioselective formation of 2′,3′-anhydro-2′,3′-secouridine (**31**), the *cis*-disubstituted 1,4-dioxane diastereoisomer of **26**, 3′-*O*-mesyl compound **19** was treated with 1N aq. NaOH. The thus formed product **31** (43%) of C(2′)—O$^-$, C(3′) cyclisation was accompanied by 3′,5′-anhydro compound **28** (21%), which was identical to the compound obtained in the analogous transformation of **15**. *cis*-Diastereoisomer **31** was characterized as the 5′-*O*-mesyl-, 5′-*O*-tosyl-, and 5′-*O*-benzoyl derivatives **32**–**34** (*Scheme 3*).

Scheme 3



Ura = uracil-1-yl

36 $R^5 = H$, $R^6 = CH_2(5')OMs$
37 $R^5 = CH_2(3')OMs$, $R^6 = H$

a) MeCN, 80°. *b*) 1N aq. NaOH, 100°. *c*) Bz_2O, py. *d*) Ac_2O, py. *e*) MsCl, py. *f*) TsCl, py. *g*) *t*-BuOK, DMF. *h*) 80% AcOH. *i*) DBU, CH_2Cl_2.

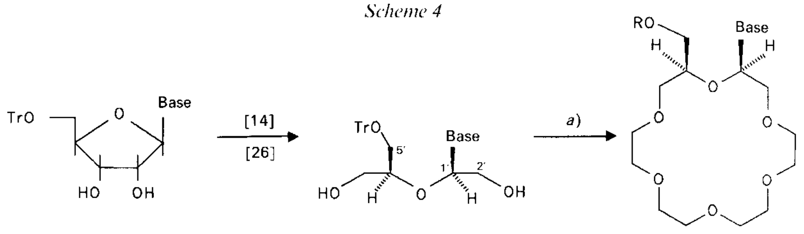
The best conditions for the generation of the *cis*-diastereoisomeric parent structure were the use of *t*-BuOK in DMF and 3′-*O*-mesyl-5′-*O*-(triphenylmethyl) compound **10**; 2′,3′-anhydro-5′-*O*-(triphenylmethyl)-2′,3′-secouridine (**35**) was formed in 99% yield. Recently, *van Aerschot et al.* [19] reported a multistep synthesis of **35** from **4** on treatment with NaOH in dioxane/H_2O; most probably it proceeded through C(2)—O$^-$, C(2′), cyclisation, C(2)—O—C(2′) ring-opening of the thus formed 2,2′-anhydro compound **9** to 3′-*O*-mesyl-5′-*O*-(triphenylmethyl) compound **10**, and C(2′)—O$^-$, C(3′) cyclisation of the latter.

Finally, an attempted C(2)—O$^-$, C(5′) cyclisation of *cis*-diastereoisomer **32** with DBU in CH_2Cl_2 [20] generated 3,3″-methylene bis[2′,3′-anhydro-5′-*O*-(methylsulfonyl)-2′,3′-secouridine] (**36**) in 44.6% yield. It is known that CH_2Cl_2 reacts with amines [21] [22]. Methylene-bridged bis-nucleosides were also studied: thus, adenosine, guanosine, and cytidine [23] produced the methylene cross-linkage at their exocyclic NH_2 groups if treated with formaldehyde, and treatment of the thymidine derivative with Bu_4NF in CH_2Cl_2

yielded the N(3)-methylene-bridged assembly [24]. Out approach to bis-uridine products was also efficient in the case of 3,3″-methylene bis[2′,5′-anhydro-3′-*O*-(methylsulfonyl)-2′,3′-secouridine] (**37**) which was formed in 48 % yield when the *trans*-diastereoisomer **25** was treated with CH_2Cl_2 in the presence of DBU. The NMR data of **36** and **37** (see *Exper. Part*) exhibited signals for the internucleosidic CH_2 group and for **32** and **25**, respectively.

2′,3′-Secouridine and -adenosine Derivatives as Synthons in the Synthesis of Chiral [18]Crown-6 Ethers. The most exciting utilization of 5′-*O*-(triphenylmethyl)-2′,3′-secouridine (**2**) [25], obtained from 5′-*O*-(triphenylmethyl)uridine (**38**) [14], was its reaction with 3,6,9-trioxaundecane-1,11-diyl bis(4-toluenesulfonate) in the presence of NaH. It yielded the novel *cis*-2-[(triphenylmethoxy)methyl]-18-(uracil-1-yl)[18]crown-6 (**39**; 50 %) (*Scheme 4*) which on detritylation in 80 % AcOH afforded *cis*-2-(hydroxymethyl)-18-(uracil-1-yl)[18]crown-6 (**40**).

Scheme 4



38 Base = uracil-1-yl (= Ura)
42 Base = N^6-Tr-adenin-9-yl (= N^6-Tr-Ade)

2 Base = Ura
41 Base = N^6-Tr-Ade

39 Base = Ura, R = Tr
40 Base = Ura, R = H
43 Base = N^6-Tr-Ade, R = Tr
44 Base = Ade, R = H
b)
b)

a) $TsOCH_2(CH_2OCH_2)_3CH_2OTs$, NaOH, THF. *b*) 80% AcOH.

Similarly, the hitherto unknown 5′-*O*,N^6-bis(triphenylmethyl)-2′,3′-secoadenosine (**41**) was synthesized by the standard $NaIO_4$ oxidative cleavage of 5′-*O*,N^6-bis(triphenylmethyl)adenosine (**42**) [26] and $NaBH_4$ reduction of the intermediate 2′,3′-dialdehyde. Subsequent reaction with 3,6,9-trioxaundecane-1,11-diyl bis(4-toluenesulfonate) in THF in the presence of NaH gave *cis*-2-[(triphenylmethoxy)methyl]-18-[N^6-(triphenylmethyl)adenin-9-yl][18]crown-6 (**43**; 50 %). Finally, detritylation in 80 % AcOH afforded *cis*-2-(adenin-9-yl)-18-(hydroxymethyl)[18]crown-6 (**44**).

The ^{1}H-NMR spectra of **40** (δ(NH) 8.97) and **44** (δ(NH_2) 5.94) exhibited strong downfield shifts in equimolar mixtures of the corresponding derivatives **39** and **43** (δ(H–N(3) of Ura) 10.26; δ(NH_2–C(6) of Ade) 6.22), indicating H-bonding interactions of the complementary Ura and Adebases.

We wish to thank the *Croatian Scientific Research Found* and the *European Communities Commission – International Cooperation* (Contract No. CI1/0523) for their support of this work.

Experimental Part

General. Solvents were dried and redistilled shortly before use. Extracts and filtrates were dried (Na_2SO_4) and evaporated *i.v.* Anal. samples were dried *i.v.* over P_2O_5 for 18 h. FC: silica gel (*Merck 60*, 230–240 mesh ASTM); in CH_2Cl_2/MeOH 40:1. Prep. TLC: silica gel activated at 110° for 60 min; in CH_2Cl_2/MeOH 9:1 (*A*) or 19:1 (*B*); products visible by UV illumination. M.p.: *Kofler* hot bench apparatus. Optical rotations ($[\alpha]_D^{20-25}$): *AA-10* automatic polarimeter (*Optical Activity Ltd.*, England). UV Spectra (λ_{max}(logε)): *Perkin-Elmer* double-beam spectrophotometer, model *124*; in EtOH. IR Spectra ($\tilde{\nu}$[cm^{-1}]): *Perkin-Elmer-297* spectrometer; solids in KBr pelletes, liquids as thin films. ^{1}H-NMR spectra (δ in ppm rel. to TMS and J in Hz): *Jeol-FX90Q* spectrometer; at 89.55 MHz. ^{13}C-NMR spectra (δ (CDCl$_3$) 77 rel. to TMS): *Jeol-FX90Q* spectrometer (at 22.5 Hz) and *Varian-Gemini-300* instrument; multiplicities from off-resonance decoupled spectra. MS: *Varian-MAT-CH-7* spectrometer; electron energy 70 eV, emission current 100 µA, ion-accelerating voltage 3 kV. High-resolution (HR) MS: *CEC-21-110C* double-focusing mass spectrometer; peak matching at 70 eV, 150 µA, and 6 kV.

5′-O-(Triphenylmethyl)-2′,3′-secouridine (= *1-{(1R)-2-Hydroxy-1-{(1S)-2-hydroxy-1-[(triphenylmethoxy)methyl]ethoxy}ethyl}uracil*; **2**) [25]. To a soln. of 5′-*O*-(triphenylmethyl)uridine [14] (1.75 g, 3.60 mmol) in dioxane/H$_2$O 5:1 (43 ml), a soln. of NaIO$_4$ (845 mg, 3.95 mmol) in H$_2$O (7 ml) was added dropwise and stirred at r.t. for 18 h. A precipitate was filtered off and the filtrate treated with NaBH$_4$ (136 mg, 3.60 mmol). After stirring for 15 min, the mixture was diluted with Me$_2$CO (0.7 ml), neutralized with 10% AcOH, and evaporated to a small volume to be partitioned between CHCl$_3$ and H$_2$O. The org. layer was dried and evaporated: 1.8 g (100%) of **2**. Colorless foam. R_f 0.35 (*B*). $[\alpha]_D = +27.5$ ($c = 0.95$, MeOH). UV: 258 (3.59). IR: 3420*s*, 1705*s*, 1685*s*, 1630 (sh), 1490*m*, 1450*m*, 1390*m*, 1265*m*, 1240*m*, 1120*s*, 1075*s*, 765*m*, 750*m*, 705*s*. Anal. calc. for $C_{28}H_{28}N_2O_6$ (488.54): C 68.84, H 5.78, N 5.73; found: C 68.78, H 6.0, N 6.96.

2′,3′-Di-O-acetyl-5′-O-(triphenylmethyl)-2′,3′-secouridine (= *1{(1R)-2-Acetoxy-1-{(1R)-2-acetoxy-1-[(triphenylmethoxy)methyl]ethoxy}ethyl}uracil*; **3**) [15]. To a soln. of **2** (573 mg, 1.17 mmol) in pyridine (2.7 ml), Ac$_2$O (2 ml, 21.3 mmol) was added. The mixture was stirred at r.t. for 1 h and then co-evaporated with EtOH, toluene, and Me$_2$CO: 672 mg (100%) of **3**. Colorless foam. R_f 0.45 (*B*). $[\alpha]_D = +19.0$ ($c = 1.04$, MeOH). UV: 257 (3.95). IR: 3220*w*, 1750*s*, 1700*s*, 1630*w*, 1500*m*, 1455*m*, 1375*s*, 1230*s*, 1080*m*, 770*m*, 750*w*, 715*m*.

2′,3′-Di-O-(methylsulfonyl)-5′-O-(triphenylmethyl)-2′,3′-secouridine (= *{(1R)-2-(Methylsulfonyloxy)-1-{(1R)-2-methylsulfonyloxy)-1-[(triphenylmethoxy)methyl]ethoxy}ethyl}uracil*; **4**) [17]. To a soln. of **2** (554 mg, 1.13 mmol) in pyridine (4.5 ml) at −20°, MsCl (0.26 ml, 3.4 mmol) was added. The mixture was then kept at +4° for 18 h and evaporated. The residue was mixed with ice/H$_2$O and extracted with CHCl$_3$ (3 × 25 ml). The org. layer was washed with aq. NaHCO$_3$ soln. and H$_2$O, dried, and co-evaporated with toluene and Me$_2$CO: 734 mg (100%) of **4**. Colorless foam. R_f 0.35 (*B*). $[\alpha]_D = +21.0$ ($c = 0.9$, MeOH). UV: 256 (4.09; [17]: 260 (4.1)). IR: 3450*w*, 1700*s*, 1630*m*, 1460*m*, 1365*s*, 1270*m*, 1180*s*, 1085*m*, 1020*m*, 975*m*, 815*m*, 770*m*, 705*m*.

2,2′-Anhydro-3′-O-(methylsulfonyl)-2′,3′-secouridine (= *(3R)-2,3-Dihydro-3-{(1R)-2-hydroxy-1-[(methylsulfonyloxy)methyl]ethoxy}-7H-oxazolo[3,2-a]pyrimidin-7-one*; **5**). To a soln. of **4** (322 mg, 0.49 mmol) in dioxane (5 ml), 1.6N aq. HCl (4 ml) was added and stirred at r.t. for 18 h. A precipitate was filtered off and the filtrate lyophilized. The residue was purified by prep. TLC (*A*, 2 developments): 123 mg (81%) of **5**. R_f 0.4 (*A*). Colorless crystals. M.p. 128–130° (EtOH/MeOH 1:1). $[\alpha]_D = +24.2$ ($c = 1.65$, MeCN). UV: 211 (4.29); infl. 261 (3.44). IR: 3400*m*, 1660*s*, 1630 (sh), 1530*s*, 1490*s*, 1350*s*, 1245*m*, 1175*s*, 1100*s*. Anal. calc. for $C_{10}H_{13}N_2O_7S$ (305.29): C 39.34, H 4.29, N 9.18; found: C 39.55, H 4.53, N 9.01.

2′-Chloro-2′-deoxy-3′-O-(methylsulfonyl)-2′,3′-secouridine (= *1{(1R)-2-Chloro-1-{(1R)-2-hydroxy-1-[(methylsulfonyloxy)methyl]ethoxy}ethyl}uracil*; **6**). To a soln. of **4** (131 mg, 0.2 mmol) in dioxane (2 ml), 1.6N HCl (1.6 ml) was added and stirred at 60° for 2.5 h. A precipitate was filtered off and the filtrate evaporated. The residue was purified by FC (CH$_2$Cl$_2$/MeOH 24:1): 30.8 mg (45%) of **6**. Colorless oil. R_f 0.3 (*A*). $[\alpha]_D = +52.7$ ($c = 1.31$, MeOH). UV: 255 (4.04). IR: 3440*s*, 1690*s*, 1465*m*, 1390*m*, 1350*m*, 1265*m*, 1175*s*, 1120*m*, 970*m*.

5′-O-Acetyl-2′-chloro-2′-deoxy-3′-O-(methylsulfonyl)-2′,3′-secouridine (= *1-{(1R)-1-{(1R)-2-Acetoxy-1-[(methylsulfonyloxy)methyl]ethoxy}-2-chloroethyl}uracil*; **7**). Acetylation of **6** (67.5 mg, 0.175 mmol) in pyridine (0.5 ml) with Ac$_2$O (0.09 ml, 0.99 mmol), standard workup, and FC (27 × 0.8 cm) gave 61 mg (80%) of **7**. R_f 0.6 (*B*). Anal. calc. for $C_{12}H_{17}ClN_2O_8S$ (384.80): C 37.46, H 4.45, N 7.28; found: C 37.22, H 4.65, N 7.56.

2′-Chloro-2′-deoxy-3′-O-(methylsulfonyl)-5′-O-(triphenylmethyl)-2′,3′-secouridine (= *1-{(1R)-2-Chloro-1-{(1R)-2-(methylsulfonyloxy)-1-[(triphenylmethoxy)methyl]ethoxy}ethyl}uracil*; **8**) [17]. A soln. of **4** (100 mg, 0.18 mmol) in DMF (10 ml) was treated with 2N aq. HCl (3 ml, 6 mmol) at r.t. for 5 h. The mixture was diluted with H$_2$O (50 ml) and extracted with CHCl$_3$ (2 × 50 ml). The org. layer was worked up by standard methods and the residue purified by prep. TLC (*A*): 94.5 mg (88.6%) of **8**. R_f 0.7 (*A*). $[\alpha]_D = +22.3$ ($c = 1.91$, MeOH). IR: 3430*w*, 1690*s*, 1630*m*, 1450*m*, 1360*m*, 1265*m*, 1175*s*, 1080*m*, 940*m*, 765*m*, 710*m*.

2,2′-Anhydro-3′-O-(methylsulfonyl)-5′-O-(triphenylmethyl)-2′,3′-secouridine (= *(3R)-2,3-Dihydro-3-{(1R)-2-methylsulfonyloxy)-1-[(triphenylmethoxy)methyl]ethoxy}-7H-oxazolo[3,2-a]pyrimidin-7-one*; **9**) [17]. To a soln. of **4** (759 mg, 1.12 mmol) in CH$_2$Cl$_2$ (12 ml, kept on molecular sieves 4 Å), DBU (0.19 ml, 1.3 mmol) was added and stirred at r.t. for 0.5 h. The mixture was evaporated and purified by FC (36 × 1.2 cm, CH$_2$Cl$_2$/MeOH 30:1): 645 mg (100%) of **9**. R_f 0.4 (*A*). Colorless crystals. M.p. 100–102° (MeOH). $[\alpha]_D = +21.0$ ($c = 0.50$, MeCN). UV: infl. 220 (4.39) and 252 (3.99; [17]: 250). IR: 1660*s*, 1635*s*, 1540*s*, 1480*s*, 1340*s*, 1240*m*, 1180*s*, 1115*s*, 1100*m*, 1080*s*, 1020*s*, 970*m*, 945*s*, 845*m*, 820*m*, 790*m*, 770*m*, 720*m*.

*3′-*O*-(Methylsulfonyl)-5′-*O*-(triphenylmethyl)-2′,3′-secouridine* (= *1-{(1*R*)-2-Hydroxy-1-{(1*R*)-2-(methylsulfonyloxy)-1-[(triphenylmethoxy)methyl]ethoxy}ethyl}uracil*; **10**). To a soln. of **9** (165 mg, 0.3 mmol) in dioxane (2 ml), 1N aq. NaOH (0.3 mmol) was added, stirred at r.t. for 18 h, evaporated, and purified by FC (27 × 0.8 cm): 158 mg (95%) of **10**. R_f 0.6 (*A*). $[\alpha]_D = +14.3$ ($c = 0.9$, $CHCl_3$). UV: 257 (3.9; [17]: 260 (4.11)). IR: 3440*m*, 1690*s*, 1630 (sh), 1450*m*, 1350*m*, 1270*m*, 1170*s*, 1080*m*, 960*m*, 820*m*, 760*m*, 710*m*.

*2′-*O*-Acetyl-3′-*O*-(methylsulfonyl)-5′-*O*-(triphenylmethyl)-2′,3′-secouridine* (= *1-{(1*R*)-2-Acetoxy-1-{(1*R*)-2-(methylsulfonyloxy)-1-[(triphenylmethoxy)methyl]ethoxy}ethyl}uracil*; **11**). To a soln. of **9** (316 mg, 0.58 mmol) in dioxane (4 ml), 1N aq. NaOH (0.58 ml) was added, stirred at r.t. for 18 h, and co-evaporated with toluene and dry EtOH. To the residue in pyridine (1.3 ml), Ac_2O (0.52 ml, 5.53 mmol) was added, stirred at r.t. for 3 h, and evaporated. The residue was partitioned between $CHCl_3$ (3 × 60 ml) and H_2O (25 ml). The org. layer was washed with aq. $NaHCO_3$ soln. and H_2O, dried, and evaporated: 328 mg (94%) of **11**. Colorless foam. R_f 0.6 (*B*). $[\alpha]_D = +32.5$ ($c = 1.96$, $CHCl_3$). UV: 256 (3.95). IR: 3460*w*, 1750*s*, 1690*s*, 1660*s*, 1630*m*, 1450*m*, 1360*m*, 1270*m*, 1230*m*, 1180*s*, 1080*m*, 960*m*, 910*m*, 770*m*, 730*m*, 710*m*. Anal. calc. for $C_{31}H_{32}N_2O_9S$ (608.67): C 61.17, H 5.30, N 4.60; found: C 61.32, H 5.53, N 4.46.

*2′,3′-Bis-*O*-(methylsulfonyl)-2′,3′-secouridine* (= *1-{(1*R*)-2-(Methylsulfonyloxy)-1-{(1*R*)-2-hydroxy-1-[(methylsulfonyloxy)methyl]ethoxy}ethyl}uracil*; **12**). A soln. of **4** (500 mg, 0.78 mmol) in MeOH/MeCN 2:1 (3 ml) was treated with *Amberlyst 15* (8 mg) and stirred at 10–15° for 5 days. The org. phase was evaporated and the residue purified by FC (36 × 1.2 cm, CH_2Cl_2/MeOH 30:1): 200 mg (99%) of TrOH (R_f 0.95, *A*) and 231 mg (74%) of **12**. Colorless foam. R_f 0.3 (*A*). $[\alpha]_D = +58.5$ ($c = 0.65$, Me_2CO). UV: 252 (3.51). IR: 3440*m*, 1690*s*, 1625 (sh), 1460*m*, 1390*s*, 1350*s*, 1270*m*, 1170*s*, 1120*m*, 1050*m*, 970*m*. Anal. calc. for $C_{17}H_{18}N_2O_{10}S_2$ (402.4): C 32.83, H 4.51, N 6.96; found: C 33.04, H 4.75, N 6.76.

*2′-*O*-Methyl-3′-*O*-(methylsulfonyl)-2′,3′-secouridine* (= *1-{(1*R*)-1-{(1*R*)-2-Hydroxy-1-[(methylsulfonyloxy)methyl]ethoxy}-2-methoxyethyl}uracil*; **13**). A soln. of **12** (315 mg, 0.87 mmol) in MeOH/MeCN 2:1 (3.5 ml) was stirred at r.t. for 18 h, then at 70–80° for 12 h and evaporated. Three foamy products were separated by FC (35 × 1.2 cm) and TLC (*A*): 60 mg (25%) of **25** (R_f 0.6; *vide infra*), 142 mg (54%) of **13** (R_f 0.45), and 16.5 mg (6.5%) of **19** (R_f 0.25) [15]. **13**: $[\alpha]_D = +44.6$ ($c = 1.12$, MeOH). UV: 257 (3.62). IR: 3400*m*, 3200*m*, 1690*s*, 1635 (sh), 1460*m*, 1390*m*, 1350*s*, 1270*m*, 1170*s*, 1110*s*, 970*m*. Anal. calc. for $C_{11}H_{18}N_2O_8S$ (338.33): C 39.05, H 5.36, N 8.28; found: C 38.98, H 5.5, N 8.46.

*2′-*O*-Acetyl-3′-*O*-(methylsulfonyl)-2′,3′-secouridine* (= *1-{(1*R*)-2-Acetoxy-1-{(1*R*)-2-hydroxy-1-[(methylsulfonyloxy)methyl]ethoxy}ethyl}uracil*; **18**). To a soln. of **11** (182 mg, 0.9 mmol) in MeOH (1 ml), *Amberlyst 15* (3 mg) was added. The mixture was stirred at r.t. for 48 h and then evaporated. Three foamy products were separated by FC (17 × 1.2 cm, CH_2Cl_2/MeOH 20:1) and TLC (*B*): 76 mg (97%) of TrOH (R_f 0.95 (*A*)), 53 mg (48%) of **18** (R_f 0.5), and 23 mg (24%) of **19** [15] (R_f 0.3; *vide infra*). **18**: Colorless oil. $[\alpha]_D = +43.1$ ($c = 1.06$, MeOH). UV: 256 (4.03). IR: 3200*m*, 1745*s*, 1690*s*, 1625 (sh), 1460*m*, 1350*s*, 1230*s*, 1170*s*, 1120*m*, 1050*m*, 960*m*.

*2′,5′-Di-*O*-acetyl-3′-*O*-(methylsulfonyl)-2′,3′-secouridine* (= *1-{(1*R*)-2-Acetoxy-1-{(1*R*)-2-acetoxy-1-[(methylsulfonyloxy)methyl]ethoxy}ethyl}uracil*; **14**). To a soln. of **18** (33 mg, 0.09 mmol) in pyridine (0.5 ml) at r.t., Ac_2O (0.042 ml, 0.45 mmol) was added, stirred for 2 h, and evaporated. The residue was purified by prep. TLC (*B*, 2 developments): 26.6 mg (72.2%) of **18**. R_f 0.7 (*A*). Colorless oil. $[\alpha]_D = +43.2$ ($c = 0.53$, $CHCl_3$). UV: 255 (3.66). IR: 3440*w*, 3240*w*, 1750*s*, 1690*s*, 1630*m*, 1460*s*, 1360*s*, 1230*s*, 1175*s*, 1110*s*, 1050*s*, 970*s*, 770*m*. Anal. calc. for $C_{14}H_{20}N_2O_{10}S$ (408.38): C 41.18, H 4.94, N 6.86; found: C 41.45, H 5.19, N 6.74.

*2′,3′-Di-*O*-acetyl-5′-*O*-(methylsulfonyl)-2′,3′-secouridine* (= *1-{(1*R*)-2-Acetoxy-1-{(1*S*)-2-acetoxy-1-[(methylsulfonyloxy)methyl]ethoxy}ethyl}uracil*; **15**). To a soln. of **20** (*vide infra*; 500 mg, 1.51 mmol) in pyridine (5.5 ml) at −20°, MsCl (0.17 ml; 2.27 mmol) was added. The mixture was kept at −20° for 18 h, the solvent removed, and the residue partitioned between $CHCl_3$ (3 × 25 ml) and ice-water. The org. layer was washed with aq. $NaHCO_3$ soln. and H_2O, dried, and evaporated: 441.2 mg (71.4%) of **15**. Colorless oil. R_f 0.5 (*B*). $[\alpha]_D = +38.4$ ($c = 0.95$, $CHCl_3$). UV: 254 (4.2). IR: 3220*m*, 1750*s*, 1690*s*, 1630*m*, 1460*m*, 1360*s*, 1230*s*, 1175*s*, 1110*m*, 1050*s*, 970*s*. Anal. calc. for $C_{14}H_{20}N_2O_{10}S$ (408.39): C 41.18, H 4.94, N 6.86; found: C 41.42, H 4.73, N 6.69.

*3′-*O*-(Methylsulfonyl)-2′,3′-secouridine* (= *1-{(1*R*)-2-hydroxy-1-{(1*R*)-2-hydroxy-1-[(methylsulfonyloxy)methyl]ethoxy}ethyl}uracil*; **19**) [15]. a) A soln. of **9** (245 mg, 0.45 mmol) in 80% AcOH (2.5 ml) was heated at 100° for 1 h. The mixture was evaporated and the residue separated by FC (35 × 1.2 cm): 92 mg (63.4%) of **19**. Identical to **19** obtained on hydrolysis of **11**. Colorless oil. R_f 0.25 (*A*). $[\alpha]_D = +37.2$ ($c = 1.66$, MeOH). UV: 261.1 (3.66). IR: 3360*s*, 1690*s*, 1625 (sh), 1460*m*, 1390*m*, 1350*s*, 1265*m*, 1170*s*, 1110*m*, 960*m*.

b) To a soln. of **4** (256 mg, 0.397 mmol) in MeCN/Me_2CO/H_2O 1:1:1 (1.8 ml), *Amberlyst 15* (4 mg) was added and stirred at r.t. for 7 days. The soln. was evaporated and the residue purified by FC (36 × 1.2 cm, CH_2Cl_2/MeOH 30:1): 103 mg (80%) of **19**. UV, IR, and NMR: identical to that described above.

Acetylation of **19** (109 mg, 0.34 mmol) in pyridine (2 ml) with Ac_2O (0.316 ml, 3.36 mmol) gave, after 2.5 h stirring at r.t., co-evaporation with toluene and EtOH, and prep. TLC (*B*, 2 developments), 101.5 mg (72.5%) of **14**. Colorless oil. UV, IR, and NMR: identical to that of **14** obtained from **18**.

*2′,3′-Di-*O*-acetyl-2′,3′-secouridine* (= *1-{(1*R*)-2-Acetoxy-1-[(1*R*)-2-acetoxy-1-(hydroxymethyl)ethoxy]ethyl}uracil*; **20**) [15]. To a soln. of the **2** (573 mg, 1.17 mmol) in pyridine (2.7 ml), Ac_2O (2 ml, 21.3 mmol) was added and stirred at r.t. for 1 h. The mixture was evaporated and the residue dissolved in 80% AcOH (18 ml) and then heated at 100° for 1 h. Standard workup and purification by FC (38 × 1.2 cm, CH_2Cl_2/MeOH 40:1 (200 ml) and 20:1 (100 ml)) gave 229 mg (77%) of **20**. Colorless oil. R_f 0.7 (*A*). $[\alpha]_D = +67.9$ ($c = 0.84$, Me_2CO). IR: 3430*m*, 3200*m*, 1745*s*, 1690*s*, 1630*m*, 1465*m*, 1380*s*, 1240*s*, 1120*m*, 1050*m*.

*2′,5′-Di-*O*-acetyl-3′-deoxy-3′-iodo-2′,3′-secouridine* (= *1-{(1*R*)-2-Acetoxy-1-[(1*R*)-2-acetoxy-1-(iodomethyl)ethoxy]ethyl}uracil*; **21**). To a soln. of **14** (345 mg, 0.84 mmol) in MeCOEt (4 ml), NaI (270 mg, 1.8 mmol) was added. The mixture was heated under reflux for 1 h. A precipitate was filtered off and the filtrate evaporated. The residue was dissolved in CH_2Cl_2 (5 ml), washed with 5% $Na_2S_2O_3$ soln. (5 ml), dried, evaporated, and purified by FC (37 × 0.8 cm): 329 mg (88.8%) of **21**. Colorless oil. R_f 0.6 (*A*). $[\alpha]_D = +59.9$ ($c = 1.39$, Me_2CO). UV: 258 (3.93). IR: 3500*w*, 3200*m*, 1750*s*, 1690*s*, 1630*m*, 1460*s*, 1390*s*, 1235*s*, 1105*s*, 1055*s*. MS: 441 ($[M + H]^+$), 329, 227, 197, 155, 112, 99, 84, 70. HR-MS: 440.1796 ($C_{13}H_{17}I_2N_7O$, calc. 440.18).

*2′,3′-Di-*O*-acetyl-5′-deoxy-5′-iodo-2′,3′-secouridine* (= *1-{(1*R*)-2-Acetoxy-1-[(1*S*)-2-acetoxy-1-(iodomethyl)ethoxy]ethyl}uracil*; **22**). To a soln. of **15** (175 mg, 0.43 mmol) in MeCOEt (3 ml), NaI (192 mg, 1.8 mmol) was added and heated under reflux for 1 h. Workup as described for **21** and purification by FC (28 × 0.8 cm) gave 173 mg (91.8%) of **22**. Colorless oil. R_f 0.6 (*A*). $[\alpha]_D = +24.7$ ($c = 0.93$, Me_2CO). UV: 257 (4.09). IR: 3480*w*, 3220*w*, 1740*s*, 1690*s*, 1630*m*, 1445*m*, 1380*s*, 1230*s*, 1100*s*, 1050*s*. MS: 441 ($[M + H]^+$), 330, 329, 227, 197, 155, 113, 112, 99, 84. HR-MS: 440.1865 ($C_{13}H_{17}I_2N_7O$, calc. 440.18).

Intramolecular Transformations of the Iodo Compounds **21** *and* **22**. To a soln. of **21** (167 mg, 0.32 mmol) in MeOH (60 ml), AgOAc (285 mg, 1.7 mmol) was added and heated under reflux for 3.5 h [18]. The mixture was then cooled to r.t., a precipitate filtered off, and the filtrate saturated on bubbling with H_2S. After filtration through a *Celite* pad, the filtrate was evaporated and the residue separated by prep. TLC (CH_2Cl_2/MeOH 40:1, 2 developments): 43 mg (25.8%) of **21** (R_f 0.6, *A*), 11.2 mg (9.0%) of **20** (R_f 0.48), identical (UV, IR, and NMR) to authentic material, and 9.3 mg (7.5%) of *2′,5′-di-*O*-acetyl-2′,3′-secouridine* (= *1-{(1*R*)-2-acetoxy-1-[(1*S*)-2-acetoxy-1-(hydroxymethyl)ethoxy]ethyl}uracil*; **23**). **23**: Colorless oil. $[\alpha]_D = +42.6$ ($c = 0.27$, Me_2CO). R_f 0.43 (*A*). UV: 259 (3.88). IR: 3420*m*, 3180*w*, 1740*s*, 1690*s*, 1625*m*, 1460*m*, 1380*m*, 1270*m*, 1230*s*, 1170*w*, 1105*m*, 1050*m*.

As described above for **21**, **22** (165 mg, 0.38 mmol) in MeOH (60 ml) and AgOAc (282 mg, 1.69 mmol; 6.5 h reflux) gave, after FC and TLC (*B*, 2 developments), 48 mg (29.1%) of **22** (R_f 0.6 *A*), 14.7 mg (11.9%) of **20** (R_f 0.48), and 10.4 mg (8.4%) of **23** (R_f 0.43), identical (IR and NMR) to **20** and **23**, resp., prepared from **21**.

Acetylation of **20** *and* **23**. To a soln. of **20**/**23** (32 mg, 0.1 mmol) in pyridine (0.5 ml), Ac_2O (0.09 ml, 0.97 mmol) was added and kept aside for 1.5 h. Standard workup gave 32 mg (89%) of *2′,3′,5′-tri-*O*-acetyl-2′,3′-secouridine* (= *1-{(1*R*)-2-Acetoxy-1-{2-acetoxy-1-[(acetoxy)methyl]ethoxy}ethyl}uracil*; **24**). Colorless oil. R_f 0.6 (*A*). $[\alpha] = +39.6$ ($c = 0.56$, Me_2CO). UV: 258 (3.64). IR: 3200*m*, 1740*s*, 1690*s*, 1630*s*, 1450*s*, 1370*s*, 1220*s*, 1170*m*, 1100*s*, 1050*s*, 975*m*. MS: 373 ($[M + H]^+$), 262, 261, 198, 197, 159, 155, 117, 112. HR-MS: 372.3254 ($C_{15}H_{20}N_2O_9$, calc. 372.33).

*2′,5′-Anhydro-3′-*O*-(methylsulfonyl)-2′,3′-secouridine* (= *1-{(2*R*,6*R*)-6-[(Methylsulfonyloxy)methyl]-1,4-dioxan-2-yl}uracil*; **25**). A soln. of **12** (187 mg, 0.47 mmol) in MeCN (4 ml) was heated at 80° for 21 h and then evaporated. The residue was separated by FC (27 × 0.8 cm): 115 mg (81%) of **25**. R_f 0.6 (*A*). M.p. 152–154° (MeOH). $[\alpha]_D = -76$ ($c = 0.5$, MeOH). UV: 255 (3.97). IR: 3460*w*, 3210*w*, 1690*s*, 1620(sh), 1450*m*, 1380*m*, 1350*s*, 1275*s*, 1170*s*, 1104*m*, 950*m*. MS: 306 (M^+), 226, 196, 195, 194, 136, 135, 134, 112, 99, 79, 69, 57. Anal. calc. for $C_{10}H_{14}N_2O_7S$ (306.29): C 39.21, H 4.61, N 9.15; found: C 38.93; H 4.91, N 9.13.

Transformations of **15** *under Basic Conditions*. A soln. of **15** (181 mg, 0.44 mmol) in H_2O (15 ml) was treated with 1N aq. NaOH (2.25 ml) and stirred at 90–100° for 2.5 h. The mixture was then neutralized with 1N aq. HCl and evaporated. Prep. TLC (*B*, 4 developments) gave 49.5 mg (49%) of *2′,5′-anhydro-2′,3′-secouridine* (= *1-[(2*R*,6*S*)-6-(hydroxymethyl)-1,4-dioxan-2-yl]uracil*; **26**) and 47 mg (46.5%) of *3′,5′-anhydro-2′,3′-secouridine* (= *1-{(1*R*)-2-hydroxy-1-[(oxetan-3-yl)oxy]ethyl}uracil*; **28**).

Data of **26**: Colorless oil. R_f 0.35 (*B*). $[\alpha]_D = -64.2$ ($c = 1.34$, MeOH). UV: 259 (3.77). IR: 3410*m*, 1730*s*, 1690*s*, 1620 (sh), 1460*m*, 1430*m*, 1390*s*, 1280*s*, 1140*m*, 1080*m*.

Data of **28**: Colorless oil. R_f 0.3 (*B*). $[\alpha]_D = +24.4$ ($c = 0.82$, MeOH). UV: 256 (3.86). IR: 3400*s*, 1690*s*, 1620*m*, 1460*m*, 1380*m*, 1270*m*, 1120*s*, 960*m*.

*2′,5′-Anhydro-3′-*O*-benzoyl-2′,3′-secouridine* (= *1-{(2*R*,6*R*)-6-[(Benzoyloxy)methyl]-1,4-dioxan-2-yl}uracil*; **27**). To a soln. of **26** (39 mg, 0.17 mmol) in pyridine (1 ml), BzCl (0.03 ml, 0.26 mmol) was added, stirred at r.t. for 18 h, and then evaporated. The residue was partitioned between H_2O (3 ml) and $CHCl_3$ (3 × 5 ml). The org.

layer was washed with aq. $NaHCO_3$ soln. and H_2O, dried, and evaporated. Prep. TLC (*B*) gave: 40.5 mg (70%) of **27**. Colorless microcrystals from Et_2O/hexane. R_f 0.4 (*B*). $[\alpha]_D = -81.0$ ($c = 0.65$, $CHCl_3$). UV: 228 (3.97), 244 (3.76), 257 (3.94). IR: 3460*m*, 3220*m*, 1720*s*, 1690*s*, 1620 (sh), 1460*m*, 1390*m*, 1310*m*, 1265*s*, 1120*m*, 1080*m*. Anal. calc. for $C_{16}H_{16}N_2O_6$ (332.32): C 57.83, H 4.85, N 8.43; found: C 58.05, H 5.05, N 8.18.

2′-O-Acetyl-3′,5′-anhydro-2′,3′-secouridine (= *1-[{(1R)-2-Acetoxy-1-[(oxetan-3-yl)oxy]ethyl}uracil*; **29**). To a soln. of **28** (47 mg, 0.206 mmol) in pyridine (1 ml), Ac_2O (0.05 ml, 0.53 mmol) was added. Standard workup and prep. TLC (*B*) gave 48 mg (86%) of **29**. Colorless oil. R_f 0.4 (*B*). $[\alpha]_D = +43.8$ ($c = 0.96$, Me_2CO). Anal. calc. for $C_{11}H_{14}N_2O_6$ (270.24): C 48.89, H 5.22, N 10.37; found: C 48.67, H 5.46, N 10.16.

3′,5′-Anhydro-2′-O-(methylsulfonyl)-2′,3′-secouridine (= *1-{(1R)-2-(Methylsulfonyloxy)-1-[(oxetan-3-yl)-oxy]ethyl}uracil*; **30**). To a soln. of **28** (29.0 mg, 0.127 mmol) in pyridine (1 ml) at −20°, MsCl (0.014 ml, 0.19 mmol) was added. The mixture was then kept at +4° for 18 h, the solvent evaporated, and the residue partitioned between AcOEt (3 × 5 ml) and H_2O. The org. layer was washed with aq. $NaHCO_3$ soln. and H_2O, dried, evaporated, and purified by prep. TLC (*B*, 2 developments): 23.9 mg (61.4%) of **30**. Colorless oil. R_f 0.4 (*B*). $[\alpha]_D = +50.2$ ($c = 1.20$, MeOH). UV: 257 (3.36). IR: 3450*m*, 3200*w*, 1690*s*, 1625 (sh), 1460*m*, 1360*s*, 1270*m*, 1175*s*, 1120*m*, 965*m*. MS: 306 (M^+), 282, 271, 197, 196, 195, 182, 177, 173, 163, 154, 113, 109, 108, 107, 100, 99, 97, 92, 70, 58. Anal. calc. for $C_{10}H_{14}N_2O_7S$ (306.29): C 39.21, H 4.61, N 9.15; found: C 39.43, H 4.45, N 9.06.

2′,3′-Anhydro-2′,3′-secouridine (= *(1-[(2R,6R)-6-(Hydroxymethyl)-1,4-dioxan-2-yl]uracil*; **31**). a) To a soln. of **19** (81 mg, 0.25 mmol) in H_2O (5 ml), 1N aq. NaOH (0.75 ml) was added. The mixture was heated under reflux for 2 h and then evaporated. The residue was separated by prep. TLC (*B*, 5 developments): 12 mg (21%) of **28** (R_f 0.30 (*B*); identical (UV, IR, and NMR) to **28** obtained from **15** and 24.5 mg (43%) of **31**. Colorless oil. R_f 0.35. $[\alpha]_D = +35.0$ ($c = 1.22$, MeOH). UV: 257 (4.22; [17]: 257 (4.0)). IR: 3440*m*, 1690*s*, 1455*m*, 1380*m*, 1265*m*, 1115*s*.

b) A soln. of **35** (*vide infra*) (309 mg, 0.66 mmol) in 80% AcOH (7 ml) as in [17] was heated at 100° for 10 min, evaporated, and purified by FC (27 × 1.2 cm, CH_2Cl_2/MeOH 30.1): 95.7 mg (64%) of **31**. R_f 0.35 (*B*). IR and NMR: identical to those described under b).

2′,3′-Anhydro-5′-O-(methylsulfonyl)-2′,3′-secouridine (= *1-{(2R,6S)-6-[(Methylsulfonyloxy)methyl]-1,4-dioxan-2-yl}uracil*; **32**). To a soln. of **31** (115 mg, 0.5 mmol) in pyridine (2 ml), at +4°, MsCl (0.057 ml, 0.76 mmol) was added and kept aside for 20 h. The mixture was co-evaporated with toluene and the residue purified by FC: 137 mg (89%) of **32**. Colorless crystals. M.p. 156–158° (MeOH). R_f 0.6 (*A*). $[\alpha]_D = +15.0$ ($c = 1.1$, MeOH). UV: 256 (3.87). IR: 3420*m*, 1690*s*, 1630*m*, 1455*m*, 1380*m*, 1350*s*, 1270*s*, 1170*s*, 1120*s*, 935*m*. Anal. calc. for $C_{10}H_{14}N_2O_7S$ (306.29): C 39.21, H 4.61, N 9.15; found: C 39.00, H 4.82, N 9.05.

2′,3′-Anhydro-5′-O-(4-Tolylsulfonyl)-2′,3′-secouridine (= *1{(2R,6S)-6-[(4-Tolylsulfonyloxy)methyl]-1,4-dioxan-2-yl}uracil*; **33**). To a soln. of **31** (75 mg, 0.33 mmol) in pyridine (2 ml) TsCl (126 mg, 0.66 mmol) was added, stirred at 35–40° for 48 h, and then co-evaporated with toluene. The residue was partitioned between ice-water and AcOEt (3 × 5 ml), the org. layer washed with H_2O, dried, and evaporated, and the residue purified by FC (27 × 0.8 cm): 69 mg (55%) of **33**. Colorless oil. R_f 0.6 (*A*). $[\alpha]_D = +32.0$ ($c = 0.64$, $CHCl_3$). UV: 221 (3.85), 258 (3.74). IR: 3430*w*, 3210*w*, 1700*s*, 1630 (sh), 1455*m*, 1385*m*, 1360*m*, 1275*s*, 1180*s*, 1120*m*, 990*m*, 940*m*. Anal. calc. for $C_{16}H_{18}N_2O_7S$ (382.39): C 50.26, H 4.74, N 7.33; found: C 50.52, H 4.86, N 7.20.

2′,3′-Anhydro-5′-O-benzoyl-2′,3′-secouridine (= *{(2R,6S)-6-[(Benzoyloxy)methyl]-1,4-dioxan-2-yl}uracil*; **34**). to a soln. of **31** (106 mg, 0.46 mmol) in pyridine (1 ml), BzCl (0.067 ml, 0.58 mmol) was added and stirred at r.t. for 18 h. The solvent was removed and the residue partitioned between $CHCl_3$ (3 × 5 ml) and H_2O (5 ml). The org. layer was washed with H_2O (2 × 5 ml), dried, and evaporated. The residue crystallized from MeOH: 125 mg (81.4%) of **34**. M.p. 146–148°. R_f 0.8 (*A*). $[\alpha]_D = +13.0$ ($c = 0.93$, $CHCl_3$). UV: 228 (4.06), 257 (3.93). IR: 3430*m*, 1765*m*, 1745*s*, 1725*s*, 1715*s*, 1625*m*, 1465*m*, 1425*m*, 1380*s*, 1330*m*, 1320*s*, 1290*s*, 1275*s*, 1120*m*, 925*m*. Anal. calc. for $C_{16}H_{16}N_2O_6$ (332.31): C 57.83, H 4.85, N 8.43; found: C 58.10, H 4.99, N 8.37.

2′,3′-Anhydro-5′-O-(triphenylmethyl)-2′,3′-secouridine (= *{(2R,6S)-6-[(Triphenylmethoxy)methyl]-1,4-dioxan-2-yl}uracil*; **35**) [17] [19]. To a soln. of **10** (413 mg, 0.73 mmol) in DMF (8.3 ml), freshly prepared *t*-BuOK (164 mg, 1.46 mmol) was added and stirred at r.t. for 15 min. The mixture was diluted with H_2O (25 ml), neutralized with 1N aq. $NaHSO_4$ soln. and partitioned between $CHCl_3$ and H_2O. The org. layer was washed with H_2O, dried, and evaporated: 341 mg (99%) of **35**. Colorless oil. R_f 0.4 (*A*). $[\alpha]_D = +4.0$ ($c = 0.5$, $CHCl_3$). UV: 256 (3.86; [21] 260 (4.10)). IR: 1690*s*, 1625*m*, 1450*m*, 1380*m*, 1265*m*, 1120*m*, 1080*m*, 760*m*, 710*m*.

3,3″-Methylenebis[2′,3′-anhydro-5′-O-(methylsulfonyl)-2′,3′-secouridine] (= *3,3″-Methylenebis{1-{(2R,6S)-6-[(methylsulfonyloxy)methyl]-1,4-dioxan-2-yl}uracil}*; **36**). To a soln. of **32** (59 mg, 0.19 mmol) in CH_2Cl_2 (2 ml), DBU (59 mg, 0.39 mmol) was added. The mixture was stirred at r.t. for 10 days and separated by TLC (*B*, 3 developments): 29 mg (48.7%) of **32** and 27 mg (44.6%) of **36**. Colorless oil. R_f 0.65 (*A*). $[\alpha]_D = +3.0$ ($c = 0.85$, Me_2CO). UV: 260.8 (3.75). IR: 3460*w*, 2920*m*, 1720*s*, 1690*s*, 1640 (sh), 1450*s*, 1405*m*, 1355*s*, 1280*s*, 1245*m*, 1175*s*, 1120*s*, 1040*m*, 970*m*, 940*m*. ^{1}H-NMR (CD_3COCD_3): 7.73 (*d*, $J = 8.2$, 2 H–C(6)); 6.03 (*s*, NCH_2N); 5.84 (*dd*, *J* = 9.9, 2.8, 2 H–C(1')); 5.71 (*d*, *J* = 8.2, 2 H–C(5)); 4.38–4.29 (*m*, 2 CH_2(5'), 2 H–C(4')); 3.89, 3.51 (2*m*, 2 CH_2(2'), 2 CH_2(3')); 3.14 (*s*, 2 Me). ^{13}C-NMR (CD_3COCD_3): 161.9 (*s*, 2 C(4)); 150.7 (*s*, 2 C(2)); 139.5 (*d*, 2 C(6)); 102.4 (*d*, 2 C(5)); 80.0 (*d*, 2 C(1')); 75.3 (*d*, 2 C(4')); 69.2 (*t*, 2 C(5')); 68.0, 66.6 (2*t*, 2 C(2'), 2 C(3')); 47.3 (*t*, NCH_2N); 37.3 (*q*, 2 Me). Anal. calc. for $C_{21}H_{28}N_4O_{14}S_2$ (624.60): C 40.38, H 4.52, N 8.97; found: C 40.19, H 4.75, N 8.87.

*3,3''-Methylenebis[2',5'-anhydro-3'-*O*-(methylsulfonyl)-2',3'-secouridine]* (*= 3,3''-Methylenebis{1-{(2*R*,6*R*)-6-[(methylsulfonyloxy)methyl]-1,4-dioxan-2-yl}uracil}*; **37**). To a soln. of **25** (51.9 mg, 0.17 mmol) in CH_2Cl_2/MeCN 2:1 (7.5 ml), DBU (117 mg, 0.77 mmol) was added. The mixture was stirred at 70° for 6.5 h and evaporated. The residue was separated by FC (27 × 0.8 cm): 14.8 mg (28.5%) of **25** and 25.4 mg (48%) of **37**. Colorless crystals. M.p. 120–122° (Me_2CO/MeCN). R_f 0.65 (*A*). $[\alpha]_D$ = –63 (*c* = 0.9, Me_2CO). UV: 258 (3.91). IR: 3440*w*, 2930*w*, 1725*s*, 1685*s*, 1630 (sh), 1450*s*, 1350*s*, 1275*s*, 1235*m*, 1175*s*, 1125*s*, 970*m*. 935*m*. ^{1}H-NMR (CD_3COCD_3): 8.04 (*d*, *J* = 8.2, 2 H–C(6)); 6.03 (*s*, NCH_2N); 5.92 (*t*, *J* = 3.5, 2 H–C(1')); 5.68 (*d*, *J* = 8.2, 2 H–C(5)); 4.5–4.25 (*m*, 2 CH_2(5'), 2 H–C(4')); 3.99 (*dd*, *J* = 10.3, 3.5, 4 H, 2 CH_2(2'), 2 CH_2(3')); 3.69 (*dd*, *J* = 10.3, 7.3, 4 H, 2 CH_2(2'), 2 CH_2(3')); 3.15 (*s*, 2 Me). ^{13}C-NMR (CD_3COCD_3): 162.1 (*s*, 2 C(4)); 151.4 (*s*, 2 C(2)); 141.4 (*d*, 2 C(6)); 101.6 (*d*, 2 C(5)); 76.8 (*d*, 2 C(1')); 69.3 (*d*, 2 C(4')); 69.0 (*t*, 2 C(5')); 67.3, 66.8 (2*t*, 2 C(2'), 2 C(3')); 47.5 (*t*, NCH_2N); 37.7 (*q*, 2 Me). MS: 624 (M^+), 528, 485, 431, 430, 335, 334, 319, 318, 236, 194, 125, 113, 99, 79. Anal. calc. for $C_{21}H_{28}N_4O_{14}S_2$ (624.60): C 40.38, H 4.52, N 8.97; found: C 40.48, H 4.66, N 8.92.

*5'-*O*-(Triphenylmethyl)uridine* (**38**) [14]. To a soln. of uridine (1.97 g, 8 mmol) in pyridine (20 ml), TrCl (2.25 g, 8 mmol) was added and stirred at 100° for 3 h. The solvent was removed, ice-water added, and the mixture extracted with $CHCl_3$ (3 × 50 ml). The org. layer was washed with aq. $NaHCO_3$ soln. and H_2O, dried, and evaporated. The residue crystallized from EtOH (20 ml): 2.39 g of **38**. M.p. 204–206° ([14]: 200°). R_f 0.6 (*A*). An additional amount of **38** (766 mg) was isolated from the mother liquor by FC (38 × 0.8 cm). Total yield 3.15 g (80.4%). $[\alpha]_D$ = +18 (*c* = 1.0, MeOH; [14]: $[\alpha]_D$ = +18.8 (*c* = 1.04, MeOH)). UV: 262.8 (3.81; [14] 262). IR: 3400*m*, 3200*m*, 1690*s*, 1680*s*, 1625 (sh), 1450*m*, 1390*m*, 1270*m*, 1215*m*, 1105*s*, 1080*m*, 1050*m*, 1000*m*, 765*m*, 745*m*, 700*m*.

cis*-2-[(Triphenylmethoxy)methyl]-18-(uracil-1-yl)[18]crown-6* (*= 1-{*cis*-18-[(Triphenylmethoxy)methyl]-1,4,7,10,13,16-hexaoxaoctadec-2-yl}uracil*; **39**). To the suspension of NaH (110 mg, 21 mmol; 50% in mineral oil) in THF (5 ml) under N_2 and heated under reflux, a soln. of **2** (489 mg, 1 mmol) and 3,6,9-trioxaundecane-1,11-diyl bis(4-toluenesulfonate) (505.5 mg, 1 mmol) in THF (5 ml) was added dropwise while stirring. The mixture was then heated under reflux for 20 h, cooled, and quenched with H_2O to be evaporated. The residue was dissolved in H_2O and extracted with CH_2Cl_2. The org. layer was dried and evaporated to a product which, on trituration with MeOH, afforded 279 mg (50%) of **39**. Colorless oil. R_f 0.35 (*A*). $[\alpha]_D$ = +23.3 (*c* = 1.05, MeOH). UV (MeOH): 212 (3.92), 285 (3.57). IR: 3420*m*, 3060*m*, 1750 (sh), 1690*s*, 1450*s*, 1382*m*, 1350*m*, 1260*s*, 1100*m*, 765*m*, 710*m*. ^{1}H-NMR ($CDCl_3$): 8.97 (br. *s*, H–N(3), Ura); 7.43 (*d*, *J* = 7.9, H–C(6), Ura); 7.27 (*m*, ArH); 6.04 (*t*, *J* = 5.2, H–C(18)); 5.54 (*d*, *J* = 7.9, H–C(5), Ura); 3.8 (*d*, *J* = 5.2, H–C(2)); 3.64 (br. *s*, $(CH_2OCH_2)_5$); 3.15 (*d*, *J* = 4.9, $TrOCH_2$). ^{13}C-NMR ($CDCl_3$): 163.1; 150.6; 143.4; 140.7; 128.4; 127.7; 127.0; 101.9; 83.2; 80.9; 77.8; 71.3; 70.9; 70.4; 63.4. MS: 646 (M^+), 403, 383, 256, 245, 244, 243, 228, 165, 105, 91, 89, 87,77, 73, 59, 57.

cis*-2-(Hydroxymethyl)-18-(uracil-1-yl)[18]crown-6* (*= 1-[*cis*-18-(Hydroxymethyl)-1,4,7,10,13,16-hexaoxaoctadec-2-yl]uracil*; **40**). A suspension of **39** (140 mg, 0.22 mmol) in 80% AcOH (0.5 ml) was heated at 80° for 15 min. A precipitate was filtered off and the filtrate evaporated. The residue was purified by prep. TLC (CH_2Cl_2/MeOH 8:2): 82.7 mg (66%) of **40**. R_f 0.25 (CH_2Cl_2/MeOH 8:2). $[\alpha]_D$ = +33.6 (*c* = 1.1, MeOH). IR: 3420*m*, 1710 (sh), 1690*s*, 1460*s*, 1385*m*, 1355*m*, 1260*s*, 1100*m*, 950*m*. UV (MeOH): 258 (3.55). ^{1}H-NMR ($CDCl_3$): 8.97 (br. *s*, H–N(3), Ura); 7.63 (*d*, *J* = 8.2, H–C(6), Ura); 6.05 (*t*, *J* = 6.2, H–C(18)); 5.71 (*d*, *J* = 8.2, H–C(5), Ura); 3.87 (*d*, *J* = 5.5, H–C(2)); 3.66 (br. *s*, CH_2OH), $(CH_2OCH_2)_5$). ^{13}C-NMR ($CDCl_3$): 163.4; 151.0; 142.2; 102.1; 84.1; 71.3; 71.0; 70.7; 62.6.

*5'-*O*,*N*^{6}-Bis(triphenylmethyl)-2',3'-secoadenosine* (*= 9-{(1*R*)-2-Hydroxy-1-{(1*S*)-2-hydroxy-1-[(triphenylmethoxy)methyl]ethoxy}ethyl}-*N*^{6}-(triphenylmethyl)adenine*; **41**). To a soln. of 5'-*O*,*N*^{6}-bis(triphenylmethyl)adenosine [26] (**42**; 384 mg, 0.51 mmol) in dioxane/H_2O 5:1 (6 ml), a soln. of $NaIO_4$ (116 mg, 0.54 mmol) in H_2O (1 ml) was added and stirred at r.t. Within a few min, a precipitate was formed. The suspension was stirred at r.t. for 18 h. Dioxane (5 ml) was then added and the mixture stirred for additional 10 min, filtered, and the cake washed with dioxane (3 ml). To the combined filtrates, $NaBH_4$ (19.3 mg, 0.51 ml) was added at r.t., and after stirring for 2 h, Me_2CO (0.1 ml) was added and stirred at r.t. for additional 5 min. The mixture was then neutralized with 10% AcOH, concentrated to a small volume, diluted with H_2O and extracted with $CHCl_3$ (10 ml). After repetitive extraction of the inorg. layer with $CHCl_3$ (5 ml), the combined org. layers were washed with H_2O (5 ml), dried, and evaporated. The residue was triturated with Me_2CO to give 243 mg (63%) of crystalline **41**. M.p. 135–137° (Me_2CO). The mother liquor afforded 100 mg of **41**, purified by prep. TLC (*B*, 2 developments). Total yield 343 mg (89%). $[\alpha]_D$ = +12.9 (*c* = 0.93, $CHCl_3$). UV: 273 (4.29). IR: 3400*m*, 1600*s*, 1575 (sh), 1485*m*, 1460*m*, 1440*m*, 1210*m*, 1100*m*, 1050*m*, 890*w*, 770*w*, 750*m*. ^{1}H-NMR (CDCl$_3$): 7.97 (*s*, H–C(8)); 7.9 (*s*, H–C(2)); 7.25 (*m*, 30 arom. H); 5.92 (*t*, *J* = 4.5, H–C(1′)); 5.42, 4.96 (2*m*, 2 OH); 3.97 (*dd*, *J* = 11.9, 3.8, CH$_2$(2′)); 3.71 (*d*, *J* = 9.4, CH$_2$(3′)); 3.61 (*dd*, *J* = 11.9, 7.8, H–C(4′)); 3.11 (*d*, *J* = 4.9, CH$_2$(5′)). ^{13}C-NMR (CDCl$_3$): 153.8 (*s*, C(6)); 151.3 (*d*, C(2)); 147.8 (*s*, C(4)); 144.5, 143.2 (2*s*, arom. C); 138.3 (*d*, C(8)); 128.7, 128.2, 127.6, 126.8 (4*d*, arom. C); 120.3 (*s*, C(5)); 86.7 (*s*, Ph$_3$*C*); 84.7 (*d*, C(1′)); 80.3 (*d*, C(4′)); 76.9 (*t*, C(2′)); 71.2 (*s*, Ph$_3$*C*); 63.5 (*t*, C(3′)); 62.5 (*t*, C(5′)). Anal. calc. for $C_{48}H_{43}N_5O_4$ (753.90): C 76.47, H 5.75, N 9.29; found: C 76.59, H 5.48, N 9.41.

cis-*2-[(Triphenylmethoxy)methyl]-18-[*N^6*-(triphenylmethyl)adenin-9-yl][18]crown-6* (= N^6*-(Triphenylmethyl)-9-*{cis-*18-[(triphenylmethoxy)methyl]-1,4,7,10,13,16-hexaoxaoctadec-2-yl*}*adenine*; **43**). To a soln. of **41** (377 mg, 0.5 mmol), 3,6,9-trioxaundecane-1,11-diyl bis(4-toluenesulfonate) (252 mg, 0.5 mmol) in THF (6 ml), NaH (55 mg, 10.5 mmol in mineral oil) was added. Workup as described for **39** afforded 230 mg (50.4%) of **43**. R_f 0.13 (*A*). $[\alpha]_D$ = +13.5 (*c* = 1.8, CHCl$_3$). UV (MeOH): 207 (5.51), 271 (4.96). IR: 3420*m*, 1605*s*, 1580*s*, 1490*m*, 1470*m*, 1450*m*, 1360*m*, 1290*s*, 1215*m*, 1110*m*, 800*m*, 760*m*, 749*m*. ^{1}H-NMR (CDCl$_3$): 8.08, 8.01 (2*s*, H–C(2), H–C(8), Ade); 7.22 (*m*, ArH); 6.19 (*t*, *J* = 5.1, H–C(18)); 4.06 (*m*, H–C(2)); 3.62 (*m*, (CH$_2$OCH$_2$)$_5$); 3.04 (*m*, TrOC*H*$_2$); 2.1 (br. *s*, NH). ^{13}C-NMR (CDCl$_3$): 154.0; 152.1; 148.8; 145.1; 143.7; 140.4; 129.9; 129.0; 128.4; 127.9; 127.7; 121.0; 86.7; 83.3; 76.2; 71.4; 71.3; 70.82; 70.6; 63.4; 53.4. MS: 912 (M^+), 243 (100, Ph$_3$C), 669, 534, 426, 377, 376, 165, 105, 61. HR-MS: 912.0891 ($C_{56}H_{57}N_5O_7$, calc. 912.06).

cis-*2-(Adenin-9-yl)-18-(hydroxymethyl)[18]crown-6* (= *9-[*cis-*18-(Hydroxymethyl)-1,4,7,10,13,16-hexaoxaoctadec-2-yl]adenine*; **44**). A suspension of **43** (180 mg, 0.2 mmol) in 80% AcOH (0.7 ml) was heated at 80° for 15 min and worked up as described for **40**. Prep. TLC gave 72 mg (85%) of **44**. Colorless oil. R_f 0.17 (CH$_2$Cl$_2$/MeOH (8:2). $[\alpha]_D$ = +2.0 (*c* = 1.2, CHCl$_3$). IR: 3342*m*, 3194*m*, 1650*s*, 1604*s*, 1584 (sh), 1428*m*, 1424*m*, 1360*m*, 1255*s*, 1215*m*, 1054 (sh), 959*m*, 842*m*. UV (MeOH): 256 (4.96). ^{1}H-NMR (CDCl$_3$): 8.29, 8.2 (2*s*, H–C(2), H–C(8), Ade); 6.25 (*m*, H–C(2)); 5.94 (br. *s*, NH$_2$); 4.22 (*m*; H–C(8)); 4.05 (*m*, C*H*$_2$OH); 3.62 (*m*, (CH$_2$OCH$_2$)$_5$, CH$_2$O*H*). ^{13}C-NMR (CDCl$_3$): 155.7; 152; 147.1; 141.4; 128.4; 83.7; 77.5; 72.1; 70.6; 70.4.

REFERENCES

[1] V. Škarić, V. Čaplar, D. Škarić, M. Žinić, *Tetrahedron Lett.* **1991,** 1821.
[2] V. Škarić, M. Hohnjec, D. Škarić, *Helv. Chim. Acta* **1976,** *59,* 2972.
[3] V. Škarić, J. Matulić-Adamić, *J. Chem. Soc., Perkin Trans. 1* **1985,** 779.
[4] V. Škarić, M. Jokić, *Croat. Chem. Acta* **1983,** *56,* 125.
[5] M. Jokić, V. Škarić, *J. Chem. Soc., Perkin Trans. 1* **1990,** 2225.
[6] V. Škarić, B. Kašnar, *Croat. Chem. Acta* **1985,** *58,* 583.
[7] H. J. Schaeffer, L. Beauchamp, P. de Miranda, G. B. Elion, D. J. Bauer, P. Collins, *Nature (London)* **1978,** *272,* 583.
[8] J. C. Martin, C. A. Dvorak, D. F. Smee, T. R. Mathews, J. P. H. Verheyden, *J. Med. Chem.* **1983,** *26,* 759.
[9] J. F. Stoddart, *Chem. Soc. Rev.* **1979,** *18,* 85.
[10] W. D. Curtis, D. A. Laider, J. F. Stoddart, *J. Chem. Soc., Perkin Trans. 1* **1977,** 1756.
[11] J.-M. Lehn, C. Sirlin, *J. Chem. Soc., Chem. Commun.* **1978,** 949.
[12] J. P. Behr, J.-M. Lehn, D. Moras, J. C. Thierry, *J. Am. Chem. Soc.* **1981,** *103,* 701.
[13] S. N. Mikhailov, V. L. Florentiev, W. Pfleiderer, *Synthesis* **1985,** 399.
[14] R. S. Tipson, in 'Synthetic Procedures in Nucleic Acid Chemistry', Eds. W. W. Zorbach and R. S. Tipson, Interscience Publishers (J. Wiley & Sons), New York–London–Sydney–Toronto, 1968, p. 441.
[15] A. S. Jones, S. Niwas, H. Tanaka, R. T. Walker, *Nucleic Acids Res.* **1986,** *14,* 5409.
[16] J. Prisbe, *J. Med. Chem.* **1986,** *29,* 2445.
[17] A. S. Jones, R. T. Walker, P. S. Wyatt, J. Balzarini, E. de Clercq, *J. Chem. Res. (M)* **1985,** 3520.
[18] V. Škarić, B. Gašpert, M. Hohnjec, *J. Chem. Soc. (C)* **1970,** 2444.
[19] A van Aerschot, G. Janssen, P. Herdweijn, *Bull. Soc. Chim. Belg.* **1990,** *99,* 769.
[20] J. A. Secrist III, *Carbohydrate Res.* **1975,** *42,* 379.
[21] J. E. Mills, C. A. Maryanoff, R. M. Cosgrovel, L. Scott, D. F. McComsey, *Org. Prep. Proced. Int.* **1984,** *16,* 97.
[22] J. E. Mills, C. A. Maryanoff, D. F. McComsey, R. C. Stanzione, L. Scott, *J. Org. Chem.* **1987,** *52,* 1857.
[23] D. C. Agathocleous, P. C. Bulman Page, R. Cosstick, I. J. Gaepin, A. G. McLennan, M. Prescott, *Tetrahedron* **1990,** *46,* 2047.
[24] K. K. Ogilvie, S. L. Beaucage, M. F. Gillen, *Tetrahedron Lett.* **1978,** 1663.
[25] O. Howarth, A. S. Jones, R.T. Walker, P. G. Wyatt, *J. Chem. Soc., Perkin Trans. 2* **1984,** 261.
[26] H.-U. Blank, D. Frahne, A. Myles, W. Pfleiderer, *Liebigs Ann. Chem.* **1970,** *742,* 34.