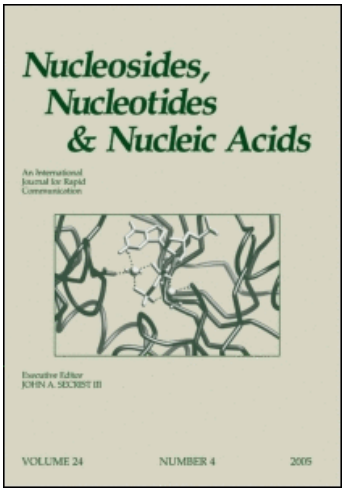

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SYNTHESIS AND PERKOW REACTION OF URIDINE DERIVATIVES

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Abstract. Several uridine derivatives with O-p-toluene sulfonyl groups in 2'- or 3'-position were prepared and their oxidation to the corresponding uloses studied. By Perkow reaction these α-tosyl ketones led to enol-phosphates which were subjected to hydrogenation and hydrolysis. This procedure represents a facile access to uridine derived deoxy uloses.

INTRODUCTION

The preparation of nucleoside analogues remains an area of active research with respect to their application for studies of metabolic processes as well as potential chemotherapeutic agents.[1-4] Therefore new mild and easy accesses to 2'- or 3'-deoxy nucleosides from simple precursors would be appreciated. Previously we could demonstrate the advantage of the Perkow reaction[5,6] for the synthesis of carbohydrate enol-phosphates[7,8] and selectively deoxygenated compounds.[8,9]

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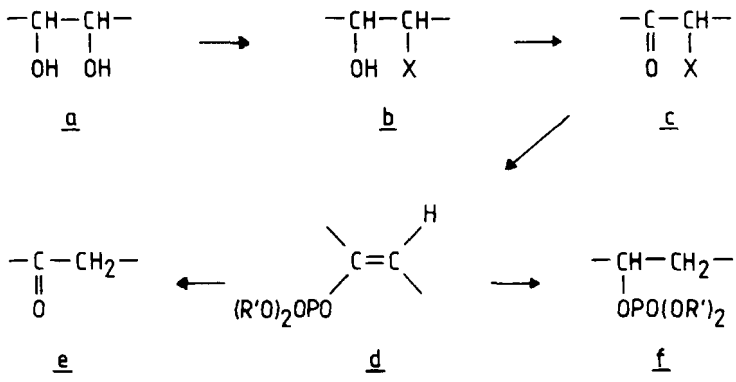
Starting with a 1,2-diol system a this as a prerequisite for the Perkow reaction has to be transformed *via* b into keton c with a leaving group X in α-position to the carbonyl function. Mild reaction with trialkyl phosphites directly yields the enolphosphate d



X = Hal
OCOR
OSO_2R

which can be either cleaved to the deoxy keton e or hydrogenated to the deoxy phosphate f. An important improvement for the application of this reaction in natural product chemistry consists of the finding that instead of the often difficult accessible α halo ketones c (X = halide) α-acyloxy or rather α-sulfonyloxy derivatives can be used successfully.[9] This and the strict neutral feature of the Perkow reaction render it of interest in the carbohydrate field and the nucleoside series which induced the present studies restricted to the chemistry of uridine derivatives.

RESULTS AND DISCUSSION

An attractive approach to a selectively tosylated uridine derivative represents the intermediate dibutyl stannylene protection first introduced by Moffatt et al..[10] In following a similar procedure uridine (1) was treated with dibutylstannic oxide in methanol and subsequently p-toluene sulfonyl chloride/triethylamine which gave 2'-O-p-toluene sulfonyl uridine (2) previously isolated crystalline from water (62%).[10] We noted that the raw material consisted of 2 and the regioisomer 3'-O-p-toluene sulfonyl uridine (5) in the ratio 2 : 5 = 7:1. Their separation was done after tritylation to compounds 4 and 6, respectively.

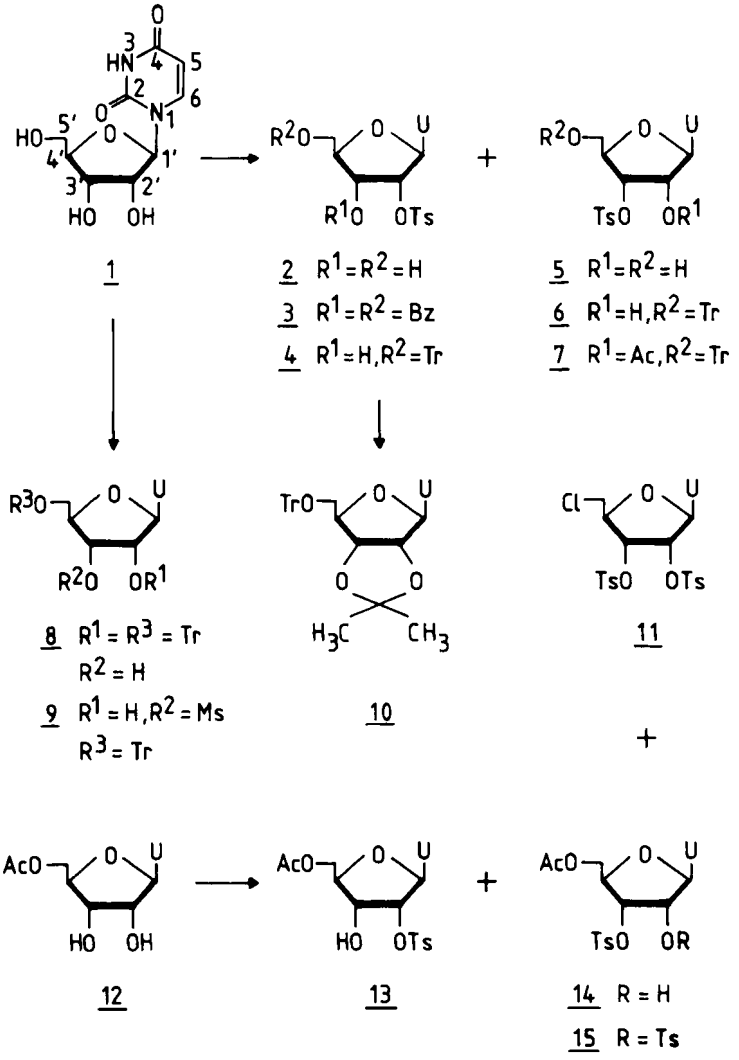
Attempts to perform a regioselective benzoylation at the primary position 5' of 2 with molar amounts of benzoyl chloride at low temperatures or with benzoyl cyanide[11] led to incomplete formation of the 2',5'-di-O-benzoate 3. As expected the selective tritylation of 2 and 5 worked smoothly and gave both the crystalline monotritylated compounds 4 (74%) and 6 (11%) after column separation. The former was prepared previously in lower yields by selective tosylation of 5'-trityl uridine.[12] The ^{1}H and ^{13}C NMR spectra of the regioisomers 4 and 6 are rather similar. A distinction based on the rules of Fromageot et al.[13]
[|δ 1'-H (2'-isomer)| > |δ 1'-H (3'-isomer)| and J(1',2') (2'-isomer) > J(1',2') (3'-isomer)] gave evidence for 4 [δ 1'-H: 6.13 and J(1',2') = 6.0 Hz]

to be the 2'-isomer and for 6 [δ 1'-H: 5.84 and J(1',2') = 5.2 Hz] to be the 3'-isomer. Furthermore, the 2'-O-acetyl derivative 7 obtained from 6 by acetylation showed a noticeable downfield shift (Δδ 0.8) of 2'-H which substantiates this assignment.

It may be noted that in contrast to 3'-isomers the 2'-O-tosyl compounds like 4 are labile with acetone. Under the conditions of a column chromatography in acetone/n-hexane 4 was completely converted to the 2',3'-O-isopropylidene-5'-O-trityl-uridine 10. The formation is understood by a double inversion at C-2': first the carbonyl group at C-2 induces an intramolecular elimination of the tosyloxy group with formation of an intermediate 2,2'-anhydro ring derivative. Subsequent nucleophilic attack at C-2' by a hydroxy group from the acetone hemiacetal linked to C-3' leads to the 2',3'-O-isopropylidene derivative in the original ribo configuration. A similar approach has been used formerly for an alternative synthesis of 3'-O-tosyl-uridine.[14]

By certain reaction conditions in the tritylation of uridine (1) the stage of the 5'-O-trityl derivative[15] can be surpassed and among other the 2',5'-di-O-trityl compound 8 is readily available.[16] After mesylation and ether cleavage the 3'-O-mesyl derivative[17] was prepared and selectively tritylated to give the crystalline uridine compound 9.

Finally, the tosylation of 5'-O-acetyl uridine 12[14] could be improved. After crystallization of the main product 5'-O-acetyl-2'-O-tosyl-uridine (13)[14] an additional 15% of the 3'-regioisomer 14, 12% of the 2',3'-ditosylate 15 and *ca.* 3% of the 5'-chloro-5'-deoxy derivative 11 could be obtained crystalline after column separation. The formation of 11 may be plausible by



nucleophilic substitution of either 15 or 2',3',5'-tri-O-tosyl uridine, formed by peresterification of traces of uridine present in 12, with N-tosyl pyridinium chloride.

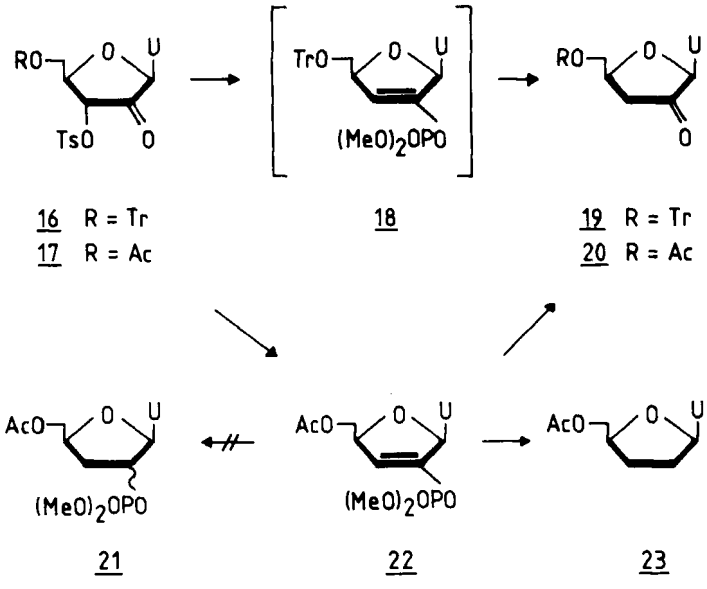
There have been several previous reports on the preparation and chemistry of keto nucleosides because they represent attractive precursors for the synthesis of modified nucleosides.[4,18-20] Both the 2',5'-di-O-trityl-3'-ulose and the 3',5'-di-O-trityl-2'-ulose of uridine were synthesized by Moffatt et al.[21] in acceptable yield. Their relative stability towards the β-elimination was explained by conformational influence owing to the large trityl groups.[21] The coupling constants support the unusual $^{2}T_{3}$(D) twist conformation with an equatorial aglyconic base unfavourably disposed for a β-elimination. In the presence of traces of base, however, they immediately eliminated uracil and the resulting enulose derivatives underwent further undefined degradations.

From the coupling constants of the 2'-O-sulfonyl derivatives 4 and 13, as well as the 3'-isomers 6, 9 and 14 [J(1',2') = 4.5-6.0, J(2',3') = 4.5-6.0, J(3',4') = 3.0-5.0 Hz; cf. table 2], however, their $^{3}T_{2}$ (D) twist conformations become evident; such conformations were discussed for several pyrimidine nucleosides.[22] Thus, there is no conformational promotion towards a hindrance of their β-elimination at hand. By several different procedures (DMSO/trifluoracetic anhydride at -75°C;[23] DMSO/phosphorus pentoxide at various temperatures;[24]

DMSO/acetic anhydride at 60°C[25]) the oxidation of both 2'-O-tosyl derivatives consequently led to extensive degradation and only uracil could be isolated and characterized.

Except for the 3'-O-mesyl compound 9 both the 3'-O-tosyl derivatives 6 and 14 could be oxydized by DMSO/P_2O_5 in moderate yields. In contrast to the expected conformationally induced tendency for β-eliminations[21] the crystalline 2'-ulose 16 and the sirupy analogue 17 turned out to be stable. The ^{1}H-NMR data of the ketones are in accord with the structures: they show a typical longe range coupling constant $^4J(1',3') = 0.5$ Hz and the 3'-H experienced a down field shift of approximately Δδ 0.6 with respect to the alcohol precursors. Furthermore the rather large coupling constants J(3',4') = 8.2 and 7.6 Hz for 16 and 17, respectively, correspond to dihedral angles Ø(3',4') > 150° which suggest $^0T_4$(D) twist conformations. Here the aglyconic uracil residue adopts an equatorial position which renders eliminations unlikely.

Treatment of the 5'-O-trityl-2'-ulose 16 with trimethyl phosphite led directly to the 3'-deoxy-2'-ulose derivative 19. Under the reaction conditions this compound obiously formed by autohydrolysis directly from the intermediate 2'-enolphosphate 18 which could not be detected by TLC or NMR studies. Generally, the enol-phosphate cleavage to the deoxy ketones is performed in



16 R = Tr
17 R = Ac

18

19 R = Tr
20 R = Ac

21 22 23

slightly alcaline medium (cf. lit.[9]), however, even trimethyl phosphite freshly distilled over sodium contained traces of dimethyl phosphite or further decomposition products which are sufficient to effect hydrolysis. A corresponding reaction of the 5'-O-acetyl compound 17 led to a mixture of the isolable enol-phosphate 22 and its saponification product 20 in a ratio 20 : 22 = 6:1. The more stabile enolphosphate compound 22 in an additional hydrolysis experiment (cf. conditions as in lit.[9]) could be transferred smoothly to the 3'-deoxy-2'-ulose 20.

The ^{1}H NMR data of the uloses 19 and 20 are similar and consistent with their structure. The large geminal coupling constant of 19 e.g. $^2J(3a',3b')$ = 18.4 Hz and the considerable size of the vicinal coupling constants J(3a',4') = 8.7 and J(3b',4') = 7.7 Hz are remarkable

and in agreement with a $^{0}T_{4}$(D) twist conformation. In the enolphosphate 22 1'-H curiously is observed as a quartet signal because the two allyl and the homoallyl coupling constants happened to be of the same size: $^{4}J(1',3') = {}^{4}J(1',P) = {}^{5}J(1',4') = 1.4$ Hz.

An alternative preparation of 3'-deoxy-2'-uloses similar to 19 and 20 was previously described by Sasaki et al.[26] starting from a difficult accessible lyxo-furanosyl uracil and another series of selective blocking and elimination steps. The present synthesis can be considered as advantageous with respect to the simple procedures and few reaction steps. Whereas the reaction series used here resembles the proposed bio-synthetic formation of cordycepin from adenosine[27] compounds of type 20 may be well suited to open an accesses to analogues of antibiotics like cordycepin.

Finally it was of interest to check the hydrogenation, and we could expect the formation of a 2'-phosphoryl-3'-deoxy nucleoside 21 with D-threo or D-erythro configuration. Surprisingly on 10% palladium/charcoal a complete hydrogenolytic cleavage of the enolester linkage was observed which led to formation of the 2',3'-dideoxy uridine derivative 23. Subsequent experiments using other hydrogenation procedures will be of interest to achieve phosphorylated uridine analogues of cordycepin.

TABLE 1 Chemical shifts (δ) at 270 MHz ($CDCl_3$)

	3	4	6[a]	7[b]	9[c]
5-H	5.66 dd	5.19 dd	5.38 d	5.35 dd	5.29 d
6-H	7.21 d	7.51 d	7.70 d	7.44 dd	7.78 d
NH	8.87 mc	8.76 mc	2.89 mc		
1'-H	5.98 d	6.13 d	5.84 d	6.21 d	5.93 d
2'-H	5.25 dd	5.15 dd	4.64 t	5.47 d	4.82 ddd
3'-H	5.67 t	4.60 dd	5.06 t	5.25 dd	5.26 t
4'-H	4.60 -	4.18 dt	4.27 mc	4.27 dt	4.46 dt
5a'-H		3.51 dd	3.36 dd	3.42 dd	3.60 dd
5b'-H	4.70 m	3.45 dd	3.21 dd	3.36 dd	3.57 dd
C_6H_4-$\underline{CH}_3$	2.37 s	2.41 s	2.41 s	2.44 s	--
Aryl-H	7.10 - 8.10 m	7.20 - 7.80 m	7.20 - 7.80 m	7.30 - 7.70 m	7.10 - 7.50 m

	10[d]	11[e]	14[f]	15[a,g]	16[a]
5-H	5.13 dd	5.49 dd	5.00 d	5.56 dd	5.75 dd
6-H	6.51 d	7.28 d	7.46 d	7.37 d	7.20 mc
NH	8.29 mc			2.86 mc	2.89 mc
1'-H	5.63 d	5.88 d	5.26 d	5.89 d	5.54 d
2'-H	4.56 dd	5.29 t	4.49 t	--	--
3'-H	4.63 dd	5.09 dd	4.87 t	5.23 dd	5.61 dd
4'-H	4.37 dt	4.34 dt	4.41 ddd	4.40 q	4.39 ddd
5a'-H	3.44 dd	3.80 dd	4.20 dd	4.26 dd	3.51 cc
5b'-H	3.37 dd	3.62 dd	4.10 dd	4.07 dd	3.27 dd
OAc	--	--	--	2.01 s	--
C_6H_4-$\underline{CH}_3$	--	2.44s,2.49s	2.43 s	2.44s,2.49s	2.44 s
Aryl-H	6.90 - 7.50 m	7.30 - 7.90 m	7.30 - 7.90 m	7.40 - 7.90 m	7.20 - 8.20 m

	17	19	20[i]	22[k]	23[l]
5-H	5.77 d	5.61 dd	5.10 d	5.59 d	5.73 dd
6-H	7.23 d	7.20 mc	5.89 d	7.49 d	7.64 d
NH		8.53 d		2.63 mc	8.42 mc
1'-H	5.09 d	5.35 s	4.19 s	5.76 q	6.04 dd
3'-H	5.42 dd	[h]	[j]	6.87 ddd	
4'-H	4.43 ddd	4.57 mc	4.35 mc	4.70 ddd	4.65 mc
5a'-H	4.50 dd	3.52 dd	4.18 dd	4.11 dd	4.43 dd
5b'-H	4.22 dd	3.39 dd	4.09 dd	3.98 dd	4.30 dd
OAc	2.09 s	--	1.68 s	1.74 s	2.10 s
C_6H_4-$\underline{CH}_3$	2.46 s	--	--	--	--
Aryl-H	7.30 - 7.90 m	7.20 - 7.50 m	--	--	--

Footnotes to Table 1

[a] in $(CD_3)_2CO$; [b] OAc 2.01 s; [c] 2'-OH 5.59 d, OSO_2-CH_3 3.23 s; [d] in C_6D_6, $C(\underline{CH}_3)_2$ 1.09 s, 1.41 s; [e] $CDCl_3/(CD_3)_2SO$ 1:1, [f] OAc 2.06 s; [g] 2'-H 5.29 t; [h] 3a'-H 2.85 dd, 3b'-H 2.62 dd; [i] in C_6D_6; [j] 3a'-H 2.49 dd, 3b'-H 2.24 dd; [k] in $C_6D_6/(CD_3)_2CO$ 1:1, $PO\underline{CH}_3$ 3.42 d and 3.45 d; [l] 2a'-, 2b'-H 2.40 m; 3a'-H 2.89 mc, 3b'-H 2.68 mc.

TABLE 2 Coupling Constants (Hz)

	3	4	6	7	9[a]	10	11	14
J(5,6)	8.0	8.2	8.0	8.0	8.0	8.0	8.0	8.0
J(5,NH)	2.2	2.0	--	2.0	--	2.0	2.2	2.0
J(1',2')	4.3	6.0	5.2	7.2	4.4	2.0	6.2	5.0
J(2',3')	5.8	5.0	5.2	5.6	5.0	6.2	6.2	5.0
J(3',4')	5.8	3.0	5.2	2.2	5.0	3.8	3.4	5.0
J(4',5a')		2.4	3.0	2.5	2.6	6.0	5.0	3.0
J(4',5b')		2.4	4.0	2.5	2.6	3.8	5.0	3.6
J(5a',5b')		11.2	11.0	11.0	11.2	10.4	12.0	12.4

	15[b]	16[c]	17[d]	19[e]	20[f]	22[g]	23[h]
J(5,6)	8.0	8.0	8.0	8.0	8.0	8.2	8.2
J(5,NH)	2.0	1.2	1.2	2.3			2.2
J(3',4')	3.8	8.2	7.6			3.4	
J(4',5a')	3.8	2.0	3.0	5.6	7.0	4.0	3.6
J(4',5b')	3.8	5.6	5.8	3.4	3.8	3.0	5.0
J(5a',5b')	12.2	10.8	12.0	10.4	11.8	12.4	12.0

Footnotes to Table 2

[a] J(2',2'-OH) ≈ 5.8; [b] J(1',2') = J(2',3') ≈ 5.8; [c] J(1',3') = 0.5; [d] J(1',3') = 0.5; [e] J(3a',3e') = 18.8, J(3a',4') = 8.7, J(3b',4') = 7.7; [f] J(3a',3b') = 18.4, J(3a',4') = 8.1, J(3b',4') = 7.7; [g] J(1',3') ≈ J(1',4') = J(1',P) ≈ 1.4, J(3',P) = 2.0, $J(P,OCH_3)$ = 11.4; [h] J(1',2a') = 3.6, J(1',2b') = 6.8, J(3a',3b') ≈ 18.6 Hz.

EXPERIMENTAL

Reactions were monitored by TLC on silica gel sheets GF_{254} (Merck). Detection: UV absorption and/or spraying with conc. sulfuric acid and subsequent heating to 150°C. Column chromatography: silica gel 60 (Merck). Preparative layer chromatography: silica gel GF Fertigplatten, 0.5 and 2.0 mm (Merck). Melting points: Mettler FP 61 (uncorrected). Optical rotation: Perkin-Elmer 241 MC and 243 in 1 dm cuvettes at 589 nm. ^1H and ^{13}C NMR:

Bruker WH 270 at 270 MHz and 67.89 MHz, respectively, with tetramethylsilane as internal standard.

3',5'-Di-O-benzoyl-2'-O-tosyl-uridine (3).

A solution of 200 mg (0.5 mmol) of unpurified 2 (prepared accoding to lit.[10]) in 5 mL of dry acetonitrile was treated with 65 mg (0.5 mmol) benzoyl cyanide in the presence of a catalytic amount of triethylamine for 30 min at room temperature. The reaction mixture was quenched with 10 mL of methanol, concentrated, taken up with water and extracted with dichloromethane. From the water phase 90 mg of 2 could be recovered. The organic phase after drying and evaporating gave 140 mg 3 (84% based on reacted 2), mp 171°C, $[\alpha]_D^{20}$ - 18.6 (c = 1.0 in chloroform).

Anal. Calcd. for $C_{30}H_{26}N_2O_{10}S$ (606.6):
C, 59.40; H, 4.32; N, 4.62; S, 5.29.
Found: C, 59.77; H, 4.33; N, 4.65; S, 5.13.

2'-O- and 3'-O-Tosyl-5'-O-trityl-uridine (4) and (6).

16.0 g (40 mmoles) of unpurified 2 was dissolved in 150 mL of dry pyridine and treated with 16.8 g (60 mmol) of trityl chloride for 4 h at room temperature. The mixture was dumped into ice water, filtered, the residue washed carefully and purified on silica gel (acetone/n-hexane 1:1). First fraction compound 4: 16.75 g (74%), mp 171-3°C (Ethanol), [lit.[12]: mp 174-5°C (Ethanol)]; ^{13}C NMR

($CDCl_3$): C-2 δ = 149.7, C-4 162.4, C-5 102.8, C-6 146.0, C-1′ 88.2, C-2′ 70.7, C-3′ 83.9, C-4′ 85.4, C-5′ 63.3, $Ph_3\underline{C}$ 80.7, C_6H_4-$\underline{C}H_3$ 21.7, Aryl-C 127.6, 127.9, 128.2, 130.2, 132.8, 139.6, 143.0.

Second fraction compound 6: 2.5 g (11%), mp 116°C, $[\alpha]_D^{20}$ +44.0 (c = 1.0 in chloroform); ^{13}C NMR ($CDCl_3$): C-2 δ = 150.9, C-4 162.9, C-5 102.9, C-6 145.3, C-1′ 89.2, C-2′ 73.9, C-3′ 81.4, C-4′ 89.2, C-5′ 62.1, $Ph_3\underline{C}$ 87.9, C_6H_4-CH_3 21.7, Aryl-C 127.5, 128.1, 128.7, 130.0, 132.9, 139.6, 143.1.

Anal. Calcd. for $C_{35}H_{32}N_2O_8S$ (640.7):
C, 65.61; H, 5.03; N, 4.37; S, 5.00
Found: C, 65.82; H, 5.13; N, 4.03; S, 4.81.

2′-O-Acetyl-3′-O-tosyl-5′-O-trityl-uridine (7).
A solution of 100 mg (0.16 mmole) of 6 was dissolved in 5 mL of dry pyridine and treated with 2 mL of acetic anhydride over night at room temperature. Repeated coevaporation with toluene gave a solid raw material which was dissolved in dichloromethane, washed successively with diluted sulfuric acid, aqueous sodium hydrogen carbonate solution, and water, dried over magnesium sulfate and evaporated to give 106 mg (99%), mp 125°C, $[\alpha]_D^{20}$ +30.0 (c = 1.0 in chloroform).
Anal. Calcd. for $C_{37}H_{34}N_2O_9S$ (682.8):
C, 65.09; H, 5.02; N, 4.10; S, 4.70.
Found: C, 65.03; H, 5.30; N, 4.23; S, 4.60.

3'-O-Mesyl-5'-O-trityl-uridine (9).

A solution of 1.6 g (5.0 mmol) of 3'-O-mesyl-uridine[17] in 15 mL dry pyridine was treated with 1.4 g (5.0 mmol) of tritylchloride at room temperature over night, then poured into ice water and the precipitate filtered over silica gel to give pure 9: 1.95 g (69%), mp 152°C, $[\alpha]_D^{20}$ +32.6 (c = 1.0 in chloroform).

Anal. Calcd. for $C_{29}H_{28}N_2O_8S$ (564.6):

C, 61.69; H, 5.00; N, 4.96; S, 5.68.

Found: C, 61.33; H, 5.08; N, 5.38; S, 5.48.

2',3'-O-Isopropylidene-5'-O-trityl-uridine (10).

In the preparation of 4 and 6 starting with 2.0 g (5.0 mmol) of unpurified 2 the raw material was purified on a silica gel column using acetone/n-hexane 1:1 to give 1.6 g (61%) of 10, mp 78°C, $[\alpha]_D^{20}$ -6.5 (c = 0.2 in chloroform); ^{13}C NMR ($CDCl_3$): C-2 δ = 150.1, C-4 163.3, C-5 113.3, C-6 141.2, C-1' 102.5, C-2' 80.8, C-3' 84.9, C-4' 92.4, C-5' 63.7, $Ph_3\underline{C}$ 86.1, $(\underline{C}H_3)_2C$ 25.5, 27.3, $(CH_3)_2\underline{C}$ 87.2, Aryl-C 127.1 - 128.5, 143.0.

Anal. Calcd. for $C_{31}H_{30}N_2O_6$ (526.6):

C, 70.71; H, 5.74; N, 5.32

Found: C, 70.39; H, 5.69; N, 5.26

Tosylation of 5'-O-acetyl-uridine.

16.6 g (58 mmol) of 12[14] were dissolved in 200 mL abs. pyridine and after addition of 16.6 g (87 mmol) tosylchloride stirred for 1 h at 0°C and then over night at

room temperature. The mixture was poured into ice water the residue filtered off, and the main product 13[14] isolated by crystallization from ethyl acetate. Yield (including additional material after column chromatography, third fraction) 15.6 g (61%), mp 172-4°C (ethyl acetate), [lit.[14]: mp 173-5°C (ethyl acetate)].

The mother liquor was processed by column chromatography (ethyl acetate/n-hexane 1:1) to give as

1. fraction: 5'-Chloro-5'-deoxy-2',3'-di-O-tosyl-uridine (11), yield 850 mg (2.6%), mp 161°C, $[\alpha]_D^{20}$ +14.7 (c = 1.0 in chloroform); ^{13}C NMR ($CDCl_3$/DMSO-D_6 1:1): C-2 δ = 149.9, C-4 162.7, C-5 102.9, C-6 140.8, C-1' 87.6, C-2' 75.0, C-3' 75.9, C-4' 81.2, C-5' 42.5, Aryl-C 127.8, 130.1, 132.1, 145.8, C_6H_4-CH_3 21.4.

Anal. Calcd. for $C_{23}H_{23}ClN_2O_9S_2$ (571.0):
C, 48.38; H, 4.06, N, 4.91; Cl, 6.21; S, 11.23.
Found: C, 48.30; H, 3.92; N, 4.91; Cl, 6.43; S, 11.15.

2. Fraction: 5'-O-Acetyl-2',3'-di-O-tosyl-uridine (15), yield 4.2 g (12%), mp 99°C, $[\alpha]_D^{20}$ +39.2 (c = 1.0 in chloroform).

Anal. Calcd. for $C_{25}H_{26}N_2O_{11}S_2$ (594.6):
C, 50.50; H, 4.41; N, 4.71; S, 10.78.
Found: C, 50.25; H, 4.34; N, 4.69; S, 10.61.

3. Fraction: additional material of 13.

4. Fraction: 5'-Acetyl-3'-O-tosyl-uridine (14), yield

3.8 g (15%), mp 142°C (decomposition), $[\alpha]_D^{20}$ + 43.8 (c = 1.0 in chloroform).

Anal. Calcd. for $C_{18}H_{20}N_2O_9S$ (440.4):

C, 49.09; H, 4.58; N, 6.36; S, 7.28.

Found: C, 48.93; H, 4.48; N, 6.17; S, 7.35.

1-(3'-O-Tosyl-5'-O-trityl-β-D-erythro-pentofuran-2'-ulosyl)uracil (16).

A solution of 530 mg (0.83 mmol) of 6 and 20 mg of phosphorus pentoxide in 20 mL of dry dimethyl sulfoxide was warmed to 60°C for 2 h, then quenched with ice water and extracted with dichloromethane. The organic layer was washed ($NaHCO_3$, water), dried ($MgSO_4$) and evaporated under high vacuum to give pure 16: 160 mg (30%), mp 115°C, $[\alpha]_D^{20}$ + 18.6 (c = 1 in chloroform).

Anal. Calcd. for $C_{35}H_{30}N_2O_8S$ (638.7):

C, 65.82; H, 4.73; N, 4.39; S, 5.02.

Found: C, 65.81; H, 4.62; N, 4.30; S, 5.26.

1-(5'-O-Acetyl-3'-O-tosyl-β-D-erythro-pentofuran-2'-ulosyl)uracil (17).

670 mg (1.5 mmol) of 14 and 20 mg of phosphorus pentoxide in 20 mL of dry DMSO were treated and worked-up as described for 16. The residue was purified by column chromatography (acetone/n-hexane 1:1) to give 220 mg (33%) colourless syrup; $[\alpha]_D^{20}$ 7.8 (c = 2.0 in chloroform).

Anal. Calcd. for $C_{18}H_8N_2O_9S$ (438.4):
C, 49.31; H, 4.14; N, 6.39; S, 7.31.
Found: C, 49.79; H, 4.18; N, 5.81; s, 7.63.

1-(3'-Deoxy-5'-O-trityl-β-D-glycero-pentofuran-2'-ulosyl)uracil (19).

120 mg (0.2 mmol) of 16 and 10 mL of freshly distilled trimethyl phosphite were stirred at 60°C for 4 h. Repeated codistillation with toluene gave a residue which was purified by column chromatography (acetone/n-hexane 1:2). Yield: 30 mg (29%) of 19 as a colourless syrup, $[\alpha]_D^{20}$ +12.6 (c = 1.5 in chloroform).

Anal. Calcd. for $C_{28}H_{24}N_2O_5$ (468.5):
C, 71.78; H, 5.16; N, 5.98.
Found: C, 71.85; H, 5.30; N, 6.24.

1-(5'-O-Acetyl-3'-deoxy-β-D-glycero-pentofuran-2'-ulosyl)uracil (20) and 1-(5'-O-Acetyl-3'-deoxy-2'-O-dimethoxyphosphoryl-β-D-glycero-pent-2'-enofuranosyl)-uracil (22).

A solution of 170 mg (0.4 mmol) of 17 in 10 mL of freshly distilled trimethyl phosphite was warmed to 60°C for 4 h, then the excess of reagent removed in vacuo and the residue separated by column chromatography (acetone/n-hexane 1:1). The first fraction was compound 20, yield 61 mg (59%) colourless syrup, $[\alpha]_D^{20}$ +14.0 (c = 3.0 in chloroform).

Anal. Calcd. for $C_{11}H_{12}N_2O_6$ (268.2):

C, 49.26; H, 4.51; N, 10.44.

Found: C, 49.17; H, 4.69; N, 10.61.

As second fraction 17 mg (11%) of compound 22 were obtained, colourless syrup, $[\alpha]_D^{20}$ -16.0 (c = 0.85 in chloroform).

Anal. Calcd. for $C_{13}H_7N_2O_9P$ (376.3):

C, 41.50; H, 4.55; N, 7.45; P, 8.23.

Found: C, 41.75; H, 4.36; N, 7.56; P, 8.06.

1-(5'-O-Acetyl-2',3'-dideoxy-β-D-glycero-pentofuranosyl)uracil (23).

11 mg (0.03 mmol) of 22 dissolved in 10 mL of ethanol were hydrogenated in the presence of 10 mg 10% palladium on charcoal for 3d. After filtration and evaporation the material was purified by preparative thin layer chromatography (acetone/n-hexane 1:1) to give compound 23: 5 mg (67%) colourless syrup, $[\alpha]_D^{20}$ +10.4 (c = 0.25 in chloroform).

Anal. Calcd. for $C_{11}H_{14}N_2O_5$ (254.2):

C, 51.97; H, 5.55; N, 11.02.

Found: C, 51.67; H, 5.15; N, 11.22.

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