The crude diketal **10c** was dissolved in anhydrous ether (50 ml), $LiAlH_4$ (400 mg) was added, and the mixture was refluxed for 16 hr. After work-up the hydroxy diketal **10d** (220 mg) was obtained as a colorless syrup, *m/e* 407 (M^+).

To a solution of the above diketal **10d** in dioxane (10 ml), 2 *N* hydrochloric acid (1 ml) was added and the mixture was stored for 20 hr at the ambient temperature. The hydroxy diketone **3b** (110 mg) was recovered with ether. The product **3b** showed mp 167–170°. A mixture melting point with authentic[1] unlabeled material (**3a**) was not depressed; ν_{max} (KBr) 3400, 1740, 1712 cm^{-1}; *m/e* 319 (M^+), 304 (M − 15), 274 (M − 45, $CH_3 \cdot CDO$), 256 (274 − 18).

Rearrangement of *19-d*-(19*R*)-19-Hydroxy-19a-methyl-5α-androstane-3,17-dione (3b) to *3β-d*-3α-Hydroxy-19a-methyl-5α-androstane-17,19-dione (4b).—A solution of the deuterated **3b** (100 mg) in methanol (50 ml) containing potassium hydroxide (100 mg) and water (0.5 ml) was refluxed for 3 hr in an atmosphere of nitrogen. The mixture was cooled, diluted with water, and neutralized with acetic acid. The product was recovered with ethyl acetate in the usual manner. The obtained residue (103 mg) was fractionated by thin layer chromatography on neutral alumina (purchased from Woelm A.G.). The plates were developed with ethyl acetate. The two major products were recovered with ethyl acetate and were identified as starting material **3b** (12 mg) and the deuterated alcohol **4b** (46 mg).

The 3α-hydroxy-*3β-d* product (**4b**), mp 170–171°, showed ν_{max} (KBr) 3550, 1730, and 1680 cm^{-1}; nmr ($CDCl_3$) τ 7.8 (s, 3 H, 19a-CH_3), 9.21 (s, 3 H, 13-CH_3); *m/e* 319 (M^+), 301 (M − 18), 276 (M − 43), 258 (276 − 18), 240 (258 − 18).

Registry No.—**3b**, 38308-99-5; **4b**, 38309-00-1; **9a**, 2951-52-2; **9b**, 14413-29-7; **9c**, 14413-27-5; **9d**, 38431-64-0; **9e**, 38309-04-5; **9f**, 38309-05-6; **9g**, 38309-06-7; **9h**, 38309-07-8; **9i**, 38309-08-9; **9j**, 38309-09-0; **9l**, 38309-10-3; **10a**, 38309-11-4; **10b**, 38312-19-5; **10c**, 38312-20-8; **10d**, 38312-21-9.

Introduction of a 2′,3′ Double Bond into 1-(5′-*O*-Benzoyl-β-D-lyxofuranosyl)uracil by Selective Elimination Reactions. A Facile Synthesis of 5′-*O*-Benzoyl-3′-deoxy-2′-ketouridine

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For the purpose of synthesizing 2′,3′-didehydrouracil nucleosides from 1-(5′-*O*-benzoyl-β-D-lyxofuranosyl)uracil (**1**) by base-induced elimination reactions, **1** was monotosylated to 1-(5′-*O*-benzoyl-2′-*O*-tosyl-β-D-lyxofuranosyl)-uracil (**2**) and 1-(5′-*O*-benzoyl-3′-*O*-tosyl-β-D-lyxofuranosyl)uracil (**3**). Mesylation of **2** and **3** gave isomers **4** and **7**, respectively. Dimesylation of **1** gave 2′,3′-di-*O*-mesyl analog **9**. Elimination reactions on **4**, **7**, and **9** gave 5′-*O*-benzoyl-3′-deoxy-2′-ketouridine (**6**). The intermediary 2′-*O*-tosyl-2′,3′-didehydro nucleoside (**5**) was isolated and characterized. Action of alcoholic ammonia on **4** gave 1-(2′-*O*-tosyl-β-D-lyxofuranosyl)uracil (**10**) *via* debenzoylation and demesylation.

In a previous paper,[1] the results of some base-catalyzed elimination reactions on 2′,3′-di- and 2′,3′,5′-tri-*O*-mesyl derivatives of 3-benzyluridine were described. One of the important features of these results was the selective 2′-hydrogen abstraction in the trans-elimination reactions regardless of the size of the 5′-*O* substituent. However, there was a known drawback in that the 3-benzyl group in the uracil skeleton cannot be removed by hydrogenolysis.[2,3]

This report describes the results of similar elimination reactions on 2′,3′-di-*O*-mesyl, 3′-*O*-mesyl-2′-*O*-tosyl, and 2′-*O*-mesyl-3′-*O*-tosyl derivatives of 1-(5′-*O*-benzoyl-β-D-lyxofuranosyl)uracil (**1**),[4] in which both the leaving groups are syn with respect to the base moiety, thus precluding cyclonucleoside formation. Further interesting situations foreseen for this series of compounds are that the sugar protons $H_{1'}$–$H_{4'}$, are all in β and trans relation to one of the leaving groups, suggesting various possible directions in β elimination, and that basic catalysts must attack, advantageously, from the less hindered bottom side of the nucleoside derivatives.

1-(5′-*O*-Benzoyl-β-D-lyxofuranosyl)uracil (**1**) was treated with 2 molar equiv of tosyl chloride to give the monotosylated compounds, 1-(5′-*O*-benzoyl-2′-*O*-tosyl-β-D-lyxofuranosyl)uracil (**2**) and 1-(5′-*O*-benzoyl-3′-*O*-tosyl-β-D-lyxofuranosyl)uracil (**3**) in 41 and 6% yield, respectively, presumably for steric reasons. Compounds **2** and **3** were crystals which included one molecule of methanol and acetone, respectively. In the nmr spectrum of **2** free of solvent, the signal of the anomeric proton appeared at δ 6.25 as a doublet with $J_{1',2'}$ = 6.8 Hz, while the resonance of $H_{2'}$ occurred at δ 5.3 as a doublet of doublets with $J_{1',2'}$ = 6.8 Hz and $J_{2',3'}$ = 4.7 Hz. The assignment of $H_{2'}$ was self-evident on the basis of a strong deshielding effect by the tosyl group, but was also confirmed by spin decoupling, since irradiation at δ 6.25 collapsed the signal at δ 5.3 to a doublet with a splitting of 4.7 Hz. Thus, the structure of **2** and therefore that of **3** was established.

The monotosylation of **1** is useful for elucidating the structure of the elimination products when another different leaving group is introduced into **2** or **3**. Hence, **2** was converted to 1-(5′-*O*-benzoyl-3′-*O*-mesyl-2′-*O*-tosyl-β-D-lyxofuranosyl)uracil (**4**) using the less bulky mesyl chloride. On treatment with excess sodium benzoate under relatively mild reaction conditions **4** gave the expected 1-(5′-*O*-benzoyl-3′-deoxy-2′-*O*-tosyl-β-D-*glycero*-pent-2′-enofuranosyl)uracil (**5**) as the sole product in 20% yield, 43% of the starting material being recovered. Some degree of resinification was also observed. The nmr spectrum of **5** is shown in Figure 1. The resonance pattern is quite similar to that of 1-(3′-deoxy-2′,5′-di-*O*-mesyl-β-D-*glycero*-pent-2′-enofuranosyl)-3-benzyluracil.[1] The

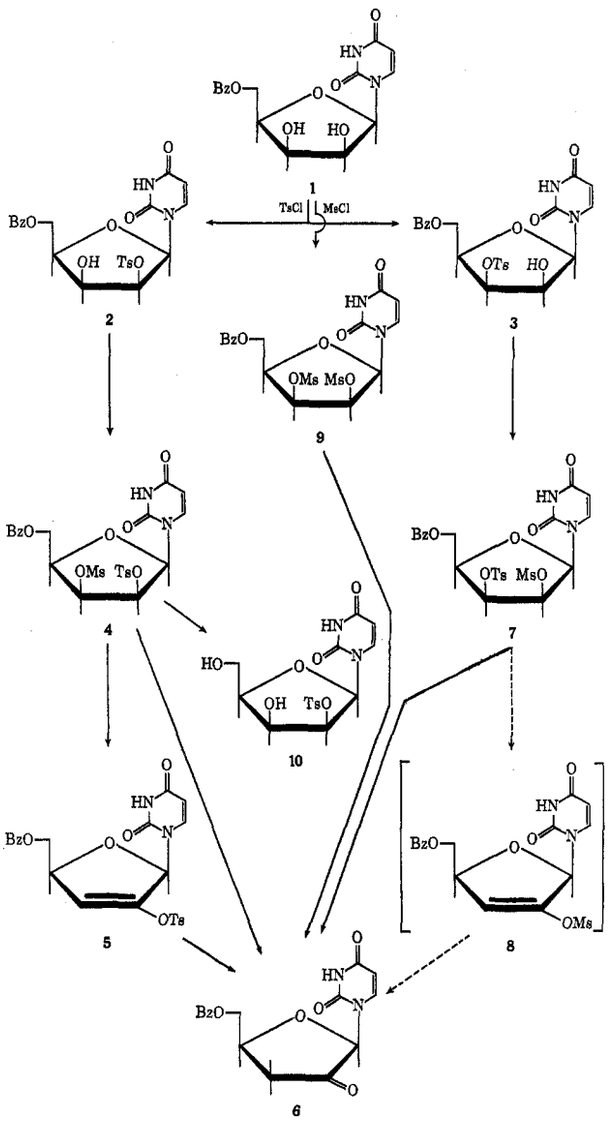
(1) T. Sasaki, K. Minamoto, and H. Suzuki, *J. Org. Chem.*, **38**, 598 (1973).
(2) N. Imura, T. Tsuruo, and T. Ukita, *Chem. Pharm. Bull.*, **16**, 1105 (1968).
(3) T. Kunieda and B. Witkop, *J. Amer. Chem. Soc.*, **93**, 3478 (1971).
(4) R. Fecher, J. F. Codington, and J. J. Fox, *ibid.*, **83**, 1889 (1961).

presence of a tosyl and not of a mesyl group in this compound and also the presence of the $H_{1'}$ signal in the nmr spectrum precluded a structure with a 1′,2′ double bond, while the presence of the $H_{4'}$ signal at an expected position of 5.15 ppm precluded a 3′,4′-didehydro structure. Reasons for the assignments of these signals are as described in detail in the previous paper.[1] Thus, the structure of **5** was unequivocally established.

Another elimination reaction of **4** was carried out using the same catalyst under relatively drastic conditions (3 hr at 120°) until the starting material disappeared, when 5′-*O*-benzoyl-3′-deoxy-2′-ketouridine (**6**) was obtained in 11% yield. The intervention of compound **5** was evidenced by thin layer chromatography as described in the Experimental Section. The ir spectrum of **6** showed the characteristic absorption at 1750 cm^{-1} for the sugar ketone.[5,6] On the other hand, 1-(5′-*O*-benzoyl-2′-*O*-mesyl-3′-*O*-tosyl-β-D-lyxofuranosyl)uracil (**7**) obtained from **3** reacted with sodium benzoate extremely rapidly to give **6** in 18% yield. In this case, the starting material **7** was almost completely consumed in 20 min at 100°. Although 2′,3′-didehydro nucleoside **8** must have intervened in this reaction, its detection by tlc was impossible.

This observation spurred us to examine a similar reaction on 1-(5′-*O*-benzoyl-2′,3′-di-*O*-mesyl-β-D-lyxofuranosyl)uracil (**9**). Compound **9** obtained from **1** reacted with sodium benzoate merely to give **6** in 21% yield. This reaction was also as rapid as in the case of **7** and did not premit detection of any intervening **8**. The unusual ease with which **5** or **8** can be converted to the keto nucleoside **6** is in contrast with the previous observations[1] on the elimination products from 2′,3′-di-*O*-mesyl-3-benzyluridine and its 5′-substituted analogs and suggests the presence of anchimeric assistance by the ionized base moiety.[7]

In the previous report,[1] the ammonia-catalyzed elimination reaction of 5′-*O*-benzoyl-2′,3′-di-*O*-mesyl-3-benzyluridine to 1-(3′-deoxy-2′-*O*-mesyl-β-D-*glycero*-pent-2′-enofuranosyl)-3-benzyluracil was described. With a view to converting **4** directly to the 5′-O-unsubstituted analog of **5** or **6**, compound **4** was heated with excess alcoholic ammonia to give, unexpectedly, 1-(2′-*O*-tosyl-β-D-lyxofuranosyl)uracil (**10**) as the sole product, which seems to have formed by simple debenzoylation and demesylation. The structural assignment is essentialy based on its nmr spectrum, in



which the anomeric proton gave a doublet at δ 6.15 with $J_{1',2'}$ = 6.8 Hz, while the signal of $H_{2'}$, appeared at δ 5.25 as a doublet of doublets with $J_{1',2'}$ = 6.8 and $J_{2',3'}$ = 4.7 Hz. These coupling constants are identical with those for $H_{1'}$ and $H_{2'}$ in compound **2**.

Thus, a tendency for 2′-hydrogen abstraction was again proved in the β-elimination reactions of 1-β-D-lyxofuranosyluracil derivatives.[9] The facile formation of **6** is quite interesting, since this series of chemical modifications is reminiscent of the observation that 3′-deoxyadenosine (cordycepin) is formed from adenosine in cultures of *Cordyceps militaris*.[10] For this biological process, a 2′,3′-en-2′-ol formed *via* a trans elimination of a molecule of water from adenosine was proposed as an intermediate.[10]

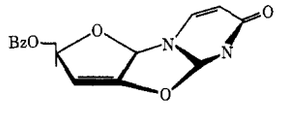
Experimental Section

All melting points are uncorrected. Electronic spectra were measured on a JASCO Model ORD/UV-5 spectrophotometer, TMS being used as an internal standard. In the case of hy-

(5) A. F. Cook and J. G. Moffatt, *J. Amer. Chem. Soc.*, **89**, 2697 (1967).

(6) U. Brodbeck and J. G. Moffatt, *J. Org. Chem.*, **35**, 3552 (1970).

(7) The reaction conditions used by us are more or less comparable with those under which 2,2,-anhydrouracil nucleosides were synthesized.[8] The transient formation of a 2,2′-anhydro-2′,3′-didehydro nucleoside (a) followed



a

by hydrolytic cleavage to give **6** might also be considered as far as a molecular model study is concerned. However, as one of the referees suggested, the nucleophilic substitution at an unsaturated 2′ carbon by uracil-2-carbonyl is unlikely. An interspacial repercussion between the ionized uracil-2-carbonyl and the electron-rich sulfonyl group seems to be the more probable reason for the formation of **6**.

(8) For examples, see (a) J. F. Codington, R. Fecher, and J. J. Fox, *J. Amer. Chem. Soc.*, **82**, 2794 (1960); (b) J. F. Codington, I. L. Doerr, and J. J. Fox, *J. Org. Chem.*, **29**, 558 (1964); (c) N. C. Yung and J. J. Fox, *J. Amer. Chem. Soc.*, **83**, 3060 (1961).

(9) The generally low yields of **5** and **6** can be explained by the concomitant formation of resinous products, which stayed immobile at the start lines of tlc plates. It might be noted that we could not detect any other noticeable side products which were movable on the tlc plates.

(10) J. N. Davidson and W. E. Cohn, *Progr. Nucl. Acid Res. Mol. Biol.*, **5**, 298 (1967).

droxyl-containing substances, measurements after D_2O addition were also carried out. Mass spectra were measured by a Hitachi RMU-D double-focusing spectrometer operating at an ionization potential of 80 eV. Solid samples were ionized by electron bombardment after sublimation directly into the electron beam at 200°. Wakogel B-5 silica gel, supplied by the Wako Pure Chemical Industries, was used for thin layer chromatography.

1-(5′-O-Benzoyl-2′-O-tosyl-β-D-lyxofuranosyl)uracil (2) and 1-(5′-O-Benzoyl-3′-O-tosyl-β-D-lyxofuranosyl)uracil (3).—To a stirred, ice-cold solution of 1-(5′-O-benzoyl-β-D-lyxofuranosyl)-uracil (1) (1.28 g, 3.7 mmol) in anhydrous pyridine (12 ml) was added tosyl chloride (1.54 g, 9.1 mmol) in several portions. After standing overnight at room temperature, the mixture was poured into ice–water (150 ml) and the semisolid precipitate was filtered, dried on a porous plate, and crystallized from methanol to give 0.7 g of colorless needles of **2**. Thin layer chromatography on the filtrate indicated the presence of two substances in comparable amounts, one of which proved to be **2**. The filtrate was evaporated to a foam and triturated with acetone to give another crystalline substance, **3** (70 mg). The filtrate separated from **3** was submitted to preparative thin layer chromatography with the use of silica gel and a solvent mixture, chloroform–ethyl acetate (1:1), to give second crops of **2** and **3**. The combined crops of **2** were recrystallized from methanol to give 0.8 g (41%) of needles, which melted at 195–197° after effervescence at 125–130°, λ_{max}^{EtOH} 227 nm (ε 29,000) and 259 (11,100).

Anal. Calcd for $C_{23}H_{22}N_2O_9S \cdot CH_3OH$: C, 53.93; H, 4.90; N, 5.24. Found: C, 53.91; H, 4.70; N, 5.18.

A portion of the methanolate **2** was dissolved in hot acetone and the solvent was evaporated. This procedure was repeated three times to give a colorless powder, mp 195°, which was used for nmr measurement after drying in a desiccator under high vacuum: nmr (DMSO-d_6) δ 2.42 (3 H, s, methyl in the tosyl group), 4.2–4.7 (4 H, m, 2 $H_{5'}$ + $H_{4'}$ + $H_{3'}$), 5.3 (1 H, dd, $J_{1',2'}$ = 6.8, $J_{2',3'}$ = 4.7 Hz, $H_{2'}$), 5.6 (1 H, dd, $J_{5,6}$ = 8, $J_{5,NH}$ = 2.25 Hz, H_5), 6.25 (1 H, d, $J_{1',2'}$ = 6.8 Hz, $H_{1'}$), 6.30 (1 H, br s, OH, lost on D_2O addition), and 7.35–8.1 (10 H, m, H_6 and aromatic protons).

On the other hand, the combined crops of **3** were recrystallized from acetone to give 0.12 g (6%) of needles (acetonate of **3**), mp 168–170°, λ_{max}^{EtOH} 225 nm (ε 31,100) and 260 (12,400).

Anal. Calcd for $C_{23}H_{22}N_2O_9S \cdot CH_3COCH_3$: C, 55.71; H, 5.04; N, 5.00. Found: C, 55.60; H, 4.92; N, 4.91.

A portion of the acetonate was repeatedly evaporated with hot chloroform to give acetone-free compound **3** as a foam, which was used for nmr measurement after drying: nmr (DMSO-d_6) δ 2.38 (3 H, s, methyl in the tosyl group), 4.45 (4 H, m, 2 $H_{5'}$ + $H_{2'}$ + $H_{4'}$), 5.35 (1 H, m, $H_{3'}$, partially merged with H_5 signal), 5.51 (1 H, dd, $J_{5,6}$ = 8, $J_{5,NH}$ = 2.25 Hz, H_5), 6.1 (1 H, d, OH, lost on D_2O addition), 6.15 (1 H, d, $J_{1',2'}$ = 6 Hz, $H_{1'}$), and 7.3–8.2 (10 H, m, aromatic protons containing H_6).

1-(5′-O-Benzoyl-3′-O-mesyl-2′-O-tosyl-β-D-lyxofuranosyl)uracil (4).—To a suspension of acetone-free **2** (502 mg, 1.02 mmol) in dry pyridine (2 ml) was added mesyl chloride (0.1 ml, 1.28 mmol) and the mixture was stirred at room temperature overnight. It was then poured into ice–water (100 ml) to give a precipitate which was filtered, dried on a porous plate, and recrystallized from methanol to give colorless needles (**4**) which gradually melted between 131 and 138° dec: yield 430 mg (72%); λ_{max}^{EtOH} 227 nm (ε 27,900) and 259 (9960); nmr ($CDCl_3$) δ 2.37 (3 H, s, methyl in the tosyl group), 3.12 (3 H, s, mesyl), 4.59 (3 H, br s, 2 $H_{5'}$ + $H_{4'}$), 5.55 (2 H, m, $H_{2'}$ and $H_{3'}$), 5.65 (1 H, d, $J_{5,6}$ = 8 Hz, H_5), 6.28 (1 H, d, $J_{1',2'}$ = 4.5 Hz, $H_{1'}$), and 7.1–8.1 (10 H, m, aromatic protons containing H_6).

Anal. Calcd for $C_{24}H_{24}N_2O_{11}S_2$: C, 49.66; H, 4.17; N, 4.83. Found: C, 49.78; H, 4.26; N, 4.91.

1-(5′-O-Benzoyl-3′-deoxy-2′-O-tosyl-β-D-*glycero*-pent-2′-enofuranosyl)uracil (5).—A mixture of 1-(5′-O-benzoyl-3′-O-mesyl-2′-O-tosyl-β-D-lyxofuranosyl)uracil (**4**) (0.3 g, 0.518 mmol) and sodium benzoate (0.3 g, 2.1 mmol) in dry DMF (5 ml) was heated at 90° for 30 min under stirring and poured into ice–water (100 ml). The precipitate was filtered, dried on a porous plate, and recrystallized from methanol to give pale-yellow needles, which were collected by filtration (0.13 g, 43%, mp 120–135°) and identified with **4** by ir and uv spectroscopy. The filtrate was concentrated and submitted to preparative thin layer chromatography with the use of a silica gel plate and a solvent mixture, chloroform–ethyl acetate (2:1), to give 50 mg (20%) of **5**: mp 149–151° (methanol); λ_{max}^{EtOH} 227 nm (ε 26,300) and 258 (8900);

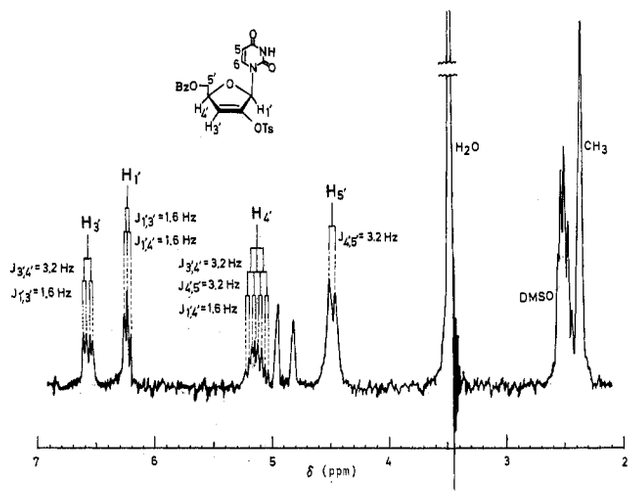


Figure 1.—Nuclear magnetic resonance spectrum of 1-(5′-O-benzoyl-3′-deoxy-2′-O-tosyl-β-D-*glycero*-pent-2′-enofuranosyl)-uracil in DMSO-d_6 + D_2O at 60 MHz.

nmr (DMSO-d_6) δ 2.4 (3 H, s, methyl in the tosyl group), 4.50 (2 H, d, $J_{4',5'}$ = 3.2 Hz, 5′-CH_2), 4.90 (1 H, d, $J_{5,6}$ = 8 Hz, H_5), 5.15 (1 H, octet, $J_{1',4'}$ = 1.6 Hz, $J_{3',4'}$ = $J_{4',5'}$ = 3.2 Hz, $H_{4'}$), 6.25 (1 H, t, $J_{1',3'}$ = $J_{1',4'}$ = 1.6 Hz, $H_{1'}$), 6.58 (1 H, dd, $J_{1',3'}$ = 1.6, $J_{3',4'}$ = 3.2 Hz, $H_{3'}$), and 7.8–8.0 (10 H, m, aromatic protons); mass spectrum *m/e* 373 (M − base), 362 (M − BzOH), 349, 251, and 207.

Anal. Calcd for $C_{23}H_{20}N_2O_8S$: C, 57.02; H, 4.16; N, 5.78. Found: C, 56.77; H, 4.25; N, 5.93.

5′-O-Benzoyl-3′-deoxy-2′-ketouridine (6).—A mixture of 1-(5′-O-benzoyl-3′-O-mesyl-2′-O-tosyl-β-D-lyxofuranosyl)uracil (**4**) (1.14 g, 1.95 mmol) and sodium benzoate (1.3 g, 9.1 mmol) in DMF (25 ml) was stirred at 120°. An aliquot of the reaction mixture was taken every 20 min and examined by tlc with the use of silica gel and a solvent mixture, chloroform–ethyl acetate (2:1). The appearance of **5** as the single product was indicated during the first 20 min, following which **5** gradually disappeared with the appearance of a new product which moved on the tlc plates slightly slower than the former. Concomitant increase in resinous products was also indicated by the deep coloration of the mixture. After 1 hr no spot for **5** was observed on tlc. After 3 hr, during which most of the starting material was consumed, the black mixture was evaporated *in vacuo* to give a tarry residue, which was triturated with water (30 ml) and extracted with ethyl acetate (200 ml). The extract obtained after evaporation of the solvent was left at room temperature with a small amount of ethanol to give a crystalline substance, which was collected by filtration. Preparative thin layer chromatography on the filtrate gave a small amount of second crop. The combined product was crystallized from methanol to give 70 mg (11%) of colorless granules: mp 195°; ir (KBr) $\nu_{C=O}$ 1680, 1705, and 1750 cm^{-1}; λ_{max}^{EtOH} 228 nm (ε 16,500) and 258 (11,400); nmr (DMSO-d_6) δ 2.8 (2 H, t, J = 8 Hz, 5′-CH_2), 4.5 (2 H, q, J = 7.8 and 4 Hz, 3′-CH_2), 5.0 (1 H, complex multiplet, $H_{4'}$), 5.6 (1 H, s, $H_{1'}$), 5.65 (1 H, d, $J_{5,6}$ = 8 Hz, H_5), and 7.2–8.1 (10 H, aromatic protons containing H_6); mass spectrum *m/e* 330 (M^+), 219 (M − base), 195 (M − $BzOCH_2$), and 208 (M − BzOH).

Anal. Calcd for $C_{16}H_{14}N_2O_6$: C, 58.18; H, 4.27; N, 8.48. Found: C, 58.26; H, 4.41; N, 8.48.

1-(5′-O-Benzoyl-2′-O-mesyl-3′-O-tosyl-β-D-lyxofuranosyl)uracil (7).—To a stirred ice-cold solution of the acetonate of **3** (0.35 g, 0.69 mmol) in anhydrous pyridine (3 ml) was added mesyl chloride (0.08 ml, 1 mmol) and the mixture was left at 0° overnight. The brown-colored solution was mixed with ethanol (1 ml), left at room temperature for 1 hr, and evaporated *in vacuo*. The residual paste was extracted with ethyl acetate (2 × 50 ml) in the presence of water (10 ml). The combined ethyl acetate solution was then washed with 5% sodium bicarbonate (10 ml) and water, and dried with sodium sulfate. Evaporation of the solvent gave 360 mg (90%) of a homogeneous foam (**7**). A portion of this material was further purified for elemental analysis by thin layer chromatography using silica gel and chloroform–ethyl acetate (1:1).

Anal. Calcd for $C_{24}H_{24}N_2O_{11}S_2$: C, 49.66; H, 4.17; N, 4.83. Found: C, 49.91; H, 4.33; N, 5.11.

Reaction of 1-(5′-*O*-Benzoyl-2′-*O*-mesyl-3′-*O*-tosyl-β-D-lyxofuranosyl)uracil (7) with Sodium Benzoate.—A mixture of **7** (360 mg, 0.62 mmol) and sodium benzoate (270 mg, 1.86 mmol) in DMF (4 ml) was stirred at 100° for 20 min. Thin layer chromatography with an aliquot of the reaction mixture indicated one main product and essentially no starting material. The mixture was poured into ice–water (50 ml) and extracted with ethyl acetate (2 × 50 ml). The ethyl acetate solution was dried with sodium sulfate and evaporated to a foam, which was submitted to preparative thin layer chromatography using silicic acid and chloroform–ethyl acetate (1:1) to give 37 mg (18%) of a crystalline substance, mp 192–194°. Its identity with **6** was confirmed by ir and uv spectroscopy.

1-(5′-*O*-Benzoyl-2′,3′-di-*O*-mesyl-β-D-lyxofuranosyl)uracil (9).—A solution of 1-(5′-*O*-benzoyl-β-D-lyxofuranosyl)uracil (**1**) (0.32 g, 0.92 mmol) in dry pyridine (3 ml) was treated with mesyl chloride (0.17 ml, 2.2 mmol) at 0° overnight and the mixture was worked up as in the case of compound **7**. The finally obtained pasty product contained trace amounts of impurities as indicated by tlc. Preparative thin layer chromatography with the use of silica gel and ethyl acetate as developer gave 0.36 g (78%) of a homogeneous foam, which was used as such for the next elimination reaction, nmr ($CDCl_3$) δ 3.15 (6 H, d, two mesyl).

Reaction of 1-(5′-*O*-Benzoyl-2′,3′-di-*O*-mesyl-β-D-lyxofuranosyl)uracil (9) with Sodium Benzoate.—A mixture of **9** (0.36 g, 0.72 mmol) and sodium benzoate (270 mg, 3.6 molar equiv) in DMF (5 ml) was stirred at 110°. Thin layer chromatography with the use of an aliquot of the reaction mixture indicated that over 50% of the starting material was converted to another faster moving substance after 15 min of reaction. After 35 min, the rest of the starting material was remarkably reduced with the appearance of a slight amount of a new product and with increase in resinous substances. It took totally 2 hr of stirring for the complete disappearance of the starting material. The mixture was now evaporated *in vacuo* as far as possible and the residue was extracted with ethyl acetate (4 × 30 ml) in the presence of water (15 ml). The ethyl acetate solution was dried with sodium sulfate and evaporated to a paste, which was submitted to preparative thin layer chromatography with the use of silica gel and ethyl acetate. Elution of the main band with ethyl acetate gave a crystalline substance, mp 192–193° (50 mg, 21%), whose identity with an authentic sample of **6** was confirmed by ir spectra and the mixture melting point determination.

1-(2′-*O*-Tosyl-β-D-lyxofuranosyl)uracil (10).—Compound **4** (0.3 g, 0.517 mmol) was combined with saturated ethanolic ammonia (16 ml) in a pressure tube, which was heated in an oil bath at 100–105° for 16 hr. After cooling, the solvent and excess ammonia were evaporated and the solid residue was crystallized from methanol to give 94 mg (45%) of colorless needles of **10**: mp 259–261°; λ_{max}^{EtOH} 225 nm (ε 14,000) and 260 (9100); nmr (DMSO-d_6) δ 2.43 (3 H, s, methyl in the tosyl group), 3.6 (3 H, br m, 2 $H_{5'}$ + $H_{4'}$), 4.15 (1 H, dd, $J_{2',3'}$ = 4.7, $J_{3',4'}$ = 3.7 Hz, $H_{3'}$), 5.25 (1 H, dd, $J_{1',2'}$ = 6.8, $J_{2',3'}$ = 4.7 Hz, $H_{2'}$), 5.6 (1 H, d, $J_{5,6}$ = 8 Hz, H_5), 6.15 (1 H, d, $J_{1',2'}$ = 6.8 Hz, $H_{1'}$), and 7.2–7.8 (5 H, m, aromatic protons containing H_6).

Registry No.—**1**, 38359-50-1; **2**, 38359-51-2; **3**, 38359-52-3; **4**, 38359-53-4; **5**, 38359-54-5; **6**, 38359-55-6; **7**, 38431-66-2; **9**, 38431-65-1; **10**, 38359-56-7.

The Use of Papain in Resolving Racemic *N*-(Alkoxycarbonyl)glycines and *N*-(Alkoxycarbonyl)alanines That Contain Small Alkoxy Groups[1]

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Papain promoted very rapid reactions at pH 4.5 between small molecular weight *N*-(alkoxycarbonyl)amino acids and *m*- or *p*-anisidine. Hindrance toward reactions was evident when ortho-substituted anilines were used. For *N*-(*tert*-butoxycarbonyl)- and *N*-(*tert*-pentyloxycarbonyl)-DL-alanines, resolution amounted to ~95 to 100%. A few *N*-(alkoxycarbonyl)glycines were used in which the asymmetric center was placed in the alkoxycarbonyl group. These groups included (*R,S*)-*N*-(*sec*-butoxycarbonyl), (*R,S*)-*N*-(1-methylbutoxycarbonyl), (*R,S*)-*N*-(2-methylbutoxycarbonyl), and (*S*)-*N*-(2-methylbutoxycarbonyl). A preference for one enantiomer was shown for each racemic mixture investigated. Anisidides formed from (*R,S*)-*N*-(2-methylbutoxycarbonyl)glycine displayed a preponderance of the *S* enantiomer to the extent of ~56% after an early period of incubation. This conclusively demonstrated the ability of papain to exert a modest stereochemical control, even though the asymmetric center is removed four or five atoms away from its usual position in *N*-acyl-DL-amino acids.

N-(*tert*-Butoxycarbonyl)- and *N*-(*tert*-pentyloxycarbonyl)amino acids have been used in solid-phase peptide syntheses of bradykinin,[2] ferredoxin,[3] ribonuclease,[4] and human growth hormone.[5] Although papain has been used to catalyze the synthesis of anilides of many *N*-acylamino acids,[6] anilides of low molecular weight *N*-(alkoxycarbonyl)amino acids have not been prepared in this manner. It was the purpose of the present research to explore the use of papain as a catalyst for reactions between a few substituted anilines and such *N*-acylamino acids, which contain only four or five carbons in the alkoxy group. By placing an asymmetric center in the alkoxy group of *N*-(alkoxycarbonyl)glycines, the zone of stereochemical control exerted by papain would be substantially altered and a considerably different perspective would therefore be achieved.

Four principal objectives were attained through this research. First, the use of *N*-*tert*-alkoxycarbonyl derivatives of glycine, DL-alanine, and L-alanine permitted a comparison to be made of their relative rates of reactions with known rates of more familiar *N*-acyl derivatives of these same amino acids. Second, by careful selection of ortho-, meta-, and para-substituted anilines, the effect of position and kind of substituent on the ability of this type of base to participate in such reactions was disclosed. Third, the extent of resolution of racemic *N*-(alkoxycarbonyl)amino acids was revealed through comparison of specific rotations of their reaction products with specific rotations of corresponding products from single enantiomers of the given *N*-acyl-

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