Anal. Calcd for $C_{21}H_{28}O_5$: C, 70.00; H, 7.78. Found: C, 70.08; H, 7.71.

3-Methoxy-14β,17α-dihydroxy-8α-estra-1,3,5(10)-trien-11-one (5a) and 3-Methoxy-14β,17α-dihydroxy-8α,9β-estra-1,3,5(10)-trien-11-one (5b). The solution of **4** (1.0 g, 2.77 mmol) in 100 mL of MeOH and 10 mL of 10% aqueous HCl was left at room temperature for 2 h. Methanol was evaporated in vacuo and the residue was extracted with $CHCl_3$. The extracts were washed with saturated aqueous $NaHCO_3$ and dried with anhydrous $MgSO_4$. Chromatography on 30 g of silica gel using hexane–ethyl acetate (95:5) as eluent afforded **5a** (0.71 g, 81%) and **5b** (0.04 g, 4.6%). The second run of the same reaction gave only compound **5a.**

5a: mp 109–112 °C (from C_6H_6); IR 1710 cm^{-1}; ^1H NMR δ 1.11 (s, 3, CH_3), 3.80 (s, 3, OCH_3), 3.95 (d, 1, $J_{9,8}$ = 6.25 Hz, H-9), 4.22 (t, 1, H-17), 6.58–6.80 (m, 2, H-2 and H-4), 6.82 ppm (d, 1, H-1).

Anal. Calcd for $C_{19}H_{24}O_4$: C, 72.15; H, 7.59. Found: C, 72.10; H, 7.52.

5b: ^1H NMR δ 1.08 (s, 3, CH_3), 3.80 (s, 3, OCH_3), 3.98 (d, 1, $J_{9,8}$ = 12.5 Hz, H-9), 4.35 (q, 1, H-17), 6.58–6.88 (m, 2, H-2 and H-4), 7.25 ppm (d, 1, H-1).

However, the regeneration of **5b** from the ^1H NMR sample gave a mixture of both epimers **5a** and **5b**; therefore, we are not giving further analytical data of **5b.**

3-Methoxy-14β-hydroxy-17α-acetoxy-8α-estra-1,3,5(10)-trien-11-one (6). The solution of **5a** (0.60 g, 1.89 mmol) in acetic anhydride (2 mL) and pyridine (4 mL) was left at room temperature for 12 h. Evaporation of pyridine and of excess of Ac_2O in vacuo followed by crystallization from methanol afforded **6** (0.62 g, 92%): mp 207–211 °C (from MeOH): IR 1710 and 1725 cm^{-1}; ^1H NMR δ 1.12 (s, 3, CH_3), 2.08 (s, 3, CH_3COO), 3.80 (s, 3, OCH_3), 3.95 (d, 1, $J_{9,8}$ = 6.25 Hz, H-9), 5.15 (t, 1, H-17), 6.68–6.80 (m, 2, H-2 and H-4), 6.85 ppm (d, 1, H-1).

Anal. Calcd for $C_{21}H_{26}O_5$: C, 70.39; H, 7.26. Found: C, 70.20; H, 7.25.

11-Thioketal of 3-Methoxy-14β-hydroxy-17α-acetoxy-8α-estra-1,3,5(10)-trien-11-one (7). To the solution of **6** (0.50 g, 1.39 mmol) in ethanedithiol (2 mL), BF_3-Et_2O (0.1 mL) was added and the mixture was stirred at room temperature for ca. 20 min until a clear solution was obtained. The reaction was then diluted with 10 mL of aqueous $NaHCO_3$ and extracted with benzene. Further standard workup gave the crude product **7**, which after recrystallization from Et_2O yielded pure **7** (0.48 g, 80%): mp 213–217 °C (from Et_2O): IR 1715 cm^{-1}; ^1H NMR δ 1.42 (s, 3, CH_3), 2.12 (s, 3, CH_3COO), 3.50 (d, 1, $J_{9,8}$ = 5 Hz, H-9), 3.85 (s, 3, OCH_3), 5.12 (t, 1, H-17), 6.55–6.72 (m, 2, H-2 and H-4), 7.80 ppm (d, 1, H-1).

Anal. Calcd for $C_{23}H_{30}O_4S_2$: C, 63.60; H, 6.92. Found: C, 63.65; H, 6.91.

3-Methoxy-8α-estra-1,3,5(10)-trien-14β,17α-diol 17-Acetate (8a). Freshly prepared Raney nickel (from 5 g of alloy) was added to the solution of the thioketal **7** (0.35 g, 0.80 mmol) in a mixture of methanol and benzene (1:1, 50 mL) and it was stirred at room temperature for ca. 3 h. Nickel was then filtered off and the solvent was evaporated in vacuo. The residue was crystallized from methanol giving **8a** (0.25 g, 91%): mp 178–188 °C (from MeOH): IR 1720 cm^{-1}; ^1H NMR δ 1.10 (s, 3, CH_3), 2.10 (s, 3, CH_3COO), 3.82 (s, 3, OCH_3), 5.20 (t, 1, H-17), 6.58–6.85 (m, 2, H-2 and H-4), 7.05 ppm (d, 1, H-1).

Anal. Calcd for $C_{21}H_{28}O_4$: C, 73.25; H, 8.13. Found: C, 73.26; H, 8.20.

3-Methoxy-14β-hydroxy-8α-estra-1,3,5(10)-trien-17-one (9). To a solution of **8a** (0.20 g, 0.58 mmol) in THF (10 mL) was added 0.05 g of LAH, and the mixture was stirred at room temperature for ca. 10 min. The reaction was quenched with aqueous $(NH_4)_2SO_4$, and after standard workup the oily diol **8b** (0.15 g, 91%) was obtained. It was dissolved in dry methylene chloride (25 mL) and oxidized with pyridinium chlorochromate (PCC)[9] (0.20 g). The compound **9** was isolated by short-column chromatography and crystallized from hexane–acetone (2:1) solution yielding pure **9** (0.13 g, 86%): mp 174–176 °C (from hexane–acetone): IR 1730 cm^{-1}; ^1H NMR δ 1.18 (s, 3, CH_3), 3.82 (s, 3, OCH_3), 6.62–6.85 (m, 2, H-2 and H-4), 7.05 ppm (d, 1, H-1); MS *m/e* 300.

Registry No.—**3,** 64069-77-8; **4,** 64035-53-6; **5a,** 64069-78-9; **5b,** 64069-79-0; **6,** 64069-80-3; **7,** 64035-54-7; **8a,** 64069-81-4; **9,** 10003-00-6; acetic anhydide, 108-24-7; ethanedithiol, 540-63-6.

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Base-Catalyzed Disproportionation Reactions of 3′,5′-Di-*O*-aroyl Derivatives of 1-β-D-Arabinofuranosyluracil

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In a recent publication,[1] we reported that 1-(2′,3′,5′-tri-*O*-benzoyl-β-D-arabinofuranosyl)uracil (iii) forms as a by-product in the synthesis of 1-(3′,5′-di-*O*-benzoyl-β-D-arabinofuranosyl)uracil (ii) from 1-(5′-*O*-benzoyl-3′-*O*-mesyl-β-D-arabinofuranosyl)uracil (i) and sodium benzoate in hot DMF and that the immediate precursor of iii is compound ii. The unusual formation of iii has posed the question of whether the 2′-*O*-benzoyl group in iii originates from the external benzoate anion of benzoic acid, or if iii forms by an intramolecular disproportionation reaction of ii. Another possibility that it results by an intramolocular benzoyl rearrangement with concomitant introduction of a second benzoyl unit from outside can not be ruled out immediately. To solve this problem, we designed a synthetic study using analogues of i and ii with different aroyl groups and sodium salts of substituted benzoic acids as basic catalysts. This report deals with some mechanistic evidences to support a disproportionation reaction in the formation of iii, the first observed example of such reactions in the nucleoside field.

Treatment of 2′,3′,5′-tri-*O*-mesyluridine (**1**)[2] with sodium *p*-chlorobenzoate by the known method[2] gave 2,2′-anhydro-(5′-*O*-*p*-chlorobenzoyl-3′-*O*-mesyl-β-D-arabinofuranosyl)-uracil (**2**) in an excellent yield. Acidic hydrolysis of **2** yielded the desired substance, 1-(5′-*O*-*p*-chlorobenzoyl-3′-*O*-mesyl-β-D-arabinofuranosyl)uracil (**3**). The structures of **2** and **3** were based on the analysis and spectroscopic data described in the Experimental Section.

The first reaction of sodium *p*-methylbenzoate on **3** was focused on the separation of two possible isomers, 1-(5′-*O*-*p*-chlorobenzoyl-3′-*O*-*p*-methylbenzoyl-β-D-arabinofuranosyl)uracil (**4a**) and 1-(5′-*O*-*p*-chlorobenzoyl-2′-*O*-*p*-methylbenzoyl-β-D-xylofuranosyl)uracil (**5**), to evaluate the approximate yields of these isomers, reducing the formations of other products as far as possible. Thus, a short-time reaction using a rather more dilute mixture of the reactants (method A) permitted isolation of **4a** and **5** in 44 and 8% yield, respectively. TLC on the reaction mixture also revealed the formation of a trace amount of a faster running substance corresponding to a triaroyl derivative like iii, but it was neglected. The structures of **4a** and **5** could be easily assigned largely on the basis of NMR data (Table I): in the spectrum of **4a,** the anomeric proton signal appeared at 6.28 ppm as a

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Table I. NMR Resonances of Uridine Derivatives at 60 MHz

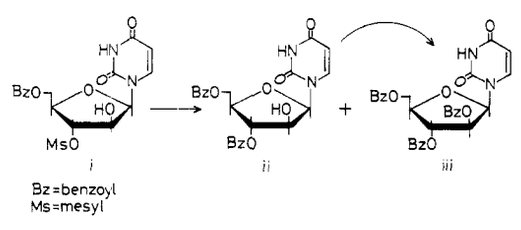
Compd	Registry no.	$C_{5'}H$	$C_{4'}H$	$C_{3'}H$	$C_{2'}H$	$C_{1'}H$	C_5H^h	NH
4a[a]	64114-32-5	4.48 (m)	4.72 (m)	5.35 (s)	*d*	6.28 (d) $J_{1',2'}$ = 3.3 Hz	5.58 (d)	10.70 (br s)
4b[c]	64114-33-6	4.3–4.6 (m)	4.6–4.9 (br s)	5.35 (s)	*d*	6.15 (d) $J_{1',2'}$ = 3.2 Hz	6.32 (d)	12.50 (br s)
5[b]	64114-34-7	4.45 (m)	4.72 (m)		5.42 (s)	5.98 (s)	5.68 (d)	10.55 (br s)
6a[a]	64114-35-8	4.85 (d) J = 4.5 Hz	4.58 (m)	5.60 (m)	5.80 (dd) $J_{1',2'}$ = 3.75 Hz $J_{2',3'}$ = 1.6 Hz	6.45 (d) $J_{1',2'}$ = 3.75 Hz	5.58 (d)	10.90 (br s)
6b	64114-36-9	4.79–5.0 (m)	4.60 (m)	5.60 (m)	5.85 (d) $J_{1',2'}$ = 3.9 Hz	6.40 (d) $J_{1',2'}$ = 3.9 Hz	6.33 (d)	*e*
7[c]	64114-79-6	3.95 (d) J = 3.4 Hz	4.32 (m)	5.32 (dd)	*d* $J_{2',3'}$ = $J_{3',4'}$ = 1.6 Hz	6.19 (d) $J_{1',2'}$ = 3.2 Hz	5.62 (d)	10.68 (br s)
8[c]	64114-37-0	4.1–4.3 (m)			4.5–4.7 (m)	6.19 (d) $J_{1',2'}$ = 3.3 Hz	5.53 (d)	10.70 (br s)
9[b]	64114-38-1	4.1–4.9 (m)		5.35 (m)	*f*	6.28 (d) $J_{1',2'}$ = 3.3 Hz	5.61 (d)	
10[b]	64114-39-2	4.85 (d) J = 4.5 Hz	4.52 (m)	5.60 (m)	5.7–5.9 (m)	6.45 (d) $J_{1',2'}$ = 3.75 Hz	*g*	

[a] In $CDCl_3/Me_2SO$-d_6(5:1). [b] In $CDCl_3$. [c] $CDCl_3/Me_2SO$-d_6(3:1). [d] In $H_{4'}$ envelope. [e] Did not appear clearly. [f] In $H_{4'}$–$H_{5'}$ envelope. [g] In $H_{2'}$ envelope. [h] All the coupling constants were 8.0 Hz.

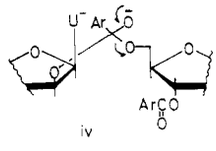
doublet ($J_{1',2'}$ = 3.3 Hz) and the aroyloxy-deshielded $C_{3'}$ proton signal at 5.35 ppm as a singlet. On the other hand, in the spectrum of **5** the signals of both the anomeric and aroyloxy deshielded $C_{2'}$ proton appeared as singlets at 5.98 and 5.42 ppm, respectively. These spectral patterns are consistent with the structure of **4a** with a cis $H_{1'}$–$H_{2'}$ relationship and that of **5** with a trans $H_{1'}$–$H_{2'}$ relationship, respectively.[3] Furthermore, it has been well established that 1-(2′,3′-anhydro-β-D-lyxofuranosyl)uracil and its 5′-*O*-substituted analogues undergo nucleophilic attacks predominantly at the $C_{3'}$ position.[4,1] Thus, the formation of the xylo isomer proved to be trivial and hence neglected in the subsequent synthetic reactions.

Reaction of **3** with the same reagent under more vigorous conditions (3.5 h at 125 °C) gave **4a,** 1-(2′,5′-di-*O*-*p*-chlorobenzoyl-3′-*O*-*p*-methylbenzoyl-β-D-arabinofuranosyl)uracil (**6a**), 1-(3′-*O*-*p*-methylbenzoyl-β-D-arabinofuranosyl)uracil (**7**), and 1-(5′-*O*-*p*-chlorobenzoyl-β-D-arabinofuranosyl)uracil (**8**) in 37.2, 11.8, 7.3, and 2.93% yield, respectively. Compounds **6a–8** exhibited uridine absorptions (sh) in the region of 260 nm and NMR resonances of $H_{1'}$ as doublets ($J_{1',2'}$ = 3.2–3.75 Hz) indicative of their arabino configurations. In the spectrum of the monoaroyl derivative (**7**), the ester-deshielded signal at 5.32 ppm did not interact with $H_{1'}$ and hence should be assigned to $H_{3'}$. Moreover, the 5′-methylene signal appeared at a significantly higher field (3.95 ppm). In contrast, the spectrum of the halogen-containing product **8** showed the 5′-methylene signal at a lower field (4.1–4.3 ppm) and the signals of $H_{2'}$ and $H_{3'}$ at the same, relatively higher field (4.5–4.7 ppm). These findings are consistent with the proposed structures **7**, and **8.** The structure of **6a** was further confirmed by an alternative synthesis (see Experimental Section). Similar treatment of **4a** with basic catalysts[5] gave **6a** in similar yields. The isolation of **6a** and its counterpart **7** let us directly

Scheme I



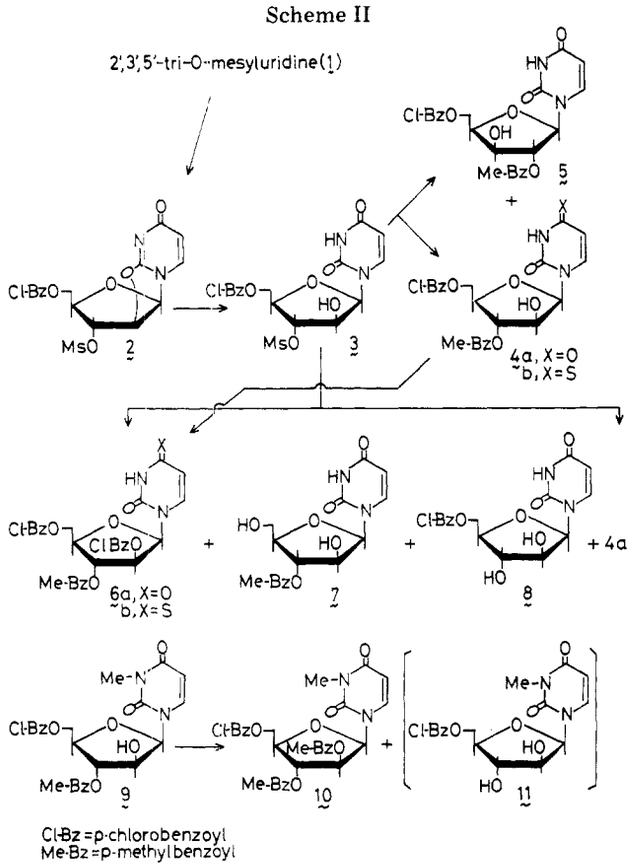
conclude that there was involved a base-catalyzed disproportionation reaction of **4a** as visualized in formula iv, also supported by separate experiments using basic catalysts other than *p*-methylbenzoate salts.[5] It must be noted here that combinations of **4a** with free aromatic acids gave only the starting materials under similar reaction conditions. The formation of the far minor product **8** could be explained in terms of hydrolysis caused by the presence of a trace of moisture, since we did not detect any trace of another counterpart (triaroyl compound) for **8.** The selective formation of



6a and **7** was interesting in view of the synthetically useful transacetylation between adenosine and its 2′,3′,5′-tri-*O*-acteyl derivative,[6] but all the attempts to improve their yields have been unsuccessful.[7] **4a** was converted to 1-(5′-*O*-*p*-chlorobenzoyl-3′-*O*-*p*-methylbenzoyl-β-D-arabinofuranosyl)-4-thiouracil (**4b**), which also gave 1-(2′,5′-di-*O*-*p*-chlorobenzoyl-3′-*O*-*p*-methylbenzoyl-β-D-arabinofuranosyl)-4-thiouracil (**6b**) as the sole triaroyl product by the action of sodium benzoate.

It seemed to be interesting to examine the effect of the ionized base moiety in the disproportionation reaction.[8] For this purpose, compound **4a** was selectively methylated at N^3 using *N,N*-dimethylformamide dimethylacetal[9] to give 1-(5′-*O*-*p*-chlorobenzoyl-β-D-arabinofuranosyl)-3-methyluracil (**9**). The structure of **9** was evident on the basis of analysis and general spectroscopic data. **9** was first treated with sodium *p*-methylbenzoate under similar conditions. The product distribution was quite similar to the reactions between **4a,b** and basic catalysts, suggesting a similar disproportionation reaction (see Experimental Section). This time only the faster moving product was isolated, and the other slower moving substance, probably **11,** was discarded because of its paucity. The triaroyl component separated in 13% yield was, surprisingly, 1-(5′-*O*-*p*-chlorobenzoyl-2′,3′-*O*-*p*-methylbenzoyl-β-D-arabinofuranosyl)-3-methyluracil (**10**) as shown by its analysis and spectroscopic data. Treatment of **9** with sodium benzoate also afforded exclusively **10** in a similar yield (12%),

Scheme II



thus precluding the possibility that the source of the introduced aroyl group is exogeneous. Thus, the protection at N^3 completely altered the direction of the disproportionation reaction, the 3'-*O*-aroyl group having been transported to the 2'-hydroxyl of another molecule of **9**. At the present stage, no obvious explanation can be given for this intriguing phenomenon even from a molecular model study.

Although we have not succeeded in raising the yields of the two main products, the triaroyl and monoaroyl compounds, and thus in raising the synthetic value of the disproportionation reactions for obtaining selectively protected monoaroyl compounds, this sequence of reactions has disclosed a new aspect of the behavior of protected arabinosides.

Experimental Section[10]

2,2'-Anhydro-1-(5'-*O*-*p*-chlorobenzoyl-3'-*O*-mesyl-β-D-arabinofuranosyl)uracil (2). A mixture of 2',3',5'-tri-*O*-mesyluridine (1) (1.0 g, 2.09 mmol) and sodium *p*-chlorobenzoate (1.12 g, 6.27 mmol) in *N*,*N*-dimethylformamide (DMF) (15 mL) was stirred at 110–115 °C for 2 h. After cooling, the mixture was poured into ice water (150 mL) under vigorous stirring. The precipitate was collected by suction, dried by pressing on a porous plate, and recrystallized from acetonitrile to give 880 mg (95%) of **2** as colorless needles: mp 223–225 °C; UV λ_{max}^{MeOH} 242 nm (ε 23 000).

Anal. Calcd for $C_{17}H_{15}N_2O_8SCl$: C, 46.07; H, 3.39; N, 6.32. Found: C, 46.11; H, 3.41; N, 6.32.

1-(5'-*O*-*p*-Chlorobenzoyl-3'-*O*-mesyl-β-D-arabinofuranosyl)uracil (3). To a stirred suspension of **2** (0.65 g, 1.45 mmol) in acetone–water (1:1) (200 mL) was added 12 N hydrochloric acid (3 mL). The mixture was stirred at room temperature for 20 h. The resulting solution was evaporated below 35 °C to remove acetone, and the separating crystals were collected by suction. Recrystallization from a mixture of acetone and water gave 0.59 g (86%) of colorless needles (**3**): mp 169–171 °C; UV λ_{max}^{MeOH} 243 (ε 28 000) and 263 nm (ε 13 200, sh).

Anal. Calcd for $C_{17}H_{17}N_2O_9SCl$: C, 44.31; H, 3.72; N, 6.08. Found: C, 44.23; H, 3.69; N, 5.94.

Reaction of 1-(5'-*O*-*p*-Chlorobenzoyl-3'-*O*-mesyl-β-D-arabinofuranosyl)uracil (3) with Sodium *p*-Methylbenzoate. Method A. Separation of 4a and 5. A mixture of **3** (0.92 g, 2 mmol) and sodium *p*-methylbenzoate (0.95 g, 6 mmol) in DMF (50 mL) was stirred at 120 °C for 70 min and cooled. TLC with an aliquot of the reaction mixture using chloroform/ethyl acetate (7:1) showed tightly running, two main spots with a tiny amount of a much faster moving substance. The consumption of the starting material was also indicated. The mixture was evaporated and the residue partitioned between chloroform (100 mL) and water (30 mL). The organic layer was dried over sodium sulfate and evaporated to a gum, which was triturated with ca. 10 mL of a solvent mixture, $CHCl_3$ (7)/ETOAc (1), to give **4a** as homogeneous crystals (154 mg). The mother liquor separated from the crystals was applied on a silica gel column (2.5 × 32 cm) and eluted with the same solvent to effect separation of the closely running components, **4a** and **5**. The slightly faster moving fraction was rechromatographed on a silica gel plate (10 × 20 cm) using the same solvent mixture (twice developed) to give 83 mg (8.3%) of **5** as a homogeneous foam: UV λ_{max}^{MeOH} 240 (ε 45 800) and 262 nm (ε 19 200).

Anal. Calcd for $C_{24}H_{21}N_2O_8Cl$: C, 57.55; H, 4.43; N, 5.59. Found: C, 57.25; H, 4.28; N, 5.39.

The second crystalline fraction was combined with the above obtained crystals and recrystallized from acetone to give 442 mg (44%) of **4a** as needles: mp 216–218 °C; UV λ_{max}^{MeOH} 240 (ε 40 000) and 261 nm (ε 16 400, sh).

Anal. Calcd for $C_{24}H_{21}N_2O_8Cl$: C, 57.55; H, 4.43; N, 5.59. Found: C, 57.60; H, 4.37; N, 4.40.

Method B. Isolation of 6a, 7, 8, and 4a. A mixture of **3** (2.235 g, 4.55 mmol) and sodium *p*-methylbenzoate (2.15 g, 13.65 mmol) in DMF (48 mL) was stirred at 125 °C for 3.5 h. After cooling, the solvent was evaporated off and the residue partitioned between ethyl acetate (100 mL) and ice water (30 mL). The organic layer was worked up as usual, charged on a silica gel column (3 × 24 cm), and eluted first with chloroform/ethyl acetate (5:1). The first fraction gave 343 mg (11.8%) of **6** as needles of mp 245–246 °C after one crystallization from a mixture of acetone and ethanol: UV λ_{max}^{MeOH} 241 (ε 70 700) and 267 nm (ε 9080, sh).

Anal. Calcd for $C_{31}H_{24}N_2O_9Cl_2$: C, 58.23; H, 3.78; N, 4.38. Found: C, 58.15; H, 3.99; N, 4.26.

The second fraction gave a semisolid mixture of **4a** and **5**, from which 847 mg (37.2%) of **4a** was obtained as crystals after crystallization from acetone and rechromatography of the overlapped fraction on a silica gel column using the same solvent mixture. The finally obtained, small amount of mixture of **4a** and **5** was neglected. The identity of **4a** with an authentic sample prepared by method A was confirmed by infrared and NMR spectroscopy.

The column was then thoroughly eluted with ethyl acetate to give a small amount of a paste, which was shown by TLC [chloroform/methanol (9:1) and ethyl acetate/chloroform (2:1)] to be a mixture of two closely running products. The mixture was charged on a silica gel plate (15 × 20 cm) and developed twice with ethyl acetate/chloroform (2:1). Elution of the slightly faster moving band with acetone and recrystallization of the obtained solid from a mixture of ethyl acetate and acetone gave 59 mg (7.3%) of **7** as needles, mp 226–229 °C; UV λ_{max}^{MeOH} 242 (ε 25 600) and 265 nm (ε 15 400, sh).

Anal. Calcd for $C_{17}H_{18}N_2O_7$: C, 56.35; H, 5.01; N, 7.73. Found: C, 56.06; H, 5.03; N, 7.53.

The slower moving band was similarly worked up to give 25 mg (2.93%) of **8**, mp 193–196 °C (from ethyl acetate); UV λ_{max}^{MeOH} 241 (ε 22 600) and 262 nm (ε 12 000, sh).

Anal. Calcd for $C_{16}H_{15}N_2O_7Cl$: C, 50.21; H, 3.95; N, 7.32. Found: C, 50.48; H, 4.08; N, 7.30.

Reaction of 1-(5'-*O*-*p*-Chlorobenzoyl-3'-*O*-*p*-methylbenzoyl-β-D-arabinofuranosyl)uracil (4a) with Sodium *p*-Methylbenzoate. A mixture of **4a** (100 mg, 0.205 mmol) and sodium *p*-methylbenzoate (130 mg, 0.82 mmol, 4 molar excess) in DMF (2.5 mL) was stirred at 125–130 °C for 19 h and worked up as in the reactions of **3**. The finally obtained ethyl acetate extract, TLC of which showed a product distribution quite similar with the reaction of **3** (method B), was submitted to preparative TLC [5 × 20 cm, chloroform/ethyl acetate (3:1)] to give 16 mg (12.5%) of **6a**, identical in all respects with an authentic specimen obtained above. The starting material and other products were discarded.

Reaction of 4a with Potassium *p*-Methylbenzoate. A mixture of **4a** (442 mg, 0.88 mmol) and potassium *p*-methylbenzoate (612 mg, 3.52 mmol, 4 molar excess) in DMF (22 mL) was stirred at 125–130 °C for 3.5 h. TLC at this stage showed a product distribution similar with the above reaction of **4a** with the same reagent. The mixture was worked up as usual and chromatographed on silica gel (32 × 2 cm) using chloroform/ethyl acetate (6:1) to give 75 mg (13.3%) of **6a** after one recrystallization. Recovery of the starting material was 36.7% (160 mg).

Alternative Synthesis of 6a. To an ice-cold stirred solution of **4a**

(100 mg, 0.2 mmol) in pyridine (2 mL) was added *p*-chlorobenzoyl chloride (0.03 mL, 0.23 mmol). The mixture was then left at room temperature for 6 h, treated with water (0.3 mL) for 5 min, and evaporated. The residue was partitioned between ethyl acetate (20 mL) and water (5 mL). TLC showed the presence of a small amount of another faster moving substance (most probably N^3-*p*-chlorobenzoyl derivative of **6a**). The ethyl acetate extract was heated in 95% pyridine at 110 °C for 2 h and cooled. The mixture was evaporated and repeatedly coevaporated with ethanol, and the residue was recrystallized from a mixture of ethanol and acetone to give 93 mg of needles of mp 245–247 °C, identical with the above-obtained sample of **6a** in all respects.

1-(5′-*O*-*p*-Chlorobenzoyl-3′-*O*-*p*-methylbenzoyl-β-D-arabinofuranosyl)4-thiouracil (4b). A mixture of **4a** (800 mg, 1.595 mmol) and phosphorus pentasulfide (710 mg, 3.19 mmol) in pyridine (25 mL) was stirred at 105 °C for 2 h and 20 min. Further phosphorus pentasulfide (300 mg) was added and the reaction continued for an additional 2 h. After cooling, the reaction mixture was partitioned between ethyl acetate (100 mL) and water (30 mL). The separated ethyl acetate layer was evaporated, the residual gum heated in water (50 mL) at 90–95 °C for 10–15 min, and the water decanted off. This procedure was repeated four times. The finally obtained solid residue was crushed with hot water, collected by suction, and recrystallized from acetonitrile to give 550 mg (67%) of **4b,** mp 254–256 °C; UV λ_{max}^{MeOH} 238 (ε 48 600) and 328 nm (ε 25 100).

Anal. Calcd for $C_{24}H_{21}N_2O_7SCl$: C, 55.77; H, 4.10; N, 5.42. Found: C, 55.64; H, 4.08; N, 5.67.

1-(2′,5′-di-*O*-*p*-Chlorobenzoyl-3′-*O*-*p*-methylbenzoyl-β-D-arabinofuranosyl)-4-thiouracil (6b). A mixture of **4b** (200 mg, 0.388 mmol) and sodium benzoate (224 mg, 1.55 mmol) in DMF (4.8 mL) was stirred at 115–120 °C for 3.5 h. After evaporation of the solvent, the residue was partitioned between ethyl acetate (50 mL) and water (10 mL). The separated organic phase was dried and evaporated, and the residue was triturated with chloroform to give 44 mg of the starting material. TLC with the filtrate using chloroform/ethyl acetate (3:1) showed the presence of a main (starting material) and two minor spots, one of which was faster moving and the other slower moving than the starting material. The filtrate was concentrated, charged on a silica gel plate (5 × 20 cm), and developed with chloroform. After usual workup, 20 mg (7.7%) of **6b,** mp 179–181 °C (from acetone + MeOH), was obtained: UV λ_{max}^{MeOH} 238 (ε 59 400) and 327 nm (ε 19 100).

Anal. Calcd for $C_{31}H_{24}N_2O_9SCl$: C, 55.45; H, 3.60; N, 4.17. Found: C, 55.21; H, 3.85; N, 4.15.

Additional starting material (56 mg) was recovered. The slower moving product was neglected.

1-(5′-*O*-*p*-Chlorobenzoyl-3′-*O*-*p*-methylbenzoyl-β-D-arabinofuranosyl)3-methyluracil (9). A mixture of **4a** (300 mg, 0.615 mmol) and *N,N*-dimethylformamide dimethylacetal (0.3 mL, 3 mmol) in chloroform (10 mL) was heated to a reflux for 4 h and cooled. The mixture was evaporated, charged on a silica gel plate (20 × 20 cm), and developed twice with chloroform/ethyl acetate (3:1). Elution of the main band with acetone gave 173 mg of a homogeneous solid, which was recrystallized from methanol to give 163 mg (52.7%) of **9** as needles of mp 173–175 °C: UV λ_{max}^{MeOH} 240 (ε 46 100) and 262 nm (ε 17 100).

Anal. Calcd for $C_{25}H_{23}N_2O_8Cl$: C, 58.31; H, 4.50; N, 5.44. Found: C, 58.54; H, 4.77; N, 5.43.

1-(5′-*O*-*p*-Chlorobenzoyl-2′,3′-di-*O*-*p*-methylbenzoyl-β-D-arabinofuranosyl)-3-methyluracil (10). Method A. A mixture of **9** (163 mg, 0.318 mmol) and sodium *p*-methylbenzoate (202 mg, 1.27 mmol, 4 molar excess) in DMF (4 mL) was stirred at 125–130 °C for 3.5 hr. TLC with an aliquot of the reaction mixture revealed the starting material as the major component with two minor products, one of which was faster moving and the other slower moving. Thus, the general pattern was similar with the case of the reactions between **4a,b** and the basic catalysts. The mixture was evaporated and the residue partitioned between ethyl acetate (30 mL) and water (7 mL). The obtained ethyl acetate extract was charged on a silica gel plate (20 × 20 cm) and developed with chloroform/ethyl acetate (3:1). The most mobile band gave 26 mg (12.9%) of **10** as needles of mp 182–184 °C after crystallization from a mixture of methanol and acetone: UV λ_{max}^{MeOH} 242 (ε 65 400) and 262 nm (ε 17 600).

Anal. Calcd for $C_{33}H_{29}N_2O_9Cl$: C, 62.61; H, 4.62; N, 4.43. Found: C, 62.43; H, 4.58; N, 4.53.

The major fraction gave 85 mg (51%) of the starting material. The other minor product was neglected.

Method B. A mixture of **9** (0.142 g, 0.277 mmol) and sodium benzoate (160 mg, 1.11 mmol, 4 molar excess) in DMF (4.5 mL) was stirred at 125–130 °C for 3.5 h. The reaction was worked up as described in method A to give 21 mg (12%) of **10,** identical with the product obtained above in terms of infrared and ultraviolet spectroscopy and mixef fusion. The other components were neglected.

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Registry No.—**1,** 59211-02-8; **2,** 64114-40-5; **3,** 64114-41-6; sodium *p*-methylbenzoate, 17264-54-9; potassium *p*-methylbenzoate, 16518-25-5; *p*-chlorobenzoylchloride, 122-01-0; phosphorus pentasulfide, 1314-80-3; sodium benzoate, 532-32-1; *N,N*-dimethylformamidedimethylacetal, 4637-24-5.

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Cyclocarbonylation of 2-*exo*-Ethynyl-7-*syn*-norbornanol to an α-Methylene δ-Lactone

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Although α-methylene butyrolactones are much more prevalent in natural products and have thus received more synthetic attention,[2] naturally occurring α-methylene valerolactones are also known, e.g., in vernolepin and vernomenin.[3] We have thus investigated the usefulness of our $PdCl_2$/thiourea catalyst system[4] in the synthesis of α-methylene valerolactones from carbon monoxide and appropriately substituted 4-pentynols.[5]

Only traces of α-methylene δ-valerolactone (1) were obtained by this method from 4-pentyn-1-ol itself, either under catalytic conditions or in the presence of 1 equiv of $PdCl_2$; most of the starting ethynyl alcohol remained unreacted even after 60 h. However, better results seemed likely with a fused-ring system where the ethynyl and hydroxyl groups were fixed in the appropriate geometry for lactone ring formation. A suitable substrate, **2a,** proved available from the treatment

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