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Note

Synthesis of diastereoisomeric uridine 2′,3′-*tert*-butylphosphonates

IRINA D. SHINGAROVA, STALINA YA. MELNIK, AND MARIA N. PREOBRAZHENSKAYA
Cancer Research Center of the U.S.S.R. Academy of Medical Sciences, 115478 Moscow (U.S.S.R.)
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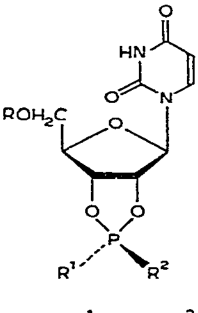
2′,3′-Adamant-1-ylphosphonates are formed by the reaction of adamant-1-ylphosphonic dichloride with nucleosides and 5′-*O*-substituted derivatives[1-3]. In further exploring this type of reaction, we have investigated the interaction of uridine (**1**) and its 5′-*O*-trityl derivative (**4**) with *tert*-butylphosphonic dichloride (**2**). Reaction of **1** and **2** in pyridine at 100° for 18 h gave 20% each of the diastereoisomeric uridine 2′,3′-*tert*-butylphosphonates (**3a** and **3b**). Likewise, **4** was converted into the diastereoisomeric 5′-*O*-trityluridine 2′,3′-*tert*-butylphosphonates (**5a**, 55.4%; **5b**, 30.6%). Detritylation of **5a** and **5b** with 90% trifluoroacetic acid furnished **3a** (95%) and **3b** (70%), respectively.

The mass spectra of **3a** and **3b** contained peaks for the molecular ion at *m/e* 346, and the fragmentation pathways were almost identical and compatible with the assigned structure. The p.m.r. data are given in Table I. The $^3J_{HP}$ values confirm that the *tert*-butylphosphonate residue is located at positions 2′ and 3′.



3a R = H, R^1 = O, R^2 = t-Bu
3b R = H, R^1 = t-Bu, R^2 = O
5a R = Tr, R^1 = O, R^2 = t-Bu
5b R = Tr, R^1 = t-Bu, R^2 = O

The configuration at phosphorus in **3a** and **3b** can be determined[3,4] on the basis of the deshielding of H-2′ and H-3′ by a *cis*-related P=O group. Thus, the signals for H-2′ and H-3′ in **3b** are at lower field than the corresponding signals in **3a**.

TABLE I

P.M.R. DATA FOR SOLUTIONS OF **3a** AND **3b** IN Me_2SO-d_6 AT 100°

Compound	*δ (p.p.m.)*[a]							
	H-6	*H-5*	*H-1′*	*H-2′*	*H-3′*	*H-4′*	*H-5′*	
3a	7.74	5.67	6.03	5.40	5.10	4.28	3.74	1.26
3b	7.74	5.68	5.94	5.48	5.24	4.23	3.72	1.33

[a]Coupling constants: **3a** $J_{5,6}$ 8, $J_{1',2'}$ 2, $J_{2',3'}$ 7, $J_{3',4'}$ 4.5, $J_{4',5'}$ 4.2, $J_{5,6}$ 8, $J_{2',P}$ 7, $J_{3',P}$ 12.8, and J_{MeP} 17.4 Hz; **3b** $J_{1',2'}$ 3, $J_{2',3'}$ 6, $J_{3',4'}$ 4.4, $J_{4',5'}$ 4.2, $J_{5,6}$ 8, $J_{2',P}$ 5.3, $J_{3',P}$ 6, and $J_{Me,P}$ 17.4 Hz.

EXPERIMENTAL

Solutions were concentrated under diminished pressure at 40°. T.l.c. was performed on Silufol UV-254 (Kavalier, Czechoslovakia), and p.l.c. on Silica Gel LSL_{254} (Chemapol, Czechoslovakia), with chloroform–methanol (*A*, 10:1; *B*, 20:1) and detection with u.v. light. Mass spectra were obtained with a Finnigan F-3020 spectrometer, and p.m.r. spectra ($CDCl_3$, internal Me_4Si) at 50° with a Varian XL-100 instrument.

*2′,3′-*tert*-Butylphosphonates* (**3a** *and* **3b**). — (*a*) To a solution of 5′-*O*-trityluridine[5] (1 g) in anhydrous pyridine (15 ml), *tert*-butylphosphonic dichloride[6] (**2**, 0.44 g) was added. The mixture was kept at 100° for 18 h, and then cooled and poured into ice–water with stirring. The solution was extracted with chloroform (4 × 50 ml), and the combined extracts were concentrated to dryness with the addition of toluene (3 × 20 ml). The residue was fractionated by t.l.c. (solvent *A*) to give **5a** (0.67 g, 55.4%), R_F 0.32 (solvent *B*), and **5b** (0.37 g, 30.6%), R_F 0.21 (solvent *B*).

Compound **5a** had $[\alpha]_D^{20}$ +7° (*c* 1, chloroform). N.m.r. data· δ 7–7.8 (H-6, Tr), 5.77 ($J_{1',2'}$ <1 Hz, H-1′), 5.59 ($J_{5,6}$ 8 Hz, H-5), 4.86–5.40 (H-2′,3′), 4.52 (H-4′), 3.36–3.60 (H-5′,5′), and 1.21 ($J_{H,P}$ 18 Hz, t-Bu).

Anal. Calc. for $C_{32}H_{33}N_2O_7P \cdot 0.5CHCl_3$: C, 60.25; H, 5.21; P, 4.78. Found: C, 59.52; H, 5.17; P, 4.76.

Compound **5b** had $[\alpha]_D^{20}$ −5° (*c* 1, chloroform). N.m.r. data: δ 7–7.8 (H-6, Tr), 5.80 ($J_{1',2'}$ 2 Hz, H-1′), 5.52 ($J_{5,6}$ 8 Hz, H-5), 5.16–5.44 (H-2′,3′), 4.27 (H-4′), 3.32–3.60 (H-5′,5′), and 1.30 ($J_{H,P}$ 18 Hz, t-Bu).

Anal. Found: C, 60.79; H, 5.38; P, 4.96.

Compound **5a** (0.64 g) was treated with 90% trifluoroacetic acid (1.6 ml) at 20–22° for 5 min. After the evaporation of the solvent, the residue was purified by t.l.c. (solvent *A*) to give **3a** (0.35 g, 95%), R_F 0.58, $[\alpha]_D^{20}$ −16° (*c* 1, methanol). Mass spectrum: *m/e* 346 (M^+), 315 $(M-CH_2OH)^+$, 235 $(M-B)^+$, 217 $(M-B-H_2O)^+$, 179 $(M-CH_2OH-BuPO_3)^+$, 139 $(BuPO_3H_3)^+$, 113 $(B+2H)^+$, 112 $(B+H)^+$, and 57 $(Bu)^+$.

Anal. Calc. for $C_{13}H_{19}N_2O_7P \cdot 0.2CHCl_3$: C, 42.83; H, 5.23; P, 8.37. Found: C, 42.93; H, 5.30; P, 8.79.

Likewise, **5b** gave **3b** (70%), R_F 0.38 (solvent *A*), $[\alpha]_D$ −22° (*c* 1, methanol). Mass spectrum: *m/e* 346 $(M)^+$, 315 $(M-CH_2OH)^+$, 235 $(M-B)^+$, 217 $(M-B-H_2O)^+$, 179 $(M-CH_2OH-BuPO_3H_3)^+$, 113 $(B+2H)^+$, 112 $(B+H)^+$, and 57 $(Bu)^+$.

Anal. Calc. for $C_{13}H_{19}N_2O_7P \cdot 0.5CHCl_3$: C, 39.94; H, 4.84; P, 7.63. Found: C, 40.02; H, 5.00; P, 7.34.

(*b*) To a solution of uridine (**1**, 0.5 g) in anhydrous pyridine (8 ml) was added **2** (0.43 g). The resulting mixture was kept at 100° for 18 h. The solvent was evaporated with the addition of toluene (3 × 20 ml), and the residue was fractionated by t.l.c. (solvent *B*) to give **3a** (0.14 g, 19.7%), **3b** (0.14 g, 19.7%), and **1** (0.23 g, 46%).

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