contacts—the suggested reason for the "light stability" of solid 1,4-naphthoquinone (I)—we are now reinvestigating the crystal structure of I.

Experimental Section

Infrared spectra were recorded (in KBr) on a Perkin-Elmer 221 spectrophotometer. Mass spectra were obtained on an M.S.9 mass spectrometer. Melting points were determined on a Gallenkamp (design no. 889339) apparatus and are uncorrected.

Photodimerization of 1,4-Naphthoquinone. i. *anti* Dimer (IIa).—A solution of I (1 g) in acetic anhydride (12.5 ml) was sealed in a Pyrex test tube and irradiated with a medium-pressure ultraviolet lamp at room temperature for 2 weeks. The off-white precipitate (0.2 g) crystallized from glacial acetic acid in colorless plates melting with decomposition at 246–248° (lit.[1] mp 244–248°). The mass of molecular ion was *m/e* 316.

ii. ***syn* Dimer (IIb). a.**—The off-white precipitate (2 g), obtained in the previous experiment, was refluxed for 18 min in methanol (50 ml). The filtrate was concentrated (15 ml), allowed to stand for 1 hr at room temperature, filtered, concentrated (8 ml), and cooled to 0°, whereupon straw-colored crystals of IIb were obtained. Recrystallization from methanol yielded off-white needles (0.005 g), melting with decomposition at 235–237°.

Anal. Calcd for $C_{20}H_{12}O_4$: C, 75.92; H, 3.9; O, 20.26. Found: C, 75.9; H, 3.9; O, 20.2.

The mass of molecular ion was *m/e* 316.

b.—A thin layer of I (1 g), recrystallized from petroleum ether (bp 50–70°), was placed between two sealed window glass plates of 1-cm thickness and placed in direct sunlight for a period of 6 weeks. The set-up was turned over weekly. The pale brown material was refluxed for 15 min in ether, the mixture filtered, and the insoluble photoproduct (IIb) washed with ether (0.15 g).

1,4,5,8-Tetraacetoxy-2,3,6,7-dibenzobiphenylene (V). a. From the *anti* Dimer (IIa).—A mixture of IIa (0.03 g), acetic anhydride (10 ml), and anhydrous sodium acetate (0.1 g) was refluxed for 4 hr and cooled to room temperature. The crystalline product (V) was filtered off, washed successively with acetic acid and water, dried, and recrystallized from acetic anhydride. Yellow needles were obtained: yield, 0.041 g (90%); mp 358–360° (lit.[2] mp 358–360°).

b. From the *syn* Dimer (IIb).—Compound IIb (0.03 g) was refluxed with a mixture of acetic anhydride (10 ml) and anhydrous as above (0.041 g).

Ketonization of 1,4,5,8-Tetrahydroxy-2,3,6,7-dibenzobiphenylene (III).—Compound III (0.025 g) was dissolved in cold concentrated sulfuric acid (2 ml) and the reddish solution poured into ice water (20 ml). The mixture was filtered and the grayish precipitate washed with water. Recrystallization from glacial acetic acid led to colorless plates of the *anti* dimer (IIa) (0.02 g).

Sulfuric Acid Hydrolyses of 1,4,5,8-Tetraacetoxy-2,3,6,7-dibenzobiphenylene (V).—Compound IV (0.05 g) was dissolved in cold concentrated sulfuric acid (3 ml) and the reddish solution poured into ice water (25 ml). The grayish precipitate was treated as above (0.044 g, 88% of IIa).

Baeyer–Villiger Oxidation of the *anti* Dimer (IIa).—Trifluoroacetic anhydride (0.98 ml) was added slowly to an ice-cooled stirred dispersion of 85% hydrogen peroxide (0.17 ml) in methylene chloride (7 ml). This solution was slowly added to a vigorously stirred suspension of anhydrous disodium hydrogen phosphate (3 g) and the *anti* dimer (IIa) (0.1 g) in methylene chloride (17 ml). The mixture was refluxed with stirring for 30 hr and cooled. The undissolved material was filtered off and washed with water, whereby the tetralactone (VI) was obtained: yield, 0.059 g; mp 350°, ν_{max}^{KBR} 1765 (s), 1592 (w), 1485 (s), 1451 (sh), 1448 (w), 1266 (s), 1250 (s), 1177 (s), 1126 (m), 1100 (m), 1033 (m), 981 (w), 969 (w), 945 (w), 905 (m), 875 (m), 776 (s), 741 (m) cm^{-1}.

Compound VI was converted into *cis,trans,cis*-tetracarbomethoxycyclobutane (VII) by refluxing VI (0.1 g) for 12 hr in methanol (6 ml) containing concentrated sulfuric acid (0.1 ml). The cooled solution was poured into cold water (10 ml) and the precipitated product extracted with ether. The ethereal solution was washed with saturated sodium bicarbonate and water and dried ($MgSO_4$). Ether was removed on a water bath. The product was recrystallized from benzene to give colorless crystals, mp 144° (lit.[3] mp 145°). The infrared spectrum was identical with that of an authentic sample of VII.

Isomerization of the *syn* Dimer (IIb) to the *anti* Dimer (IIa).—Compound IIb (0.02 g) was dissolved in cold concentrated sulfuric acid (1.5 ml). Th solution was poured into ice water (20 ml) and a grayish precipitate was obtained. Recrystallization from acetic acid produced IIa in colorless plates (0.018 g).

Registry No.—IIa, 14734-19-1; IIb, 14734-20-4.

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Nucleosides. XLVI. Selectively Methylated Derivatives of Spongouridine

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In view of the biological activity recently found in nucleosides containing an arabino moiety,[2] it was of interest to prepare partially methylated derivatives of 1-β-D-arabinofuranosyluracil (spongouridine). The present paper reports the synthesis and properties of two dimethylated nucleosides, 1-(2-*O*-methyl-β-D-arabinofuranosyl)-3-methyluracil (IV) and 1-(3-*O*-methyl-β-D-arabinofuranosyl)-3-methyluracil (IX).

The synthesis of IV utilized the 3′,5′-di-*O*-trityl nucleoside II, which had been prepared in this laboratory by two routes,[3] namely, tritylation of the 5′-*O*-trityl nucleoside I to yield IIa and cleavage of the ditrityl anhydro nucleoside V to give IIb. Although the structure of IIb had been unequivocally established, there remained some incertitude regarding the structure of IIa. The assignment of a 3′,5′-di-*O*-trityl structure to IIa was based upon its physical properties, which were similar to those of IIb. Melting points, however, were over a 15° range, and infrared spectra, although identical, possessed broad peaks. Furthermore, it has been our experience that infrared spectra of some tritylated nucleosides of different structure are similar. Therefore, the possibility that the 2′,5′- and 3′,5′-di-*O*-trityl compounds would possess nearly identical properties could not be discounted. Fortunately, methylation of IIa by the method of Kuhn and coworkers[4] gave, after detritylation, colorless crystals which were shown to have a 2′-*O*-methyl structure IV, as described below, thus confirming the previously assigned 3′,5′-di-*O*-trityl structure for IIa.

The 3′-*O*-methyl isomer of IV, compound IX, was prepared in crystalline form from 2,2′-anhydro-1-β-D-arabinofuranosyluracil (VI) by the methylation procedure of Kuhn, *et al.*[4] It is of interest to note that

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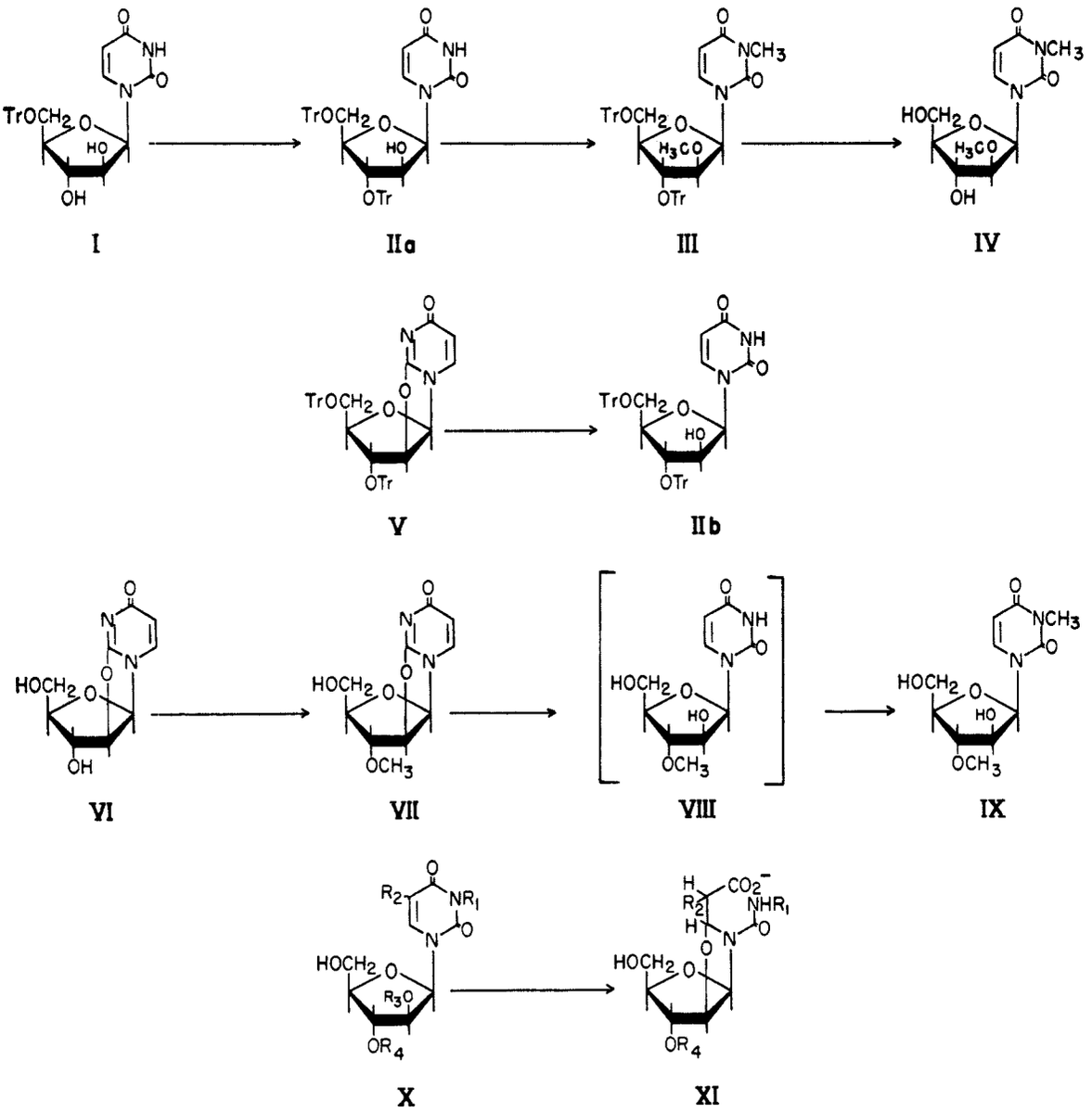

the primary site of methylation appears to be the secondary 3′ position rather than the primary 5′ position. In this connection it may be noted that in the permethylation of spongouridine by the same procedure,[4] nmr spectra of aliquots removed during the course of the reaction exhibited the triplet characteristic of the 5′-hydroxyl group after methylation at the 2′, 3′, and 3 positions was complete. It is probable that methylation of O-3′ in VI occurred prior to cleavage of the 2,2′-anhydro bond to give VII. The splitting of this bond through the action of silver hydroxide and a small amount of moisture present in the reaction mixture probably gave intermediate VIII, which was then methylated at N-3 to yield IX.

The position of the *O*-methyl group of IX was established by nmr studies. In DMSO-d_6 IX exhibited a doublet and a triplet, which disappeared upon the addition of D_2O and must have been due to secondary (2′ or 3′) hydroxyl and primary (5′) hydroxyl groups, respectively. In addition, a multiplet at τ 5.80 became a quartet. Therefore, this quartet must have been due to a proton on the carbon atom bearing the free hydroxyl. Field sweep decoupling from the center of the quartet (ν = +104 Hz) collapsed the H-1′ doublet to a singlet. Hence, the τ 5.80 peak is H-2′ ($J_{1',2'} \sim 4.2$ Hz and $J_{2',3'} \sim 2.2$ Hz). This proves the *O*-methyl group in IX is on C-3′.

The nmr spectrum of IV was complicated by the fact that the signal for H–3′ was partially buried under the signal for H-2′. Nevertheless, in DMSO-d_6 two OH peaks (τ 4.44 and 5.03) were clearly visible. These disappeared upon the addition of D_2O. Compound IV, as well as IX, consumed no periodate, indicating the presence of a methoxyl at either C-2′ or C-3′. Since the methoxyl group in IX had been established at C-3′, the substituent on the sugar moiety of IV had to be at C-2′.

Both IV and IX give signals for two methyl groups. In each case the *N*-methyl peak was assigned to the higher field signal (τ 6.82) by comparison with the *N*-methyl peak of 3-methyluridine (τ 6.80). The chemical shifts of the *O*-methyl peaks in IV and IX are consistent with their assigned positions. The methoxyl signal (τ 6.73) for the 2′-*O*-methyl compound IV occurs 0.10 ppm to higher field than the methoxyl signal for 3′-*O*-methyl compound (IX). This is consistent

with the findings of Cushley, *et al.*,[5] that the C-2′ acetyl signal in acetylated furanosyl pyrimidine nucleosides is shifted to higher field than the C-3′ or C-5′ acetyl signals when the C-1′ and C-2′ substituents are *cis*. This diamagnetic shift was attributed to the anisotropic effect of the 5,6 double bond. Since the C-1′, C-2′ substituents in IV are also *cis*, one would expect the C-2′ methoxyl signal in IV to be significantly more shielded than the C-3′ methoxyl in IX. It appears likely therefore that the method[5] for establishing the anomeric configuration of acetylated pyrimidine nucleosides is equally applicable to their methylated counterparts. The H-2′ signal in IV, established by a field sweep decoupling experiment from H-1′ ($\nu = -134$ Hz), occurs 0.22 ppm to higher field than H-2′ in IX and 0.19 ppm to higher field than H-2′ in spongouridine in accord with the greater shielding effect of methoxyl *vs.* hydroxyl.

It is of interest to note that the anomeric signal (H-1′) in IV is found 0.23 ppm downfield from H-1′ in IX, and 0.18 ppm downfield from H-1′ in spongouridine apparently due to deshielding by the C-2′ methoxyl group.

The behavior of IV and IX in aqueous base was consistent with the structures assigned. IV was relatively stable in NaOH (0.1 *N*) and its ultraviolet absorption spectrum remained essentially unaltered after 1 hr at 25°. Compound IX, on the other hand, exhibited marked instability in NaOH (0.1 *N*) with the rapid loss of selective absorption in the ultraviolet region ($t_{1/2}$ = 22 min at 25°). The reactivity of IX is readily explained by the presence of a 2′ hydroxyl group in an "up" (arabino) position. The reactivity of such a structure is consistent with the findings recently reported[6] for the reaction of 1-(β-D-arabinofuranosyl)-5-fluoro-3-methyluracil (X, R_1 = CH_3, R_2 = F, R_3 and R_4 = H) in aqueous base. Treatment of this compound with NaOH (0.1 *N*) resulted in attack by the 2′-hydroxy anion on C-6 of the uracil moiety to form a 6,2′-anhydro bridge with concomitant cleavage of the N_3–C_4 bond to give the open-chain ureide structure XI (R_1 = CH_3, R_4 = H, R_2 = F). It is probable that the product formed upon treating IX with base had a similar ureide structure, namely, XI (R_1 and R_4 = CH_3, R_2 = H).

The addition of base to a solution of IX causes an immediate bathochromic shift of the maximum of 5 mμ (261 to 266 mμ). This shift is probably due to the localization of the π electrons of the 5,6-double bond caused by polarization due to the proximity of the *O*-2′ anion.

Experimental Section

Nmr spectra were recorded on a Varian A-60 spectrometer equipped with a spin decoupler (Varian, Model V-6058A). Melting points were determined by the capillary method and are corrected. Microanalyses were made by the Spang Microanalytical Laboratories, Ann Arbor, Mich.

1-(2-*O*-Methyl-β-D-arabinofuranosyl)-3-methyluracil (IV).—The preparation of 1-(3,5-di-*O*-trityl-β-D-arabinofuranosyl)uracil (II) from 1-(5-*O*-trityl-β-D-arabinofuranosyl)uracil (I) was carried out as previously described[3] except that II was separated from unreacted I on alumina (Bio-Rad, AG 7), using ethanol–ethyl acetate as the eluant. Compound II (0.40 g, 0.55 mmole) in dimethylformamide (10 ml) was stirred for 22 hr at 23–25° with methyl iodide (0.80 g, 5.6 mmoles) and silver oxide (0.35 g, 1.5 mmole). Compound III was obtained as a colorless solid (0.42 g). Without further purification III (0.20 g), dissolved in ether (10 ml), was treated with anhydrous ethereal HCl (20 ml, 50% saturated). Colorless crystals (0.07 g, 96%) were obtained, which upon recrystallization from ethanol gave needles, mp 198–200°, $[\alpha]^{25}D$ +127° (*c* 0.2, EtOH). The proton nmr spectrum determined in DMSO-d_6 consisted of H-6 (τ 2.28, doublet, $J_{5,6}$ = 8.0 Hz), H-1′ (τ 3.80, doublet, $J_{1',2'}$ = 5.1 Hz), H-5 (τ 4.26, doublet), OH (C-3′) (τ 4.44, doublet, $J_{OH,H\text{-}3'}$ ~4.5 Hz), OH(C-5′) (τ ~5.03, broad peak), H-2′, H-3′ (τ ~6.07, multiplet), H-4′, H-5′, H-5′ (τ ~6.34, narrow multiplet), –O–CH_3 (τ 6.73, singlet), –N–CH_3 (τ 6.82, singlet).

Anal. Calcd for $C_{11}H_{16}N_2O_6$: C, 48.52; H, 5.92; N, 10.29. Found: C, 48.68; H, 5.96; N, 10.31.

1-(3-*O*-Methyl-β-D-arabinofuranosyl)-3-methyluracil (IX).—The reaction of 2,2′-anhydro-1-β-D-arabinofuranosyluracil (VI, 0.23 g, 1.0 mmole) with methyl iodide (0.90 g, 6.3 mmoles) and silver oxide (0.46 g, 2.0 mmoles) in dimethylformamide (5 ml) for 69 hr with stirring gave, after crystallization from ethanol, 0.04 g (15%), of colorless prisms, mp 127–131°, $[\alpha]^{25}D$ +130° (*c*, 0.2, EtOH). The proton spectrum determined in DMSO-d_6 consisted of H-6 (τ 2.31, doublet, $J_{5,6}$ = 8.0 Hz), H-1′ (τ 4.03, doublet, $J_{1',2'}$ = 4.2 Hz), H-5 (τ 4.21, doublet), OH (C-2′) (τ 4.38, doublet, $J_{OH,H\text{-}2'}$ = 5.0 Hz), OH (C-5′) (τ 4.92, triplet, splitting of 5.2 Hz), H-2′ (τ ~5.80, multiplet), H-3′, H-4′, H-5′, H-5′ (τ ~6.30, multiplet), –O–CH_3 (τ 6.63, singlet), –N–CH_3 (τ 6.82 singlet).

Anal. Calcd for $C_{11}H_{16}N_2O_6$: C, 48.52; H, 5.92; N, 10.29. Found: C, 48.52; H, 5.85; N, 10.25.

Registry No.—IV, 15040-83-2; IX, 15040-84-3.

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Synthesis and Catalytic Hydrogenation of 3α,19-Dihydroxycholest-5-ene and Its Derivatives[1]

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Considerable progress has been made recently in the synthesis of 19-substituted steroids,[3-5] especially as intermediates for synthesis of 19-nor steroids. However, 19-substituted steroids having a 3α substituent have not yet been reported. The present Note reports a convenient synthesis of 3α,19-dihydroxycholest-5-ene and its derivatives, together with the catalytic hydrogenation of the above compounds.[6]

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