determined by NMR and by capillary VPC analysis (80 °C). Ratios and characteristic NMR data are presented in Table II.

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**Registry No.** (*E*)-Dimethyl(1,1-dimethylethyl)[(1-methoxy-1-propenyl)oxy]silane, 84784-58-7; (*Z*)-dimethyl(1,1-dimethylethyl)[(1-methoxy-1-propenyl)oxy]silane, 84784-64-5; (*E*)-dimethyl(1,1-dimethylethyl)[(1-ethoxy-1-propenyl)oxy]silane, 89043-55-0; (*Z*)-dimethyl(1,1-dimethylethyl)[(1-ethoxy-1-propenyl)oxy]silane, 73967-98-3; (*E*)-dimethyl(1,1-dimethylethyl)[[1-(1-methylethoxy)-1-propenyl]oxy]silane, 89043-56-1; (*Z*)-dimethyl(1,1-dimethylethyl)[[1-(1-methylethoxy)-1-propenyl]oxy]silane, 89043-57-2; (*E*)-dimethyl[[1-(1,1-dimethylethoxy)-1-propenyl]oxy](1,1-dimethylethyl)silane, 89043-58-3; (*Z*)-dimethyl[[1-(1,1-dimethylethoxy)-1-propenyl]oxy](1,1-dimethylethyl)silane, 89043-59-4; (*E*)-dimethyl(1,1-dimethylethyl)[[3-methyl-1-(1-methylethoxy)-1-buten-1-yl]oxy]silane, 89043-60-7; (*Z*)-dimethyl(1,1-dimethylethyl)[[3-methyl-1-(1-methylethoxy)-1-buten-1-yl]oxy]silane, 89043-61-8; (*E*)-(1,1-dimethylethyl)diphenyl[[1-(1-methylethoxy)-1-propenyl]oxy]silane, 89043-62-9; (*Z*)-(1,1-dimethylethyl)diphenyl[[1-(1-methylethoxy)-1-propenyl]oxy]silane, 89043-63-0; (*E*)-[[1-(1-methylethoxy)-1-propenyl]oxy]triethylsilane, 89043-64-1; (*Z*)-[[1-(1-methylethoxy)-1-propenyl]oxy]triethylsilane, 89043-65-2; diisopropylethylammonium perchlorate, 16473-89-5; perchloric acid, 7601-90-3; diisopropylethylamine, 7087-68-5.

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## Reaction of Formaldehyde with Nucleosides: Addition to 2′,3′,5′-Triacetyl 9-β-D-Arabinofuranosyladenine

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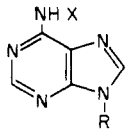
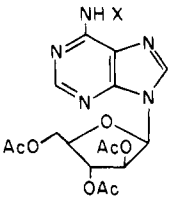
The reactions between nucleosides and formaldehyde have been extensively investigated.[1-3] Since the initial discovery that this reaction occurs with amino groups in both RNA and DNA, it has been used as a probe for undisrupted secondary structure in nucleic acids, as these regions are resistant to attack by formaldehyde.[4] Controversy exists regarding the nature of the reaction products and the functional group(s) that react with formaldehyde. These reactions have been generally carried out in aqueous solution, and since the products are labile and difficult to purify, they have not been well characterized. Such diverse products as Schiff bases,[5] monomethylol[6] and dimethylol[7] derivatives, and dimeric methylene compounds[8] have been suggested. Spectral[9] and kinetic[9a,10] evidence has been presented for the product from adenosine, the most studied nucleoside, suggestive of the $N^6$-hydroxymethyl structure **1**. It is generally agreed[2] that



1, X = $CH_2OH$
2, X = $CH_2OEt$



3, X = H
4, X = $CH_2OCH_2OH$
5, X = $CH_2OCH_2OAc$
6, X = $CH_2OCH_2OCO$-*t*-Bu

this product would be favored at equilibrium over the stronger bases that result from reaction at the N-1, N-3, or N-7 positions. It was shown more recently[11] that 2′,3′-*O*-isoprolylideneadenosine when reacted with formaldehyde in refluxing ethanol gave the *N*-ethoxymethyl derivative **2**. In connection with our interest in low-melting and lipophilic derivatives of adenosinearabinoside (ara-A) which may have increased skin permeability,[12] we studied the reaction of ara-A derivatives with formaldehyde. In this paper we present spectral evidence for the structure of a product isolated for the first time, in a reaction of an adenine pentose derivative with formaldehyde in aqueous solution.

2′,3′,5′-Triacetyl ara-A[13] (**3**) chosen for its solubility in nonaqueous solvents was readily prepared without significant formation of $N^6$-acetylated product by reacting ara-A in excess acetic anhydride and pyridine at 0 °C. Initial experiments showed the formation of a mixture of several compounds when **3** reacted with formaldehyde. However, it was possible to obtain one major product if the reaction was carried out in 5 M aqueous formaldehyde at 0 °C. This product could be extracted into dichloromethane. A $^1H$ NMR spectrum of this unstable adduct **4** in deuteriochloroform showed two new peaks, one at δ 5.5, which overlapped with the multiplet due to 2′-H and 3′-H (at δ 5.3–5.65) and the other at δ 5.15. The integrated area of the complex accounted for six protons, suggesting that the product may not be a monomethylol adduct.[9a] Other changes in the spectrum compared to that of **3** were the downfield shift of the anomeric doublet from δ 6.56 to 6.63 and of $C_2$-H and $C_8$-H each downfield by 0.13 ppm.

To determine the number and position of the methylene units, the adduct was acetylated with acetic anhydride and pyridine at 0 °C. The NMR spectrum[14] of the thin-layer chromatographically purified product showed only one additional acetate group. The methylene resonance at δ 5.15 in the $^1H$ NMR spectrum of **4** moved downfield and merged with the other methylene among the 2′-H and 3′-H multiplet on acetylation. The only other additional feature observed in the $^1H$ NMR spectrum of **5** was a broad triplet for one proton (exchangeable with $D_2O$) at δ 7.7 assigned to $NHCH_2$. Two methylene carbons at δ 72.23 and 88.03 assigned[14] to $NHCH_2O$ and $OCH_2O$, respectively, were present in the $^{13}C$ NMR, consistent with structure **5** for

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this acetate ester of the adduct 4. A molecular ion at $m/e$ 495 in agreement with a molecular formula of $C_{20}H_{25}N_5O_{10}$ and a UV maximum at 263 nm ($\epsilon$ 14610) in ethanol in accordance with monoalkyl substitution[9] on $N^6$ support the above structure assignment.

Further confirmation of the *N*-(hydroxymethoxy)methyl structure for the adduct 4 was provided by the off-resonance decoupled $^{13}C$ NMR spectrum of the pivalate ester 6, which showed methylene triplets at $\delta$ 70.32 and 86.34.

Prolonging reaction at 0 °C or conducting the reaction at room temperature resulted in the conversion of this initially formed mono *N*-(hydroxymethoxy)methyl derivative to another product, presumably a diadduct. Proper characterization of this adduct proved to be difficult because of its instability.

Stable monomethylol derivatives[15] are formed in the reaction of formaldehyde with amides, imides, and pyrimidine bases, where intramolecular hydrogen bonding to the carbonyl oxygen stabilize such adducts. The formation of a *N*-(hydroxymethoxy)methyl adduct in the present case may, likewise, be attributed to the stabilization by intramolecular hydrogen bonding involving either the amino or hydroxyl hydrogen in a six-membered cyclic arrangement.

## Experimental Section

The following spectrometers were used: IR, Beckman AccuLab 4; $^1H$ NMR, Varian T-60; $^{13}C$ NMR, Varian FT-80A; UV, Cary 14; mass spectrum, Riber R10-10 interphased with PDP-8A computer. Chemical shifts are reported in parts per million relative to tetramethylsilane as internal reference. Column chromatography was performed on silica gel 60 (E. Merck). Precoated silica gel 60 F254 (E. Merck) or Analtech GHLF plates were used for thin-layer chromatography.

**2′,3′,5′-Triacetyl 6-[[(Hydroxymethoxy)methyl]amino]-purine-9-β-D-arabinoside (4).** 2′,3′,5′-Triacetyl arabinosyladenine[13] (200 mg) was dissolved in ice-cold 5 M aqueous formaldehyde (5 mL) and kept stirred at 0–4 °C. The reaction was monitored by TLC [silica gel, dichloromethane–acetone (1:1)]. When most of the starting material had disappeared (after 28 h), the reaction mixture was extracted with dichloromethane and the extract was washed twice with water. After the extract was dried ($Na_2SO_4$), the solvent was removed to furnish a thick glue (0.28 g). The product was contaminated with some polymeric formaldehyde. Attempted purification by chromatography resulted in its decomposition: $^1H$ NMR ($CDCl_3$) $\delta$ 1.96 (s, 3 H), 2.13 and 2.16 (s, 3 H each), 4.2–4.6 (m, 3 H), 5.1–5.7 (m, 6 H, $NCH_2OCH_2$ and 2′-H and 3′-H), 6.03 (d, $J$ = 4 Hz, 1 H), 8.11 (s, 1 H), 8.46 (s, 1 H). (Polymeric formaldehyde peaks were at 4.8–5.0).

**2″,3″,5″-Triacetyl 6-[(3′-Acetoxy-2′-oxapropyl)amino]-purine-9-β-D-arabinoside (5).** The above (hydroxymethoxy)-methyl derivative 4 (280 mg) was dissolved in ice-cold dry pyridine (2.5 mL), and acetic anhydride (2.5 mL) was added with stirring. After 17 h at 0–4 °C, the excess acetylating agent was destroyed with crushed ice. The solvents were distilled off in vacuum at room temperature. The residue was taken in water and washed twice with ether. The ether washings were discarded. The aqueous layer was then extracted with dichloromethane. The dichloromethane extract was washed once with water and then with brine. After drying ($Na_2SO_4$), the organic extract was evaporated to yield an oily residue (285 mg) which on preparative thin-layer chromatography (silica gel, ethyl acetate) afforded the pure ester 5 (110 mg) as a thick oil: $^1H$ NMR ($CDCl_3$) $\delta$ 1.93 (s, 3 H), 2.08, 2.15, 2.18 (s, 3 H each), 4.2–4.6 (m, 3 H), 5.3–5.7 (m, 6 H), 6.63 (d, 1 H, $J$ = 4 Hz), 7.7 (br t, 1 H, $J$ = 6 Hz), 8.11 (s, 1 H), 8.45 (s, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 21.42, 21.57, 21.83, 22.13, 64.13, 72.23, 75.95, 77.0, 81.14, 84.32, 88.03, 120.51, 141.0, 150.86, 154.35, 155.39, 169.77, 170.72, 171.61, 171.84; IR (film) 1738 $cm^{-1}$ (C=O); UV max (EtOH) 263 nm ($\epsilon$ 14610); mass spectrum, $m/e$ 495 ($M^+$), 465, 452, 436, 392 ($M^+ - CH_2OCH_2OCOCH_3$); chemical ionization ($NH_3$) 496 $(M + 1)^+$.

**2″,3″,5″-Triacetyl 6-[(3′-Pivaloxy-2′oxapropyl)amino]-purine-9-β-D-arabinoside (6).** To an ice-cold solution of the 6-[[(hydroxymethoxy)methyl]amino]purine 4 (1 g) in dichloromethane (40 mL) were added dry pyridine (5 mL) and pivalic anhydride (5 mL), and the reaction mixture was kept stirring at 0–4 °C for 48 h. After stirring with methanol (5 mL) for 1 h, the solvents were evaporated off in vacuum at room temperature. The residue was diluted with water and extracted with dichloromethane. The residue (1.54 g) obtained on washing, drying ($Na_2SO_4$), and evaporation of the solvent was chromatographed on silica gel. Elution with dichloromethane–ethyl acetate (1:1) furnished the pure pivalate ester 6 (152 mg) as a hygroscopic foam: $^1H$ NMR ($CDCl_3$) $\delta$ 1.23 (s, 9 H), 1.93, 2.15, 2.16 (s, 3 H each) 4.2–4.6 (m, 3 H), 5.4–5.65 (m, 6 H), 6.65 (d, 1 H, $J$ = 4 Hz), 7.4 (br t, 1 H, $J$ = 7 Hz), 8.1 (s, 1 H), 8.46 (s, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.59 (q), 20.0 (q), 26.3 (q), 38.16 (s), 62.39 (t), 70.32 (t), 74.18 (d), 75.27 (d), 79.33 (d), 82.49 (d), 86.34 (t), 118.98 (s), 139.32 (d), 149.19 (s), 152.43 (d), 153.64 (s), 167.9 (s), 168.88 (s), 169.77 (s), 177.47 (s); IR (KBr) 1745 (C=O); UV max (EtOH) 263 nm ($\epsilon$ 18660); mass spectrum, chemical ionization ($NH_3$) $m/e$ 538, $(M + 1)^+$.

**Acknowledgment.** Helpful discussions with Prof. R. G. Carlson, Department of Chemistry, University of Kansas, is gratefully acknowledged.

**Registry No.** 3, 15830-52-1; 4, 89178-18-7; 5, 89178-19-8; 6, 89178-20-1; formaldehyde, 50-00-0.

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## Novel Base-Induced Double Epimerization of Ethyl 2-*endo*,3-*exo*-3-Nitro-7-oxabicyclo[2.2.1]heptane-2-carboxylate

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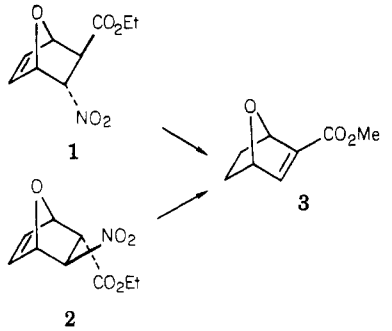
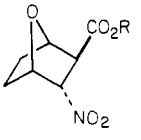
The racemic Diels–Alder adducts 1 and 2 obtained from furan and ethyl β-nitroacrylate[1] represent useful intermediates for the preparation of (+)-methyl (1*R*,4*S*)-7-oxabicyclo[2.2.1]hept-2-ene-2-carboxylate (3), a key intermediate in our recently completed synthesis of (+)-compactin.[2] In this connection we have shown that ester 4,




4, R = Et
5, R = H

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