teration, whereas the other (assigned to the β protons) collapsed to a singlet.

Registry No.—**7**, 18703-68-9; **8**, 30689-46-4; **9**, 30689-47-5; **11**, 30689-48-6; **12**, 30689-49-7; **13**, 30689-50-0; **14**, 30439-20-4; *cis*-**15**, 30689-52-2; *trans*-**15**, 30689-53-3; *cis*-**16**, 30689-54-4; *trans*-**16**, 30689-55-5; **17**, 30689-56-6; *trans*-**18**, 30689-57-7; *trans*-**19**, 30689-58-8; **20**, 30689-59-9; **22**, 20841-66-1; **23**, 30689-61-3; **24**, 24132-27-2; **25**, 30689-63-5; (+)-**26**, 30412-89-6; **28**, 30689-65-7; **29**, 30689-66-8; **30**, 30758-78-2; **31**, 30758-79-3; (+)-**32**, 30412-92-1; **33**, 30689-68-0; **34**, 30758-80-6; **37**, 30689-69-1; **38**, 30689-70-4.

Nucleosides. XIII. The Concurrent Introduction of Two Different Blocking Groups Into Some Ribonucleosides[1a,b]

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The reaction of adenosine, cytidine, and guanosine with *p*-nitrobenzaldehyde and ethyl orthoformate in the presence of trifluoroacetic acid in dimethylformamide affords the corresponding *N*-(α-ethoxy-*p*-nitrobenzyl)-2′,3′-*O*-ethoxymethylene derivatives **1a**, **3b**, and **4**, respectively, in excellent yields. Benzoylation of **1a** in pyridine effected, as well, concurrent elimination of the elements of ethanol to give the 5′-*O*-benzoyl-*N*-(*p*-nitro)benzylidene derivative **2**. On the other hand, uridine and *p*-nitrobenzaldehyde in the presence of *p*-toluenesulfonic acid gave 2′,3′-*O*-*p*-nitrobenzylideneuridine (**5a**). Possible reaction paths for these transformations, which constitute useful procedures for the simultaneous introduction of two different blocking groups into certain nucleosides, are discussed.

Several useful procedures have been developed for masking the cis glycol system of a ribonucleoside by condensation with a suitable aldehyde or ketone under acid catalysis. Unfavorable equilibria that arise in certain cases of acetal and ketal formation can be overcome through the use of ketals[2] or ethyl orthoformate.[3,4] The latter has also found application in effecting acetal formation with benzaldehyde and derivatives thereof that carry a para substituent capable of increasing electron density at the carbonyl function by resonance (R^+) effects.[5] By contrast, 2′,3′-*O*-benzylidene nucleosides that carry a para (R^-) substituent are, to our knowledge, unknown. The present communication describes the results of an attempt to prepare 2′,3′-*O*-(*p*-nitrobenzylidene)adenosine, which was required in an unrelated study, and which led instead to a novel and useful procedure for the concurrent introduction of two different blocking groups into certain nucleosides.

The reaction of adenosine and excess *p*-nitrobenzaldehyde in a mixture of dimethylformamide (DMF) and ethyl orthoformate containing trifluoroacetic acid gave a chromatographically homogeneous solid (90% yield) to which the structure N^6-(α-ethoxy-*p*-nitrobenzyl)-2′,3′-*O*-ethoxymethyleneadenosine (**1a**) was assigned on the basis of chemical and spectral (ir, uv, and nmr) evidence along with both elemental and ethoxyl analyses. The absence of a free amino group in the structure, which was evident from its ir spectrum ($CHCl_3$), was confirmed by the failure of **1a** to react with dimethylformamide dimethyl acetal.[6] The hydrolysis of **1a** with 88% formic acid at room temperature for 5 min gave *p*-nitrobenzaldehyde and adenosine 2′(3′)-formate. The latter was shown to be identical with the product of formic acid hydrolysis[7] of 2′,3′-*O*-ethoxymethyleneadenosine (**1b**).[8]

The benzoylation of **1a** in pyridine at room temperature promoted the elimination of the elements of ethanol from the N,O mixed acetal in addition to effecting esterification of the primary (C′-5) alcohol residue and thereby provided the Schiff base **2**.

Cytidine, like adenosine, gave the corresponding N,O mixed acetal **3b** in high yield. Surprisingly, the yield of the corresponding derivative of cytosine **3a** is significantly lower (35%) under the same conditions with 55% of the heterocycle being recovered unchanged. Acid hydrolysis of **3a** and **3b** afforded *p*-nitrobenzaldehyde and cytosine [or cytidine-2′(3′)-formate]. The latter was easily hydrolyzed in alkali to cytidine.

The same reaction applied to guanosine gave a (tlc) chromatographically homogeneous solid which, on acid hydrolysis, yielded *p*-nitrobenzaldehyde and guanosine 2′(3′)-formate as the only detectable products. Accordingly, the structure N^4-(α-ethoxy-*p*-nitrobenzyl)-2′,3′-*O*-ethoxymethyleneguanosine (**4**) was assigned to the product. Whereas this assignment is supported by spectral (ir, uv) data, all attempts to obtain an acceptable elemental analysis have been unsuccessful.

The importance of ethyl orthoformate to the formation of the mixed acetals is indicated by the fact that adenosine is recovered unchanged when the ortho ester is omitted from the reaction mixture. These observa-

(1) (a) This investigation was supported in part by U. S. Public Health Service Research Grant No. FR 5529 from the National Cancer Institute and in part by an institutional grant to the Detroit Institute of Cancer Research Division of the Michigan Cancer Foundation from the United Foundation of Greater Detroit. (b) Presented in part at the 158th National Meeting of the American Chemical Society, New York, N. Y., Sept 1969, Abstract CARB 16. (c) To whom correspondence should be addressed: Detroit Institute of Cancer Research, Detroit, Mich.

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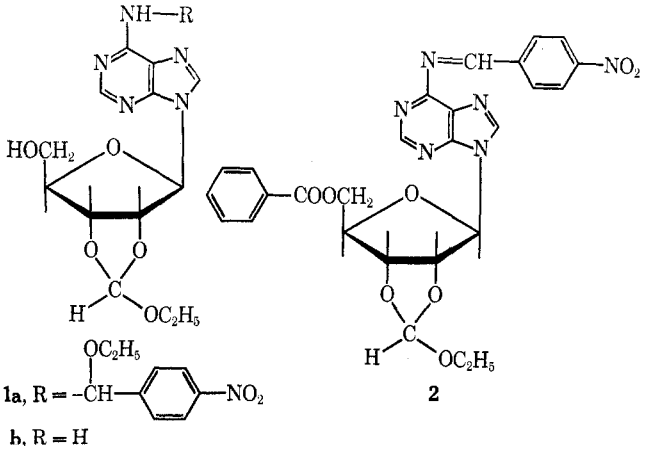
tions parallel a report of the catalytic influence of ethyl orthoformate in the condensation of *p*-nitrobenzaldehyde with active methylene compounds in acetic anhydride.[9] The effect was ascribed to the "basic properties of ethyl orthoformate," but a detailed interpretation of the reaction was not provided.

Substitution of *p*-nitrobenzaldehyde diethyl acetal (*vide infra*) for the aldehyde itself in a mixture that contained adenosine, ethyl orthoformate, and trifluoroacetic acid gave 2′,3′-*O*-ethoxymethyleneadenosine (**1b**) instead of **1a**. Replacement of trifluoroacetic acid by hydrogen chloride in the reaction of adenosine with *p*-nitrobenzaldehyde and ethyl orthoformate again yielded **1a**. The omission of acid from the reaction mixture leads only to the recovery of the reactants. By contrast, the reaction of *p*-bromoaniline and *p*-nitrobenzaldehyde in DMF affords the corresponding Schiff base in good yield after 1 hr at ambient temperature.

Despite unsuccessful attempts to devise a general synthesis of 2′,3′-*O*-(*p*-nitrobenzylidene)ribonucleosides, the desired reaction was effected in the case of uridine with *p*-nitrobenzaldehyde in 1,2-dimethoxyethane and in the presence of *p*-toluenesulfonic acid to give **5a** in 58% yield. Substitution of dioxane for 1,2-dimethoxyethane led to a mixture of **5a** and a product that was identified as 2′,3′-*O*-ethylideneuridine (**5b**). These observations indicate that dioxane (in acid) undergoes a prior cleavage to acetaldehyde which is consumed in the acid-catalyzed formation of **5b**.[10]

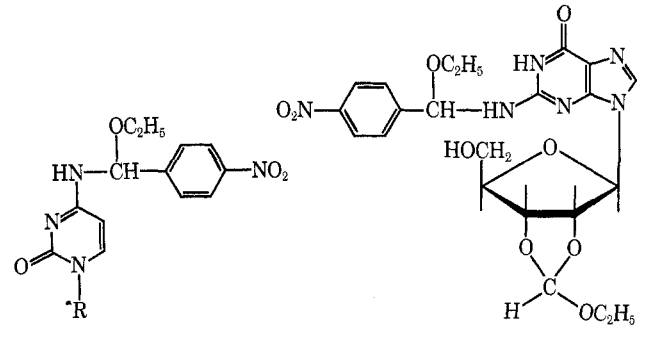
It would seem that any plausible reaction path to the N,O mixed acetals (**9**, Scheme I) should include the formation of the diethoxycarbonium ion **6**, generated from reaction with ethyl orthoformate. Interaction of **6** and *p*-nitrobenzaldehyde would lead to the ethyloxonium cation **7** with which alkylation of the exocyclic amino groups of the heterocyclic bases could be effected. Alternatively, the formation of **9** may be explained by initial attack of **6** (Scheme II) on the exocyclic amino



1a, R = –CH(OC$_2$H$_5$)–C$_6$H$_4$–NO$_2$

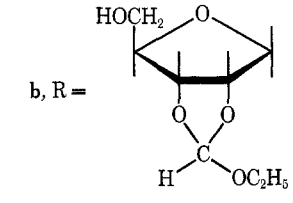
b, R = H

2

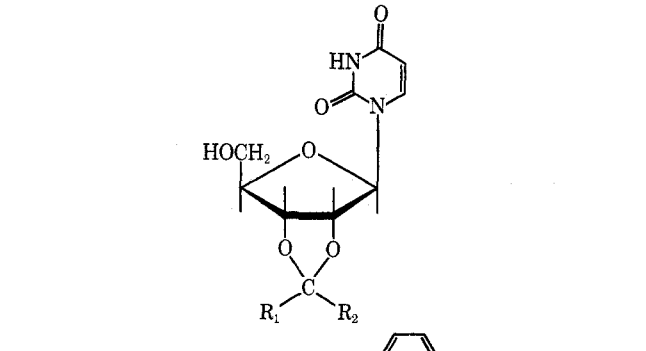


3a, R = H

4



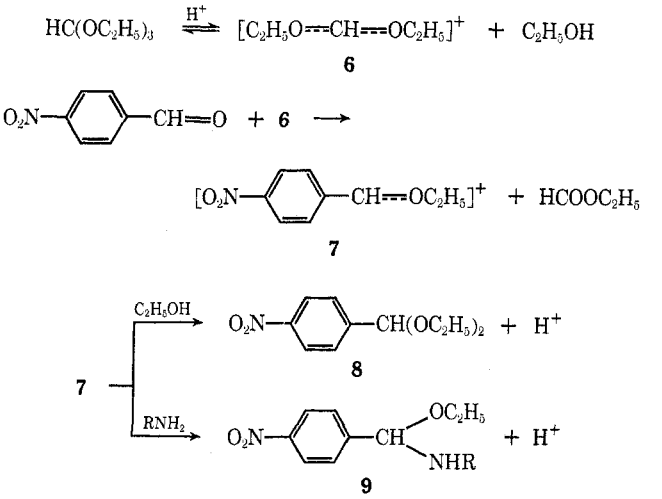
b, R =



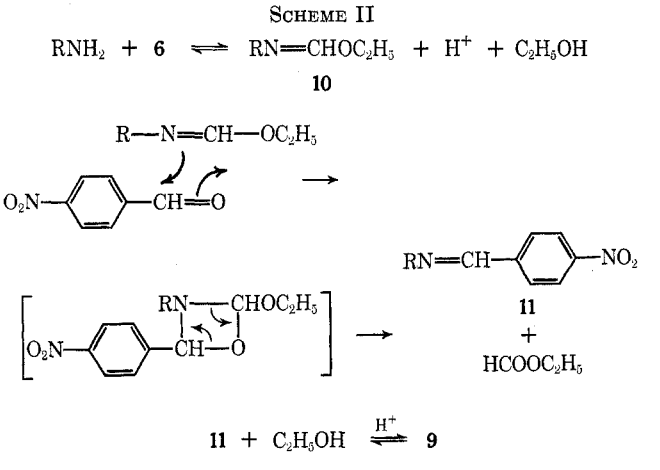
5a, R$_1$ = H; R$_2$ = O$_2$N–C$_6$H$_4$–

b, R$_1$ = H; R$_2$ = CH$_3$

Scheme I



Scheme II



R = heterocyclic residue

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(10) J. Žemlička, *J. Org. Chem.*, **36**, 2383 (1971).

group of the heterocycle to give an *N*-ethoxymethylene intermediate **10**. The addition of aldehyde to the latter, *via* a four-center mechanism, leads to the Schiff base **11** from which the product **9** would be derived on acid ethanolysis. A clear choice between these two paths cannot be made on the basis of the present evidence.

It should be noted that the conditions, which on the one hand promote the intervention of **7**, deplete the concentration of the free amine. Thus, the increase of **7** in hydrochloric acid relative to trifluoroacetic acid[11] may be offset by the quantity of heterocyclic base that is "protected" from electrophilic attack by **6** or **7** as a consequence of the increase in the protonated form of the base. It is apparently the control exercised by the nature of the acid that determines the product (**1a** or **1b**) derived from adenosine.

The isolation of 2′,3′-*O*-ethoxymethylene nucleosides, **1**, **2**, and **3** instead of corresponding *p*-nitrobenzylidene derivatives is apparently due to the fact that *p*-nitrobenzaldehyde, unlike benzaldehyde and (R^+) para-substituted derivatives, fails to enter into acetal interchange (transacetalation) with the 2′,3′-*O*-ethoxymethylene intermediates under the imposed conditions.[12] The modifying influence of the *p*-nitro substituent on the additive power of the carbonyl group would be expected to facilitate the formation of a hydrate or a hemiacetal as do the electronegative substituents in, for example, chloral and α-fluoro ketones[13] (hemiketal). By the same reasoning, a marked decrease should be observed in the ease of conversion of the initial carbonyl addition product to an acetal or ketal. This is evidently the case with fluoro ketones hemiketals for which it was necessary to devise a novel base-catalyzed process to effect ketalization.[14] By contrast, *p*-nitrobenzaldehyde diethyl acetal is readily obtained in good yield from the action of ethyl orthoformate in ethanol on the aldehyde in the presence of anhydrous hydrogen chloride.[15] However, this acetalation fails when trifluoroacetic acid is substituted for hydrogen chloride. This finding, along with the fact that both catalysts are ineffective in the acetalation of adenosine, cytidine, and guanosine, indicates the importance of considerations other than the influence of an electronegative substituent in benzaldehyde to the success of the reaction.

Experimental Section

General Procedures.—Evaporations were carried out *in vacuo* at bath temperatures below 40° unless stated otherwise. The petroleum ether used in the study was of a 30–60° range. Melting points were determined on a Thomas-Hoover apparatus (capillary method) and are uncorrected. Analytical samples were dried at 0.02 mm and room temperature over P_2O_5. Microanalyses were performed by Micro-Tech Laboratories Inc., Skokie, Ill. Thin layer chromatography (tlc) was carried out on silica gel GF (E. Merck-AG); preparative tlc was accomplished on 20 × 20 cm plates coated with a 2-mm loose layer of (70–325 mesh) silica gel (E. Merck) containing 2% fluorescent indicator[16] in chloroform–methanol mixtures: S_1 (4:1), S_2 (9:1), S_3 (9.5:0.5), and cyclohexane–benzene (1:1, S_4). Paper chromatography was performed on Whatman No. 4 paper with which the following solvents were used: S_5, 2-propanol–ammonium hydroxide–water (7:1:2); S_6, 1-butanol–water (saturated); S_7, 1-butanol–acetic acid–water (5:2:3). Optical rotations were determined with a Perkin-Elmer Model 141 spectropolarimeter in the specified solvent. Infrared spectra were measured (KBr) with a Perkin-Elmer Model 21 spectrometer. Nuclear magnetic resonance spectra were obtained using a Varian A-60A spectrometer with TMS as internal reference in deuteriochloroform and with DSS in DMSO-d_6.

Reaction of Adenosine, *p*-Nitrobenzaldehyde, and Ethyl Orthoformate. A. Trifluoroacetic Acid as Catalyst (1a).—A mixture of adenosine (1.08 g, 4 mmol), *p*-nitrobenzaldehyde (1.8 g, 12 mmol), ethyl orthoformate (3.36 ml, 20 mmol), and trifluoroacetic acid (0.8 ml, 10.8 mmol) in 50 ml of dimethylformamide (DMF) was first stirred magnetically at room temperature until the reaction mixture was homogeneous and then maintained at ambient temperature for 6 days.[17] Excess (2 ml) triethylamine was added and the alkaline solution was evaporated to dryness at 45° and 0.1 mm. The residue was dissolved in methylene chloride, and the solution was washed twice with 25 ml of saturated sodium bicarbonate and dried over magnesium sulfate. The filtered solution was reduced in volume to *ca.* 20 ml and the crude product separated as a syrup upon successive addition of 50 ml of ether and 200 ml of petroleum ether. The residue, after decantation of the mixed solvents, precipitated from 10 ml of methylene chloride as a yellow amorphous powder on addition first of 50 ml of ether and 250 ml of petroleum ether. The solid (1.62 g, 81% yield), which showed an indefinite melting point, gave a single spot on a tlc plate developed with either solvent system S_3 or chloroform. An analytical sample was purified by preparative tlc using solvent system S_2 containing 0.1% of triethylamine. The band corresponding to **1a** was eluted with the same solvent system and the filtered solution was evaporated to dryness. The sample was precipitated from chloroform on addition of ether followed by petroleum ether: uv max (1% $CHCl_3$ in EtOH) 267 nm (ε 23,300), min 237 (7600); ir (KBr) 3300 cm^{-1} (OH), absence of NH_2; nmr ($CDCl_3$) δ 8.12 and 7.65 (doublet of doublets, 4, *p*-nitrophenyl, AA′BB′), 6.04 (d, 1, H-1′), 1.25 (6, m, two CH_3).

Anal. Calcd for $C_{22}H_{26}N_6O_8$: C, 52.58; H, 5.22; N, 16.73; C_2H_5O, 17.94. Found: C, 52.78; H, 4.96; N, 16.90; C_2H_5O, 17.72.

When ethyl orthoformate was omitted from the reaction mixture, no reaction was observed (after 6 days at room temperature).

Adenosine also constituted the major nucleosidic component when *p*-nitrobenzaldehyde and ethyl orthoformate were replaced by diethyl acetal **8**.

Hydrogen Chloride as Catalyst (1b).—A mixture of adenosine (0.13 g, 0.5 mmol), *p*-nitrobenzaldehyde (0.225 g, 1.5 mmol), ethyl orthoformate (0.21 ml, 1.1 mmol), and 4.47 *M* hydrogen chloride in dimethylformamide (0.25 ml, 1.1 mmol) in 5.0 ml of dimethylformamide was maintained at room temperature for 24 hr. The reaction mixture was made alkaline with triethylamine (0.28 ml, 2 mmol), the triethylamine hydrochloride was removed by filtration, and the filtrate evaporated to dryness. The residue was dissolved in 5 ml of chloroform and precipitated by the successive addition of 25 ml of ether and 50 ml of petroleum ether. A second precipitation by the same procedure gave 0.113 g (57% yield) of product **1c** in the form of an amorphous solid which was identical both spectrally (ir and uv) and on the basis of tlc with an authentic sample[8] of 2′,3′-*O*-ethoxymethyleneadenosine (**1b**).

N^6-*p*-Nitrobenzylidene-5′-*O*-benzoyl-2′,3′-*O*-ethoxymethyleneadenosine (2).—To a stirred solution of 0.5 g (1 mmol) of **1a** in 10 ml of dry pyridine, cooled to 0° by an ice–salt bath, was added 0.58 ml (5 mmol) of benzoyl chloride. The reaction mixture was then maintained at room temperature for 40 hr after which 5 ml of methanol was added and the solution was evaporated to dryness. The residue was dissolved in $CHCl_3$ and the solution was shaken first with 10 ml of a saturated solution of sodium bicarbonate and then with water. Evaporation of the

(11) Hydrochloric acid is about ten times stronger than trifluoroacetic acid: T. Gramstad, *Tidsskr. Kjemi, Bergv. Met.*, **19**, 62 (1959).

(12) The acetalation of ribonucleosides with *p*-dimethylaminobenzaldehyde and ethyl orthoformate with trichloracetic acid as catalyst is reported[4] to lead to the formation of some 2′,3′-*O*-ethoxymethylene ribonucleosides in addition to the expected 2′,3′-*O*-(*p*-dimethylaminobenzylidene)ribonucleosides. Apparently, protonation of the dimethylamino group suppresses its activating (R^+) influence.

(13) R. F. Reed, "Properties and Reactions of Bonds in Organic Molecules," Elsevier, New York, N. Y., 1968, p 354.

(14) H. E. Simmons, Jr., and D. W. Wiley, *J. Amer. Chem. Soc.*, **82**, 2288 (1960).

(15) T. H. Fife and L. K. Rao, *J. Org. Chem.*, **30**, 1942 (1965).

(16) Leuchtpigment ZS Super, Ridel-De Haën AG, Hannover, Germany.

(17) Subsequently, it was established that a 24-hr reaction period is sufficient.

dried organic layer gave an amorphous residue which was precipitated from ether (25 ml) by the addition of petroleum ether (150 ml). The solid (0.32 g, 57% yield) appeared to be homogeneous on tlc (solvent S_3). An analytical sample was obtained as an amorphous powder by subjecting the crude solid first to preparative tlc (solvent S_2) and then precipitation of the eluted (S_2) material from ether–petroleum ether: uv max (1% $CHCl_3$ in EtOH) 270 nm (ϵ 21,000), min 243 (14,300); ir (KBr) 3400 (NH, broad band), 1735 (C=O), 1683 cm^{-1} (C=N).

Anal. Calcd for $C_{27}H_{24}N_6O_8$: C, 57.85; H, 4.32; N, 15.00. Found: C, 57.85; H, 4.56; N, 14.77.

2′,3′-*O*-(*p*-Nitrobenzylideneuridine) (5a).—A solution of 0.24 g (1 mmol) of uridine, 0.3 g (2 mmol) of *p*-nitrobenzaldehyde, and 0.114 g of *p*-toluenesulfonic acid in 100 ml of 1,2-dimethoxyethane was heated just to reflux and 70 ml of solvent was removed by distillation in 2.5 hr. Additional 1,2-dimethoxyethane (50 ml) was introduced and then 15 ml of solvent was collected in 2.25 hr on distillation. Benzene (50 ml) was next added to the reaction flask and 100 ml of the solvent mixture was distilled off in 3.5 hr. Next, a 1:1 mixture (40 ml) of benzene–1,2-dimethoxyethane was added and 40 ml of the solvent mixture was removed by distillation in 2.5 hr. Fresh *p*-nitrobenzaldehyde (0.3 g, 2 mmol) and 1,2-dimethoxyethane (50 ml) were added to the reaction vessel and distillation was continued for 6 hr during which time 50 ml of solvent was collected. On cooling, a yellow solid was deposited which was collected, washed with 10 ml of 1:1 mixture of benzene–1,2-dimethoxyethane, and air-dried, wt 0.22 g (58% yield), mp 247–248°. Recrystallization of the product from nitromethane[18] (20 ml/0.1 g) provided an analytical sample, which was dried at 100° and 0.05 mm: mp 268–270°; $[\alpha]^{24}D$ −10.3°, $[\alpha]^{24}_{436}$ −23° (*c* 0.25, DMF); uv max (EtOH) 262 nm (ϵ 19,800), min 229 (5100); nmr (DMSO-d_6) δ 8.23 and 7.74 (4, doublet of doublets AA′BB′, *p*-nitrophenyl), 5.85 (2, d, $H_{1'}$).

Anal. Calcd for $C_{16}H_{15}N_3O_8$: C, 50.93; H, 4.01; N, 11.14. Found: C, 50.86; H, 4.18; N, 11.17.

N^4-(α-Ethoxy-*p*-nitrobenzyl)cytosine (3a).—A solution of cytosine hemihydrate (0.11 g, 0.92 mmol), *p*-nitrobenzaldehyde (0.45 g, 3 mmol), and ethyl orthoformate (0.42 ml, 2.5 mmol) in 10 ml of DMF containing trifluoroacetic acid (0.2 ml, 2.69 mmol) was maintained at room temperature for 9 days. A second addition of both *p*-nitrobenzaldehyde (0.225 g, 1.5 mmol) and ethyl orthoformate was then made and the mixture was stored at room temperature for an additional 13 days. Excess triethylamine (1 ml) was added and the reaction mixture was evaporated to dryness. The syrupy residue was triturated successively with 10 ml each of chloroform, ether, and petroleum ether. The residue solidified following a second trituration with chloroform (20 ml) which was collected, washed with acetone, and dried. The ir and nmr spectra of the latter (0.06 g) were essentially superimposable with the corresponding spectra of cytosine. The combined filtrates were evaporated to dryness and the residue was partitioned between $CHCl_3$ (20 ml) and saturated $NaHCO_3$ (10 ml). Following a second washing with $NaHCO_3$, the aqueous layer was extracted with $CHCl_3$ and the combined, dried ($MgSO_4$) extracts were evaporated to dryness. The residue was precipitated from chloroform (5 ml) by sequential addition of ether (25 ml) and petroleum ether (50 ml). The amorphous product (0.075 g, 27% yield), which gave a single spot on tlc (S_1), showed an indefinite melting point (foaming at 125–135° with decomposition at 215–218°): uv max (EtOH) 276 nm (ϵ 15,400), min 232 (9900); nmr ($CDCl_3$) δ 8.31, 7.61 (doublet of doublets, 4, *p*-nitrophenyl, AA′BB′), 1.25 (t, 3, CH_3 of ethoxyl).

Anal. Calcd for $C_{13}H_{14}N_4O_4 \cdot 0.5H_2O$: C, 52.17; H, 5.05; N, 18.72. Found: C, 52.33; H, 4.86; N, 18.44.

N^4-(α-Ethoxy-*p*-nitrobenzyl)-2′,3′-*O*-ethoxymethylenecytidine (3b).—A mixture of cytidine (0.96 g, 4 mmol), ethyl orthoformate (3.4 ml, 20 mmol), and trifluoroacetic acid (0.8 ml, 10.8 mmol) in 50 ml of DMF was maintained at room temperature for 10 days. The reaction mixture was made alkaline with excess triethylamine (3 ml) and the solution was evaporated to dryness at 55° (0.05 mm). The residue was dissolved in chloroform (100 ml) and the solution was washed twice with saturated $NaHCO_3$ (40 ml) and then with water. The dried ($MgSO_4$) chloroform extract was evaporated to dryness and the residue, which was redissolved in chloroform (15 ml), separated as an oil upon successive addition of ether (75 ml) and petroleum ether (200 ml). The solvents were decanted and the residual syrup was again dissolved in chloroform from which it precipitated as an amorphous solid on successive addition of ether and petroleum ether. The product was collected and washed with ether, wt 1.33 g (67% yield). An analytical sample was obtained following preparative tlc (S_2 + 0.1% triethylamine). The major uv-absorbing zone[19] was first eluted with S_2 and the residue, after evaporation of the solvent, separated from a mixture of chloroform, ether, and petroleum ether as an amorphous solid of indefinite melting point: uv max (1% $CHCl_3$ in EtOH) 278 nm (ϵ 13,600), min 230 (7300); ir (KBr) 3380 cm^{-1} (broad band, NH and OH); nmr ($CDCl_3$) δ 7.66 and 8.10 (doublet of doublets, 4, *p*-nitrophenyl, AA′BB′), 1.18 (m, 6, CH_3 residue in 2 ethoxy groups).

Anal. Calcd for $C_{21}H_{26}N_4O_9 \cdot H_2O$: C, 50.80; H, 5.69; N, 11.29; C_2H_5O, 18.15. Found: C, 51.01; H, 5.26; N, 11.37; C_2H_5O, 17.50.

Reaction of Guanosine, *p*-Nitrobenzaldehyde, and Ethyl Orthoformate.—A solution of guanosine (1.13 g, 4 mmol), *p*-nitrobenzaldehyde (2.7 g, 18 mmol), ethyl orthoformate (2.9 ml, 17.1 mmol), and trifluoroacetic acid (0.8 ml, 10.8 mmol) in DMF (40 ml) was stirred at ambient temperature for 50 hr. Triethylamine (2.2 ml, 16 mmol) was then added and the mixture was evaporated to dryness at 45° (0.1 mm). The residue was dissolved in chloroform (100 ml), the solution was washed with a saturated solution of sodium bicarbonate (two 40-ml portions), and the dried chloroform extract was evaporated to dryness *in vacuo*. The residue was dissolved in dichloromethane (15 ml) and a yellow solid **4** was precipitated by the addition of ether (50 ml) and petroleum ether (30–60°), wt 1.78 g (86% yield), which retained a small amount of *p*-nitrobenzaldehyde according to tlc (S_1). The analytical sample was purified by preparative tlc (S_1, in which dichloromethane was substituted for chloroform and 0.1 ml of triethylamine/100 ml of solvent mixture), the main uv-absorbing (yellow) zone was eluted with the same solvent system, and the eluate was evaporated to dryness *in vacuo*. The product **4** was precipitated as described above as a chromatographically (tlc) homogeneous solid: uv max (1% $CHCl_3$ in EtOH) 259 nm (ϵ 21,000), min 232 (8600); ir (KBr) 3100–3300 (OH), 1700 cm^{-1} (CO, guanosine); ir ($CHCl_3$) absence of NH_2; nmr ($CDCl_3$), the *p*-nitrophenyl group, $H_{1'}$, and ethoxyl protons all appeared as poorly resolved signals.

Anal. Calcd for $C_{22}H_{26}N_6O_9$: N, 16.24. Found: N, 16.43.

***p*-Bromo-*N*-(*p*-nitrobenzylidene)aniline.**—A solution of *p*-nitrobenzaldehyde (0.15 g, 1 mmol) and *p*-bromoaniline (0.17 g, 1 mmol) in DMF (5 ml) was held at room temperature for 1 hr. The reaction mixture was evaporated to dryness at 40° (0.1 mm) and the residue crystallized from benzene–ethanol (1:1) as a yellow solid: wt 0.13 g (43% yield); mp 160–163° (lit.[20] 162–164°); nmr ($CDCl_3$) δ 8.16 (s, 1, CH=), 7.69 and 7.99 (two d, 4, AA′BB′ of *p*-nitrophenyl), 6.78, 7.20 (two d, 4, AA′BB′ of *p*-bromophenyl).

Registry No.—**1a**, 30765-26-5; **2**, 30765-27-6; **3a**, 30826-39-2; **3b**, 30765-28-7; **4**, 30765-29-8; **5a**, 30765-30-1; *p*-bromo-*N*-(*p*-nitrobenzylidene)aniline, 10480-19-0.

(18) Purification of this material may also be achieved by precipitation from pyridine on the addition of water, or from dimethyl sulfoxide by the addition of methanol.

(19) On tlc, the zone travels as a double spot, which suggests the possibility that the product **3b** is a mixture of diastereoisomers.

(20) P. K. Kadaba, *Tetrahedron*, **22**, 2453 (1966).