The Photocycloaddition Reactions of Uridine and Related Compounds with 2,3-Dimethyl-2-butene

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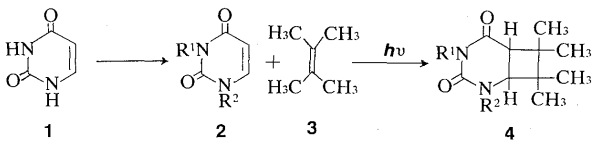
The photochemical reactions of uracil and 5-fluorouracil derivatives with simple alkenes have been investigated. Photocycloaddition of uracil or 5-fluorouracil derivatives and 2,3-dimethyl-2-butene in acetone gave an enantiomeric mixture of cross cycloadducts (4, 7) in moderate yields. Under similar conditions, diastereomers of 4-substituted 7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione nucleosides (14—17) were formed from uridine or 5-fluorouridine derivatives in good yields. The structures and stereochemistry of these cycloadducts of the nucleoside series were elucidated on the basis of the proton nuclear magnetic resonance spectra and X-ray crystallographic analysis.

Keywords ribonucleoside; photocycloaddition; X-ray crystallographic analysis; 2,4-diazabicyclo[4.2.0]octane; Vorbrüggen ribosylation; ^{1}H-NMR

Photochemical cycloaddition reactions between nucleobases, *viz.*, uracil derivatives, and simple olefins have been extensively investigated.[2,3)] Many workers[4)] have also studied the photodimerizations of pyrimidine nucleosides. However, the photoadditions between nucleosides and simple alkenes have received little attention except for the work of Charlton and Lai,[5)] who have prepared the 2,3-dimethyl-2-butene adducts of uridine derivatives. We considered that these photocyclizations might provide a route to a variety of bicyclic pyrimidine nucleosides, and it was anticipated that these adducts might be useful for biological studies. They might also serve as useful intermediates for syntheses of naturally occurring nucleobases of nucleosides.[6)] Earlier studies by Swenton *et al.*[2)] on the reaction of 1,3-dimethyluracil or 5-fluoro-1,3-dimethyluracil with isobutene showed that cycloadditions of this type take place in a stereoselective way. That means that the cyclization of a symmetrical olefin, *viz.*, 2,3-dimethyl-2-butene, and uracil (**2b** or **6c**) may give rise to a relatively uncomplicated mixture from which each product could be easily fractionated. Thus, we carried out the acetone-sensitized cycloaddition of 1,3-dialkyluracils and symmetrical olefins. In the present paper we describe the outcome of the above-mentioned reactions including the structural elucidation of products.

Photoaddition was performed in acetone at room temperature by the use of a 400 W high-pressure mercury lamp fitted with a Pyrex filter.

The acetone-sensitized cycloaddition of 1,3-dimethyluracil (**2b**) and 2,3-dimethyl-2-butene (**3**) proceeded smoothly, leading to the formation of the cycloadduct (**4b**) in 76% yield. The similar photocycloaddition of 1,3-diethyluracil (**2d**) also proceeded to give the adduct (**4d**) in 56% yield.



1 2 3 4

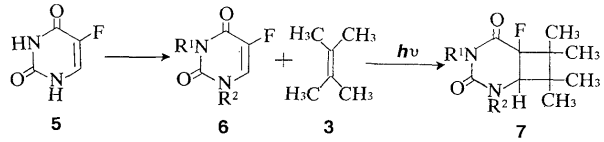
a : R¹=H, R²=CH₃
b : R¹=R²=CH₃
c : R¹=H, R²=CH₂CH₃
d : R¹=R²=CH₂CH₃
e : R¹=H, R²=CH₂C₆H₅
f : R¹=R²=CH₂C₆H₅

Chart 1

The structures of these products (*cf.* **4b** and **4d**) were elucidated by spectral [mass spectra (MS) and nuclear magnetic resonance (NMR)] as well as elemental analyses. NMR data for both adducts are consistent with cyclobutane structures; for example, in the ^{1}H-NMR spectrum of **4b**, signals at δ 5.71 and 7.15 due to the 5,6-vinyl protons in **2b** are absent, while new signals appeared at δ 2.9 and 3.6 ppm. In addition, the splitting pattern of **4d** is characteristic of the cyclobutane ring. The signals appeared as a pair of doublets and those due to hydrogens of four methyl groups appeared as four separate singlets (δ 0.93, 0.97, 1.12, and 1.23). These compounds (**4b**, **d**) showed differentiation-inducing and growth-inhibitory activities towards HL-60 cells.[7)]

This finding of differentiation-inducing activity of the cyclobutane ring system prompted us to prepare 2,4-diazabicyclo[4.2.0]octane-3,5-dione derivatives and nucleosides thereof.

Alkylation of uracil (**1**) or 5-fluorouracil (**5**) with alkyl halide (MeI or EtI) in dry acetone gave 1-alkyl- or 3-alkyluracils or 1,3-dialkyluracils (**2**, **6**) in moderate yields. Aralkylation of **1** and **5** with benzyl chloride [K_2CO_3 in dimethylsulfoxide (DMSO)] afforded 1-benzyluracil (**2e**) and 1-benzyl-5-fluorouracil (**6f**) in 57% and 62% yields, respectively. 1,3-Dibenzyluracil (**2f**) and 1,3-dibenzyl-5-fluorouracil (**6g**) were obtained in 79% and 72% yields from the reaction of **1** and **5**, respectively, with benzyl chloride using 60% NaH in *N*,*N*-dimethylformamide (DMF). The structures of the products were confirmed by spectral (MS, NMR, and ultraviolet (UV)) as well as elemental analyses. The acetone-sensitized photocycloaddition of **2** and **6** with **3** afforded **4** and **7**, respectively, in excellent yields. The



5 6 3 7

a : R¹=H, R²=CH₃
b : R¹=CH₃, R²=H
c : R¹=R²=CH₃
d : R¹=H, R²=CH₂CH₃
e : R¹=R²=CH₂CH₃
f : R¹=H, R²=CH₂C₆H₅
g : R¹=R²=CH₂C₆H₅

Chart 2

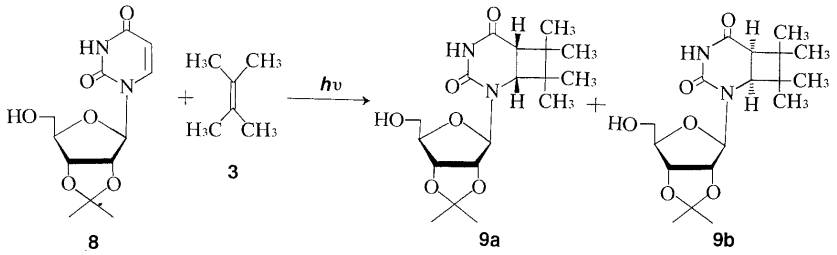
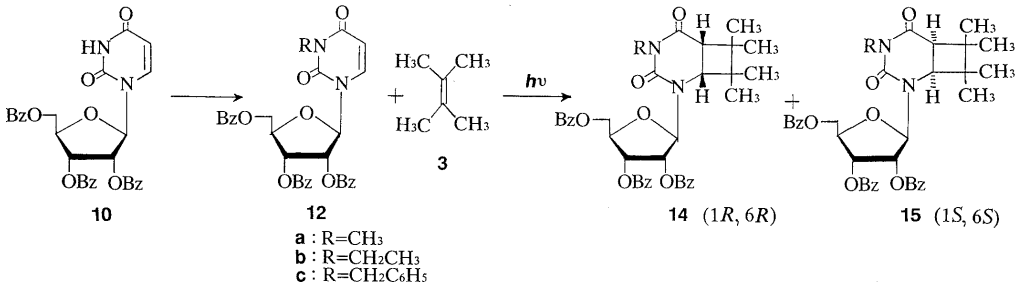


Chart 3



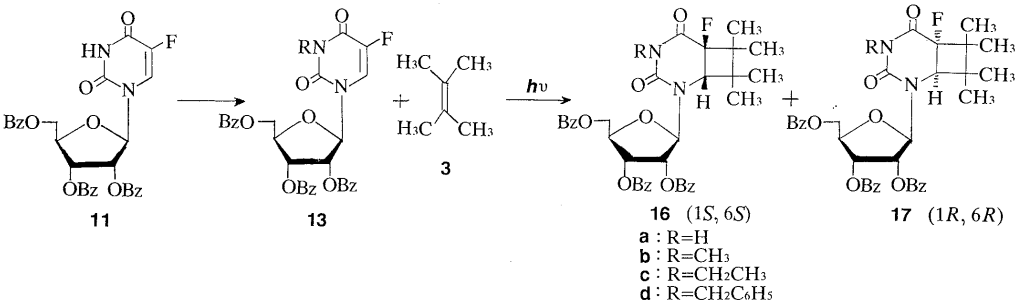


Chart 4

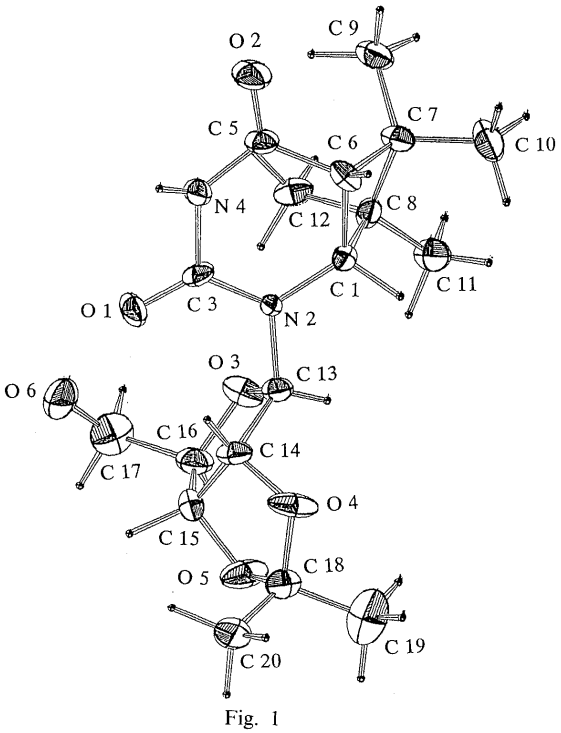


Fig. 1

structures of **4** and **7** were established on the basis of MS and NMR, and elemental analyses (Charts 1 and 2). Analogously, the photocycloaddition between **8** and **3** afforded two adducts (**9a** and **b**) in the ratio of 9 : 1 (54% and 6% isolated yields). The MS and NMR data of these compounds are consistent with the assigned cycloadduct structures (**9a** and **9b**). The structure of **9a** including the stereochemistry was definitively established by means of an X-ray crystal structure analysis. A perspective drawing of **9a** is shown in Fig. 1 on the basis of the absolute configuration of D-ribose. The absolute configurations at C-1 and C-6 were both assigned as *R*. Taking the above results into consideration, we anticipate that the second adduct (**9b**) has the 1*S*, 6*S* configuration.

Ribosylation of **1** and **5** were performed according to the general procedure (Vorbrüggen procedure)[8,9] to give **10** and **11**. 3-Alkyl-2′,3′,5′-tri-*O*-benzoyluridines (**12**, **13**) were obtained in good yields on treatment of **10** or **11** with various alkyl halides. In addition, the photocycloadducts **14**—**17** were obtaine from **11**, **12**, and **13** with **3**. Compounds **14a**, **15a** and **16a**, **17a** were isolated by preparative thin-layer chromatography (TLC) developed with $CHCl_3$–EtOH (10 : 1). The configurations of these compounds (**14a**, **15a** and **16a**, **17a**) were confirmed by NMR; the NMR data of **14a** and **16a** were quite similar to the NMR data of **9a**, and those of **15a** and **17a** are similar to those of **9b**. Photoaddition involving the uridine derivatives (**12b**, **c** and **13b**, **c**) afforded two major products, which could not be separated. However, it was found by means of NMR that the reaction mixture consists of two major products. The configurations as well as structures of these compounds

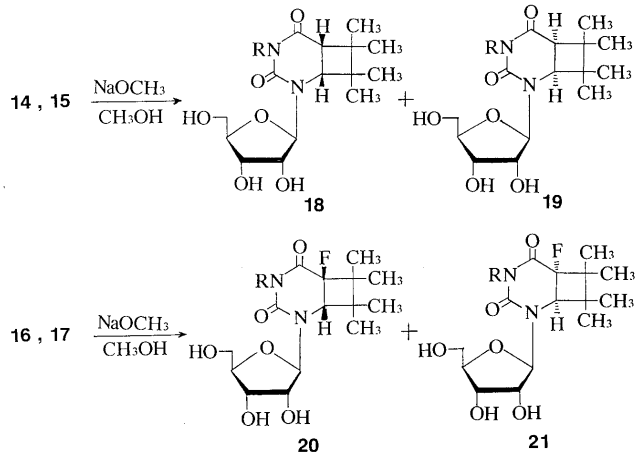


Chart 5

TABLE I. Product Distribution in Cycloaddition

Products	Yield (%)	Ratio of diastereomers *endo* : *exo*[11]
9a, **9b**	60	9 : 1[a]
14a, **15a**	64	1.2 : 1[a]
14b, **15b**	91	3 : 2[b]
14c, **15c**	93	3 : 2[b]
16a, **17a**	92	5 : 2[a]
16b, **17b**	99	5 : 2[b]
16c, **17c**	96	3 : 1[b]
16d, **17d**	92	3 : 1[b]

a) The ratio was determined from the isolated yields. *b*) The ratio was estimated from the NMR spectra.

(**14b**, **c**, **15b**, **c** and **16b—d**, **17b—d**) were determined by NMR as described above, and the ratios of the respective products were determined on the basis of the integration of anomeric proton signal in the ^{1}H-NMR spectra. Finally, 7,7,8,8-tetramethyl-2-(*β*-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-diones (**18—21**) were prepared in excellent yields by treating **14—17** with sodium methoxide in MeOH at 50—60 °C.

It is worth noting that some of the products (**4b**, **d**, **6b**, **d**, **e**, **g**, and **9a**) exhibit differentiation-inducing and growth-inhibitory activities towards HL-60 cells.[7,10]

The results may be summarized as follows. i) 2,4-Diazabicyclo[4.2.0]octane-3,5-diones were prepared from the uracil derivatives by acetone-sensitized irradiation. ii) Diastereomeric 2,4-diazabicyclo[4.2.0]octane-3,5-dione nucleosides were prepared from uridine derivatives in an analogous way, and these diastereomeric nucleosides were isolated by preparative TLC. iii) The structure and stereochemistry of 2,4-diazabicyclo[4.2.0]octane-3,5-dione nucleosides were confirmed by ^{1}H-NMR and X-ray crystallographic analyses. iv) Some of the products (**4b**, **d**, **6b**, **d**, **e**, **g**, and **9a**) showed differentiation-inducing and growth-inhibitory activities towards HL-60 cells.[7,10]

Finally, some interesting observations in the present studies are worthy of comment. Of the pair of diastereomers produced by the addition reactions, the "*endo*"-adduct is predominant as compared with the "*exo*"-adduct[11] (see Table I). This outcome of the cycloaddition may be explained by the relative rates of competing reactions, by analogy with another cycloaddition, *viz.*, the Diels–Alder reaction, where the "*endo*"-addition takes place faster. Namely, under our reaction conditions (kinetically controlled conditions), the "endo"-addition occurs faster, so the "*endo*"-cycloadduct is the major product. Elucidation of the exact mode of the reaction will require further studies. Nevertheless, it is interesting that the ratio of the "endo" adduct and the "*exo*"-adduct has something to do with the nature of the protecting groups in the sugar portion. The predominance of the "*endo*"-product with 2′,3′-*O*-isopropylideneuridine is very marked. A similar propensity associated with a reaction involving 2′,3′-*O*-isopropylideneuridine has been reported quite often, *e.g.*, in the 5-hydroxymethylation of 2′,3′-*O*-isopropylideneuridine.[12]

Experimental

General Melting points were determined in a capillary tube and are uncorrected. MS were recorded on a JEOL D-100 instrument. ^{1}H-NMR spectra were recorded on a Varian EM-390 NMR spectrometer or Varian VXR-300 spectrometer with Me_4Si (TMS) as an internal standard in $CDCl_3$ or in DMSO-d_6. Microanalyses were performed by the staff of the Microanalytical Laboratory of this school. The cell dimensions and diffraction intensities were measured on a Rigaku four-circle diffractometer, using graphite-monochromated Cu K_α radiation. Column chromatography was performed on Wakogel C-200. TLC was performed on Kieselgel 60 GF_{254} (20 cm × 20, Merck) and spots were detected under UV light. Unless otherwise stated, the solvents were removed in a rotary evaporator coupled to a water aspirator (*ca.* 20 mmHg).

Reaction of Uracil (1) with Methyl Iodide A mixture of uracil (**1**, 2.24 g, 20 mmol), methyl iodide (4.26 g, 30 mmol) and potassium carbonate (1.38 g, 10 mmol) in dry acetone (40 ml) was stirred at 60—70 °C for 24 h in a sealed steel tube. The resulting solution was filtered to remove potassium carbonate and the unreacted uracil (1.15 g), and the filtrate was concentrated *in vacuo*. The residue in $CHCl_3$ was chromatography over silica gel and eluted with $CHCl_3$ to give **2a** and **2b**.

1-Methyluracil (2a) Recrystallization of **2a** from $CHCl_3$–EtOH (1 : 1) afforded 212 mg (17%) as white needles, mp 232—233 °C (lit.[13] mp 233—234 °C. MS *m/z*: 126 (M^+). ^{1}H-NMR (DMSO-d_6) δ: 3.21 (3H, s, NCH_3), 5.46 (1H, d, 5-H, J=7.8 Hz), 7.58 (1H, d, 6-H, J=7.8 Hz), 11.12 (1H, br, NH). UV λ_{max}^{EtOH} nm (log ε): 263 (3.87). UV $\lambda_{max}^{1\ N\ NaOH-EtOH\ (1:10)}$ nm (log ε): 263 (3.65). *Anal.* Calcd for $C_5H_6N_2O_2$: C, 47.62; H, 4.80; N, 22.22. Found: C, 47.54; H, 4.85; N, 22.06.

1,3-Dimethyluracil (2b) This compound was recrystallized from $CHCl_3$ to give 415 mg (30%) as white needles, mp 123—125 °C (lit.[13] mp 125 °C). MS *m/z*: 140 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 3.33, 3.40 (3H each, s, NCH_3), 5.71 (1H, d, 5-H, J=7.8 Hz), 7.15 (1H, d, 6-H, J=7.8 Hz).

Reaction of 1 with Ethyl Iodide A mixture of **1** (1.12 g, 10 mmol), ethyl iodide (2.34 g, 15 mmol) and potassium carbonate (0.69 g, 5 mmol) was added to dry acetone (20 ml). The resulting mixture was worked up according to the procedure described above for **2a** to give **2c** (120 mg, 22%) as white crystals, **2d** (215 mg, 23%) as a colorless oil, and unreacted uracil (682 mg) as a white powder.

1-Ethyluracil (2c) This compound had mp 145—146 °C (lit.[13] mp 145—146 °C). MS *m/z*: 140 (M^+). ^{1}H-NMR (DMSO-d_6) δ: 1.16 (3H, t, $CH_2\underline{CH}_3$, J=7.2 Hz), 3.69 (2H, q, $\underline{CH}_2CH_3$, J=7.2 Hz), 5.50 (1H, d, 5-H, J=7.8 Hz), 7.67 (1H, d, 6-H, J=7.8 Hz), 11.13 (1H, br, NH). UV λ_{max}^{EtOH} nm (log ε): 263 (3.96). UV $\lambda_{max}^{1\ N\ NaOH-EtOH\ (1:10)}$ nm (log ε): 263 (3.81). *Anal.* Calcd for $C_6H_8N_2O_2$: C, 51.42; H, 5.75; N, 19.99. Found: C, 51.19; H, 5.97; N, 19.81.

1,3-Diethyluracil (2d) This compound was obtained as oil (lit.[14] mp 14—15 °C). MS *m/z*: 168 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 1.21, 1.30 (3H each, t, $CH_2\underline{CH}_3$, J=7.2 Hz), 3.80, 3.99 (2H each, q, $\underline{CH}_2CH_3$, J=7.2 Hz), 5.69 (1H, d, 5-H, J=8.0 Hz), 7.15 (1H, d, 6-H, J=8.0 Hz). *Anal.* Calcd for $C_8H_{12}N_2O_2$: C, 57.13; H, 7.19; N, 16.66. Found: C, 57.02; H, 7.24; N, 16.40.

1-Benzyluracil (2e) A mixture of **1** (1.12 g, 10 mmol), benzyl chloride (1.89 g, 15 mmol), and potassium carbonate (0.69 g 5 mmol) in DMSO (20 ml) was stirred at 60—70 °C for 1h. A 4% aqueous solution of NaOH (20 ml) was added to the hot reaction solution. The mixture was extracted with benzene (20 ml × 3), and the aqueous phase was adjusted to pH 2—3 with concentrated HCl. On standing in a refrigerator, crystals precipitated was collected by filtration, and washed with water. The crude product was purified by recrystallization from MeOH to give **2e** (1.15 g, 57%) as white

needles, mp 171—173 °C (lit.[15] mp 173 °C). MS *m/z*: 202 (M^+). ^{1}H-NMR (DMSO-d_6) δ: 4.85 (2H, s, $C\underline{H}_2C_6H_5$), 5.53 (1H, d, 5-H, J=7.8 Hz), 7.70 (1H, d, 6-H, J=7.8 Hz), 7.18—7.35 (5H, m, $CH_2C_6\underline{H}_5$), 11.23 (1H, br, NH). UV λ_{max}^{EtOH} nm (log ε): 261 (3.84). UV $\lambda_{max}^{1\,N\,NaOH-EtOH\,(1:10)}$ nm (log ε): 261 (3.70). *Anal.* Calcd for $C_{11}H_{10}N_2O_2$: C, 65.33; H, 4.98; N, 13.86. Found: C, 65.21; H, 5.04; N, 13.65.

1,3-Dibenzyluracil (2f) A solution of **1** (2.24 g, 20 mmol) in DMF (40 ml) was treated with 60% NaH (1.60 g, 40 mmol), and the resulting mixture was stirred at 40—50 °C for 1 h. After the evolution of hydrogen gas ceased, benzyl chloride (3.78 g, 30 mmol) was added to the reaction mixture, and the whole was stirred at 50—60 °C for 2 h. A 4% aqueous solution of NaOH (20 ml) was added to the resultant reaction solution, which was then extracted with AcOEt (30 ml × 3). The combined extracts were dried (Na_2SO_4), and concentrated *in vacuo* to dryness. The residue was recrystallized from $CHCl_3$–hexane (1 : 1) to give **2f** (4.62 g, 79%) as colorless prisms, mp 71—72 °C. MS *m/z*: 292 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 4.87, 5.11 (2H each, s, $C\underline{H}_2C_6H_5 \times 2$), 5.68 (1H, d, 5-H, J=7.8 Hz), 7.06 (1H, d, 6-H, J=5.4 Hz), 7.16—7.57 (10H, m, $CH_2C_6\underline{H}_5 \times 2$). *Anal.* Calcd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58. Found: C, 73.70; H, 5.64; N, 9.31.

Reaction of 5-Fluorouracil (5) with Methyl Iodide A mixture of 5-fluorouracil (**5**, 1.30 g, 10 mmol), methyl iodide (2.13 g, 15 mmol), and potassium carbonate (0.69 g, 5 mmol) in dry acetone (20 ml) was stirred at 60—70 °C for 24 h. The resulting solution was filtered, and the filtrate was concentrated *in vacuo*. The resulting residue was taken up in a small volume of $CHCl_3$, and fractionated by silica gel column chromatography with $CHCl_3$ to give **6a**, **b**, and **6c**.

5-Fluoro-1-methyluracil (6a) This compound was recrystallized from acetone–EtOH (1 : 1) yield, 777 mg (27%, pale yellow needles), mp 255—257 °C (lit.[16] mp 257—260 °C). MS *m/z*: 144 (M^+). ^{1}H-NMR (DMSO-d_6) δ: 3.23 (3H, s, NCH_3), 7.98 (1H, d, 6-H, J=6.0 Hz), 11.60 (1H, br, NH). UV λ_{max}^{EtOH} nm (log ε): 271 (3.96). UV $\lambda_{max}^{1\,N\,NaOH-EtOH\,(1:10)}$ nm (log ε): 269 (3.79). *Anal.* Calcd for $C_5H_5FN_2O_2$: C, 41.67; H, 3.47; N, 19.44. Found: C, 41.40; H, 3.43; N, 19.20.

5-Fluoro-3-methyluracil (6b) This compound was recrystallized from acetone–EtOH (1 : 1) to give 355 mg (12%) as white needles, mp 170—171 °C. MS *m/z*: 144 (M^+). ^{1}H-NMR (DMSO-d_6) δ: 3.21 (3H, s, NCH_3), 7.76 (1H, d, 6-H, J=5.7 Hz), 11.02 (1H, br, NH). UV λ_{max}^{EtOH} nm (log ε): 263 (3.81). UV $\lambda_{max}^{1\,N\,NaOH-EtOH\,(1:10)}$ nm (log ε): 293 (3.96). *Anal.* Calcd for $C_5H_5FN_2O_2$: C, 41.67; H, 3.47; N, 19.44. Found: C, 41.42; H, 3.52; N, 19.24.

5-Fluoro-1,3-dimethyluracil (6c) Recrystallization of **7c** from $CHCl_3$–hexane (1 : 1) gave 550 mg (17%) as white needles, mp 128—129 °C (lit.[17] mp 128—130 °C). MS *m/z*: 158 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 3.36, 3.38 (3H each, s, NCH_3), 7.30 (1H, d, 6-H, J=5.4 Hz). *Anal.* Calcd for $C_6H_7FN_2O_2$: C, 45.57; H, 4.43; N, 17.72. Found: C, 45.79; H, 4.56; N, 17.47.

Reaction of 5 with Ethyl Iodide A mixture of **5** (1.30 g, 10 mmol), ethyl iodide (2.34 g, 15 mmol), and potassium carbonate (0.69 g, 5 mmol) was added to dry acetone (20 ml). The mixture was treated as described above to give **6d** (553 mg, 35%) and **6e** (409 mg, 22%), each as white needles.

1-Ethyl-5-fluorouracil (6d) This compound showed mp 183—184 °C. MS *m/z*: 158 (M^+). ^{1}H-NMR (DMSO-d_6) δ: 1.15 (3H, t, $CH_2C\underline{H}_3$, J=7.2 Hz), 3.64 (2H, q, $C\underline{H}_2CH_3$, J=7.2 Hz), 8.07 (1H, d, 6-H, J=6.3 Hz), 11.67 (1H, br, NH). UV λ_{max}^{EtOH} nm (log ε): 270 (3.79). UV $\lambda_{max}^{1\,N\,NaOH-EtOH\,(1:10)}$ nm (log ε): 270 (3.69). *Anal.* Calcd for $C_6H_7FN_2O_2$: C, 45.57; H, 4.43; N, 17.72. Found: C, 45.58; H, 4.46; N, 17.62.

1,3-Diethyl-5-fluorouracil (6e) This compound showed mp 66—68 °C. MS *m/z*: 186 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 1.20, 1.29 (3H each, t, $CH_2C\underline{H}_3$, J=7.2 Hz), 3.77, 4.00 (2H each, q, $C\underline{H}_2CH_3$, J=7.2 Hz), 7.23 (1H, d, 6-H, J=5.7 Hz). *Anal.* Calcd for $C_8H_{11}FN_2O_2$: C, 51.61; H, 5.91; N, 15.05. Found: C, 51.50; H, 6.15; N, 14.99.

1-Benzyl-5-fluorouracil (6f) A mixture of **5** (6.50 g, 50 mmol), benzyl chloride (9.53 g, 75 mmol), and potassium carbonate (3.45 g, 25 mmol) in DMSO (100 ml) was treated according to the procedure described above for **2e** to give **6f** (6.80 g, 62%) as white needles, mp 170—171 °C (lit.[18] mp 173—174 °C). MS *m/z*: 220 (M^+). ^{1}H-NMR (DMSO-d_6) δ: 4.89 (2H, s, $C\underline{H}_2C_6H_5$), 7.18 (1H, d, 6-H, J=5.4 Hz), 7.26—7.43 (5H, m, $CH_2C_6\underline{H}_5$), 9.10 (1H, br, NH). UV λ_{max}^{EtOH} nm (log ε): 271 (3.98). UV $\lambda_{max}^{1\,N\,NaOH-EtOH\,(1:10)}$ nm (log ε): 269 (3.57). *Anal.* Calcd for $C_{11}H_9FN_2O_2$: C, 60.00; H, 4.09; N, 12.73. Found: C, 60.22; H, 4.30; N, 12.51.

1,3-Dibenzyl-5-fluorouracil (6g) Compound **5** (1.30 g, 10 mmol) was dissolved in DMF (20 ml), and 60% NaH (1.20 g, 30 mmol) was added to the resulting solution. The mixture was treated according to the procedure described above for **2f** to give **6g** (2.22 g, 72%) as white needles, mp 148—149 °C. MS *m/z*: 310 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 4.35 (2H, s, $C\underline{H}_2C_6H_5$), 4.88, 5.15 (1H each, s, $C\underline{H}_2C_6H_5$), 7.15 (1H, d, 6-H, J=5.4 Hz), 7.20—7.57 (10H, m, $CH_2C_6\underline{H}_5 \times 2$). *Anal.* Calcd for $C_{18}H_{15}FN_2O_2$: C, 69.68; H, 4.84; N, 9.03. Found: C, 69.57; H, 4.88; N, 9.28.

General Procedure for the Synthesis of 3-Alkyl-2′,3′,5′-tri-*O*-benzoyluridines (12a—c) A mixture of 2′,3′,5′-tri-*O*-benzoyluridine (**10**, 5 mmol)[8] and 60% NaH (5 mmol) in DMF (50 ml) was stirred at 60 °C for 1 h. Alkyl halide (7.5 mmol) was added, and the mixture was stirred at 60—70 °C for 10 h. Water (50 ml) was added to the solution, and the mixture was extracted with $CHCl_3$ (30 ml × 3). The combined extracts were dried (Na_2SO_4), and then the filtrate was concentrated *in vacuo*. The residue was taken up in a small volume of $CHCl_3$, and subjected to column chromatography on silica gel with $CHCl_3$–EtOH (20 : 1). The fraction containing the desired product was collected and concentrated, and the residue was recrystallized from an appropriate solvent; yields, melting points, and MS data are listed in Table II.

2′,3′,5′,-Tri-*O*-benzoyl-3-methyluridine (12a) ^{1}H-NMR ($CDCl_3$) δ: 3.30 (3H, s, NCH_3), 4.50—4.88 (3H, m, 4′-H, 5′-H), 5.65 (1H, d, 5-H, J=7.8 Hz), 5.77 (1H, dd, 2′-H, J=4.8, 6.0 Hz), 5.90 (1H, dd, 3′-H, J=4.2, 6.0 Hz), 6.22 (1H, d, 1′-H, J=4.8 Hz), 7.33 (1H, d, 6-H, J=7.8 Hz), 7.24—7.65, 7.83—8.21 (15H, m, $C_6H_5 \times 3$). *Anal.* Calcd for $C_{31}H_{26}N_2O_9$: C, 65.26; H, 4.59; N, 4.91. Found: C, 65.12; H, 4.75; N, 4.79.

2′,3′,5′-Tri-*O*-benzoyl-3-ethyluridine (12b) ^{1}H-NMR ($CDCl_3$) δ: 1.17 (3H, t, $CH_2C\underline{H}_3$, J=7.2 Hz), 3.95 (2H, q, $C\underline{H}_2CH_3$, J=7.2 Hz), 4.54—4.90 (3H, m, 4′-H, 5′-H), 5.62 (1H, d, 5-H, J=8.2 Hz), 5.76 (1H, dd, 2′-H, J=4.8, 6.0 Hz), 5.90 (1H, dd, 3′-H, J=4.2, 6.0 Hz), 6.28 (1H, d, 1′-H, J=4.8 Hz), 7.34 (1H, d, 6-H, J=8.2 Hz), 7.25—7.68, 7.86—8.20 (15H, m, $C_6H_5 \times 3$). *Anal.* Calcd for $C_{32}H_{28}N_2O_9$: C, 65.75; H, 4.83; N, 4.79. Found: C, 65.64; H, 4.87; N, 4.68.

2′,3′,5′-Tri-*O*-benzoyl-3-bezyluridine (12c) ^{1}H-NMR ($CDCl_3$) δ: 4.52—4.90 (3H, m, 4′-H, 5′-H), 5.03, 5.06 (1H each, s, $C\underline{H}_2C_6H_5$), 5.65

TABLE II. Reactions of **10**, **11** with Alkylating Agents

Starting material	Alkylating agent	60% NaH	K_2CO_3	Solvent	Product		
					Yield (%)	mp[a] (°C)	MS (*m/z*)
10 2.78 g, 5 mmol	MeI 1.07 g, 7.5 mmol	0.20 g, 5 mmol	—	DMF	40	57—60	570
10 2.78 g, 5 mmol	EtI 1.17 g, 7.5 mmol	0.20 g, 5 mmol	—	DMF	59	75—76	584
10 2.78 g, 5 mmol	BnCl 0.95 g, 7.5 mmol	0.20 g, 5 mmol	—	DMF	55	76—78	646
11 2.87 g, 5 mmol	MeI 1.07 g, 7.5 mmol	—	345 mg, 2.5 mmol	Acetone	57	88—89	588
11 5.74 g, 10 mmol	EtI 2.34 g, 15 mmol	—	0.69 g, 5 mmol	Acetone	55	72—73	602
11 5.74 g, 10 mmol	BnCl 1.91 g, 15 mmol	—	0.69 g, 5 mmol	Acetone	54	77—78	664

a) Recrystallized from $CHCl_3$–hexane (1 : 1).

TABLE III. Photocycloaddition Reactions of **2** or **6** with **3** in Acetone at Room Temperature

Starting material	Product			*Anal.* Calcd (%)			Found (%)		
	Yield (%)	mp[a] (°C)	MS (*m/z*)	C	H	N	C	H	N
2a	77	154—156	210	62.83	8.63	13.32	62.79	8.81	13.15
2b	76	69—70	224	64.25	8.99	12.49	64.18	9.05	12.37
2c	68	183—184	224	64.25	8.99	12.49	64.16	9.15	12.36
2d	56	Oil	252	66.63	9.59	11.10	66.38	9.47	11.09
2e	89	144—145	286	71.30	7.74	9.78	71.41	7.90	9.95
2f	73	Oil	376	76.56	7.50	7.44	76.51	7.66	7.31
6a	56	130—131	228	57.89	7.46	12.28	57.63	7.44	12.08
6b	99	123—124	228	57.89	7.46	12.28	58.01	7.04	12.10
6c	93	136—137	242	59.50	7.85	11.57	59.77	7.67	11.39
6d	41	Oil	242	59.50	7.85	11.57	59.60	7.79	11.32
6e	81	Oil	270	62.22	8.52	10.37	62.18	8.79	10.60
6f	99	159—160	304	67.11	6.91	9.21	67.37	7.19	9.28
6g	93	98—100	394	73.10	6.85	7.11	72.98	7.03	6.92

a) Recrystallized from $CHCl_3$–hexane (1 : 1).

(1H, d, 5-H, J=8.4 Hz), 5.70 (1H, t, 2′-H, J=5.4 Hz), 5.90 (1H dd, 3′-H, J=4.2, 5.4 Hz), 6.33 (1H, d, 1′-H, J=5.4 Hz), 7.18—7.63, 7.80—8.18 (21H, m, C_6H_5×4, 6-H). *Anal.* Calcd for $C_{37}H_{30}N_2O_9$: C, 68.72; H, 4.68; N, 4.33. Found: C, 68.75; H, 4.81; N, 4.17.

General Procedure for the Synthesis of 3-Alkyl-2′,3′,5′-tri-*O*-benzoyl-5-fluorouridines (13a—c) A mixture of 2′,3′,5′-tri-*O*-benzoyl-5-fluorouridine (**11**)[9], alkyl halide and potassium carbonate in dry acetone was stirred at 60—70 °C for 7 h, then filtered, and the filtrate was concentrated. The residue was taken up in a small volume of $CHCl_3$, and subjected to column chromatography on silica gel, with $CHCl_3$–EtOH (20 : 1). The crude product was recrystallized from an appropriate solvent; yields, melting points, and MS data are listed in Table II.

2′,3′,5′-Tri-*O*-benzoyl-5-fluoro-3-methyluridine (13a) ^{1}H-NMR ($CDCl_3$) δ: 3.30 (3H, s, NCH_3), 4.58—4.80 (3H, m, 4′-H, 5′-H), 5.63—5.93 (2H, m, 2′-H, 3′-H), 6.27 (1H, d, 1′-H, J=5.4 Hz), 7.24—7.70, 7.85—8.20 (16H, m, C_6H_5×3, 6-H). *Anal.* Calcd for $C_{31}H_{25}FN_2O_9$: C, 63.27; H, 4.25; N, 4.76. Found: C, 63.56; H, 4.40; N, 4.68.

2′,3′,5′-Tri-*O*-benzoyl-3-ethyl-5-fluorouridine (13b) ^{1}H-NMR ($CDCl_3$) δ: 1.14 (3H, t, $CH_2C\underline{H}_3$, J=7.2 Hz), 3.96 (2H, q, $C\underline{H}_2CH_3$, J=7.2 Hz), 4.60—4.83 (3H, m, 4′-H, 5′-H), 5.63—5.97 (2H, m, 2′-H, 3′-H), 6.33 (1H, d, 1′-H, J=5.4 Hz), 7.20—7.73, 7.87—8.22 (16H, m, C_6H_5×3, 6-H). *Anal.* Calcd for $C_{32}H_{27}FN_2O_9$: C, 63,79; H, 4.49; N, 4.65. Found: C, 63.57; H, 4.56; N. 4.51.

2′,3′,5′-Tri-*O*-benzoyl-3-benzyl-5-fluorouridine (13c) ^{1}H-NMR ($CDCl_3$) δ: 4.63—4.80 (3H, m, 4′-H, 5′-H), 5.08 (2H, s, $C\underline{H}_2C_6H_5$), 5.53—5.95 (2H, m, 2′-H, 3′-H), 6.40 (1H, d, 1′-H, J=5.4 Hz), 7.17—7.67, 7.75—8.20 (21H, m, C_6H_5×4, 6-H). *Anal.* Calcd for $C_{37}H_{29}FN_2O_9$: C, 66.87; H, 4.37; N, 4.22. Found: C, 66.74; H, 4.42; N, 4.12.

General Procedure for Photocycloaddition of 2 or 6 to 2,3-Dimethyl-2-butene (3) A solution of **2** or **6** (2 mmol) and 2,3-dimethyl-2-butene (**3**, 1.68 g, 20 mmol) in dry acetone (600 ml) was irradiated with a 400 W high-pressure mercury lamp through a Pyrex filter under a nitrogen atmosphere for 72 h. After evaporation of the solvent, the residue was subjected to column chromatography on silica gel with $CHCl_3$–EtOH (10 : 1). A fraction containing the product was collected and evaporated to dryness, and the residue was recrystallized from an appropriate solvent to give an analytical sample of **4** or **7**; yields, melting points, MS data, and combustion values are listed in Table III.

2,7,7,8,8-Pentamethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (4a) ^{1}H-NMR ($CDCl_3$) δ: 1.00, 1.03, 1.12, 1.27 (3H each, s, CCH_3), 2.96 (3H, s, NCH_3), 2.94 (1H, d, 6-H, J=10.2 Hz), 3.65 (1H, d, 1-H, J=10.2 Hz), 8.08 (1H, br, NH).

2,4,7,7,8,8-Hexamethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (4b) ^{1}H-NMR ($CDCl_3$) δ: 0.93, 0.97, 1.12, 1.23 (3H each, s, CCH_3), 2.93, 3.20 (3H each, s, NCH_3), 2.98 (1H, d, 6-H, J=9.6 Hz), 3.58 (1H, d, 1-H, J=9.6 Hz).

2-Ethyl-7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (4c) ^{1}H-NMR ($CDCl_3$) δ: 0.99, 1.02, 1.09, 1.24 (3H each, s, CCH_3), 1.09 (3H, t, $CH_2C\underline{H}_3$, J=7.2 Hz), 2.90, 3.77 (1H each, m, $C\underline{H}_2CH_3$), 2.88 (1H, d, 6-H, J=10.2 Hz), 3.76 (1H, d, 1-H, J=10.2 Hz), 8.37 (1H, br, NH).

2,4-Diethyl-7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (4d) ^{1}H-NMR ($CDCl_3$) δ: 0.93, 0.96, 1.09, 1.25 (3H each, s, CCH_3), 1.15, 1.21 (3H each, t, $CH_2C\underline{H}_3$, J=7.0 Hz), 2.93 (1H, d, 6-H, J=10.2 Hz), 3.67 (1H, d, 1-H, J=10.2 Hz), 2.71—3.10 (1H, m, $C\underline{H}_2CH_3$), 3.63—4.05 (1H, m, $C\underline{H}_2CH_3$), 3.88 (2H, q, $C\underline{H}_2CH_3$, J=7.0 Hz).

2-Benzyl-7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (4e) ^{1}H-NMR ($CDCl_3$) δ: 0.84, 0.86, 0.89, 1.11 (3H each, s, CCH_3), 2.82 (1H, d, 6-H, J=9.6 Hz), 3.71 (1H, d, 1-H, J=9.6 Hz), 4.01, 4.87 (1H, each, d, $C\underline{H}_2C_6H_5$, J=15.0 Hz), 7.22—7.43 (5H, m, $CH_2C_6\underline{H}_5$), 10.12 (1H, br, NH).

2,4-Dibenzyl-7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (4f) ^{1}H-NMR ($CDCl_3$) δ: 0.79, 0.88, 0.96, 1.15 (3H each, s, CCH_3), 2.85 (1H, d, 6-H, J=10.0 Hz), 3.60 (1H, d, 1-H, J=10.0 Hz), 3.84, 5.22 (1H each, d, $C\underline{H}_2C_6H_5$, J=15.0 Hz), 5.06 (2H, s, $C\underline{H}_2C_6H_5$), 7.20—7.57 (10H, m, $CH_2C_6\underline{H}_5$×2).

6-Fluoro-2,7,7,8,8-pentamethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (7a) ^{1}H-NMR ($CDCl_3$) δ: 0.92, 1.05, 1.18, 1.18 (3H each, s, CCH_3), 2.99 (3H, s, NCH_3), 3.73 (1H, d, 1-H, J=22.8 Hz), 8.22 (1H, br, NH).

6-Fluoro-4,7,7,8,8-pentamethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (7b) ^{1}H-NMR ($CDCl_3$) δ: 0.87, 1.01, 1.12 (3H each, s, CCH_3), 1.20 (3H, d, CCH_3, J=3.9 Hz), 3.21 (3H, s, NCH_3), 3.83 (1H, d, 1-H, J=22.8 Hz), 7.00 (1H, br, NH).

6-Fluoro-2,4,7,7,8,8-hexamethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (7c) ^{1}H-NNR ($CDCl_3$) δ: 0.82, 0.99, 1.18 (3H each, s, CCH_3), 1.21 (3H, d, CCH_3, J=4.2 Hz), 3.00, 3.22 (3H each, s, NCH_3), 3.78 (1H, d, 1-H, J=22.8 Hz).

2-Ethyl-6-fluoro-7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (7d) ^{1}H-NMR ($CDCl_3$) δ: 0.82, 1.00, 1.14, 1.18 (3H each, s, CCH_3), 1.14 (3H, t, $CH_2C\underline{H}_3$, J=7.2 Hz), 3.75 (1H, d, 1-H, J=22.8 Hz), 3.91 (2H, q, $C\underline{H}_2CH_3$, J=7.2 Hz), 8.43 (1H, br, NH).

2,4-Diethyl-6-fluoro-7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]-octane-3,5-dione (7e) ^{1}H-NMR ($CDCl_3$) δ: 0.82, 1.01, 1.18 (3H, each, s, CCH_3), 1.25 (3H, d, CCH_3, J=3.9 Hz), 1.15 (3H, m, $CH_2C\underline{H}_3$), 1.23 (3H, t, $CH_2C\underline{H}_3$, J=7.2 Hz), 3.07, 3.68 (1H each, m, $C\underline{H}_2CH_3$), 3.72 (1H, d, 1-H, J=22.8 Hz), 3.92 (2H, q, $C\underline{H}_2CH_3$, J=7.2 Hz).

2-Benzyl-6-fluoro-7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (7f) ^{1}H-NMR ($CDCl_3$) δ: 0.88, 0.95, 1.02, 1.10 (3H each, s, CCH_3), 3.72 (1H, d, 1-H, J=22.8 Hz), 4.13, 4.99 (1H each, d, $C\underline{H}_2C_6H_5$, J=15.0 Hz), 7.18—7.47 (5H, m, $CH_2C_6\underline{H}_5$), 8.47 (1H, br, NH).

2,4-Dibenzyl-6-fluoro-7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]-octane-3,5-dione (7g) ^{1}H-NMR ($CDCl_3$) δ: 0.58, 0.87, 0.91 (3H each, s, CCH_3), 1.11 (3H, d, CCH_3, J=3.9 Hz), 3.68 (1H, d, 1-H, J=22.8 Hz), 4.11, 5.01 (1H each, d, $C\underline{H}_2C_6H_5$, J=14.4 Hz), 5.09 (2H, s, $C\underline{H}_2C_6H_5$), 7.15—7.56 (10H, m, $CH_2C_6\underline{H}_5$×2).

Photoaddition of 2′,3′-*O*-Isopropylideneuridine (8) to 3 A solution of 2′,3′-*O*-isopropylideneuridine (**8**, 1.50 g, 5.28 mmol) and **3** (4.40 g, 52.8 mmol) in dry acetone (600 ml) was irradiated with a 400 W high-pressure mercury lamp through an Pyrex filter under nitrogen atmosphere for 48 h. After evaporation of the solvent, the residue was subjected to preparative TLC (precoated TLC plates, Silica gel 60F-254, Merck) with $CHCl_3$ to give **9a** (1.05 g, 54%) as colorless needles (mp 218—219 °C from $CHCl_3$) and **9b** (117 mg, 6%) as a colorless syrup. The ratio of **9a** and **9b** was 9 : 1 as determined from the isolated yields.

TABLE IV. Atomic Coordinates (10^4) with Their Standard Deviations in Parentheses and Equivalent Isotropic Temperature Factors

Atom	x	y	z	B_{eq}	Atom	x	y	z	B_{eq}
O1	−1874 (6)	9738 (3)	8811 (10)	5.0	C8	−116 (9)	8549 (4)	4876 (12)	3.1
O2	−3757 (7)	8319 (3)	5917 (12)	5.7	C9	−1494 (10)	7627 (4)	4603 (17)	4.5
O3	818 (5)	9741 (2)	7560 (10)	3.9	C10	−997 (12)	8165 (5)	1816 (17)	6.0
O4	−269 (7)	10861 (3)	5099 (10)	5.1	C11	1130 (10)	8571 (4)	3999 (18)	5.1
O5	1306 (7)	11050 (3)	6960 (11)	5.7	C12	46 (9)	8367 (4)	6851 (15)	4.0
O6	−101 (9)	10046 (4)	11266 (10)	6.6	C13	−39 (8)	9914 (3)	6188 (14)	3.2
N2	−1024 (6)	9478 (3)	6105 (9)	2.2	C14	−428 (8)	10510 (4)	6615 (15)	3.6
N4	−2747 (7)	9023 (3)	7266 (11)	3.5	C15	515 (11)	10708 (4)	8017 (14)	4.3
C1	−938 (8)	9082 (3)	4673 (12)	2.7	C16	1223 (9)	10206 (4)	8633 (16)	4.4
C3	−1860 (8)	9445 (4)	7443 (14)	3.1	C17	1061 (13)	10047 (5)	10651 (18)	6.2
C5	−2926 (8)	8652 (4)	5878 (15)	3.5	C18	597 (9)	11283 (4)	5517 (14)	3.9
C6	−2067 (8)	8710 (3)	4296 (13)	3.0	C19	1419 (14)	11342 (7)	3878 (22)	8.2
C7	−1176 (8)	8204 (4)	3851 (15)	3.4	C20	−29 (14)	11830 (4)	6037 (19)	6.5

TABLE V. Bond Lengths (Å) with Their Standard Deviations in Parentheses

O1–C3	1.225 (12)	C5–C6	1.499 (13)
O2–C5	1.202 (11)	C6–C1	1.538 (12)
O3–C13	1.434 (11)	C6–C7	1.582 (12)
O3–C16	1.429 (12)	C7–C8	1.604 (13)
O4–C14	1.405 (12)	C7–C9	1.521 (13)
O4–C18	1.411 (12)	C7–C10	1.514 (16)
O5–C15	1.417 (13)	C8–C11	1.502 (15)
O5–C18	1.425 (12)	C8–C12	1.528 (13)
O6–C17	1.342 (16)	C13–C14	1.514 (12)
N2–C1	1.418 (10)	C14–C15	1.529 (14)
N2–C3	1.342 (11)	C15–C16	1.492 (14)
N2–C13	1.493 (10)	C16–C17	1.544 (17)
N4–C3	1.399 (11)	C18–C19	1.508 (18)
N4–C5	1.365 (12)	C18–C20	1.518 (15)
C1–C8	1.559 (12)		

TABLE VI. Bond Angles (°) with Their Standard Deviations in Parentheses

C3–N2–C1	123.4 (6)	C19–C18–C20	112.8 (10)
C3–N4–C5	129.2 (8)	O1–C3–N4	118.4 (8)
C13–N2–C1	116.5 (6)	O1–C3–N2	125.4 (8)
C13–N2–C3	119.8 (6)	N4–C3–N2	116.2 (8)
C13–O3–C16	111.5 (6)	O2–C5–N4	121.0 (9)
C14–O4–C18	109.4 (7)	O2–C5–C6	123.2 (9)
C15–O5–C18	107.8 (7)	N4–C5–C6	115.7 (7)
O3–C13–N2	107.2 (6)	C5–C6–C1	114.2 (7)
O3–C13–C14	107.7 (7)	C5–C6–C7	118.2 (7)
N2–C13–C14	117.3 (7)	C1–C6–C7	89.3 (6)
O4–C14–C13	110.9 (8)	N2–C1–C6	117.7 (7)
O4–C14–C15	105.7 (7)	N2–C1–C8	120.5 (7)
C13–C14–C15	103.9 (7)	C6–C1–C8	90.4 (6)
O5–C15–C14	102.3 (7)	C1–C8–C7	87.7 (6)
O5–C15–C16	108.3 (8)	C1–C8–C11	116.6 (7)
C14–C15–C16	107.7 (8)	C1–C8–C12	112.8 (7)
O3–C16–C15	107.0 (8)	C7–C8–C11	117.6 (8)
O3–C16–C17	107.9 (8)	C7–C8–C12	112.7 (7)
C15–C16–C17	115.4 (9)	C11–C8–C12	108.4 (8)
O6–C17–C16	115.7 (10)	C6–C7–C8	87.2 (6)
O4–C18–O5	104.3 (7)	C6–C7–C10	109.3 (8)
O4–C18–C19	106.8 (9)	C6–C7–C9	118.3 (8)
O4–C18–C20	111.5 (8)	C8–C7–C10	113.9 (8)
O5–C18–C19	108.3 (9)	C8–C7–C9	117.0 (8)
O5–C18–C20	112.8 (8)	C10–C7–C9	109.6 (8)

(1*R*,6*R*)-2-(2,3-*O*-Isopropylidene-β-D-ribofuranosyl)-7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (9a) mp 218—219 °C. MS *m/z*: 368 (M^+). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 1.00, 1.07, 1.08, 1.23 (3H each, s, CCH_3), 1.33, 1.53 (3H each, s, isopropylidene), 2.93 (1H, d, 6-H, J=10.0 Hz), 2.95 (1H, br, 5′-OH), 3.68—3.86 (2H, m, 5′-H), 3.87 (1H, d, 1-H, J=10.0 Hz), 4.17 (1H, dd, 4′-H, J=3.3, 6.3 Hz), 4.82 (1H, d, 1′-H, J=3.0 Hz), 4.97 (1H, dd, 3′-H, J=3.3, 6.6 Hz), 5.09 (1H, dd, 2′-H, J=3.0, 6.6 Hz), 8.14 (1H, br, NH). *Anal.* Calcd for $C_{18}H_{28}N_2O_6$: C, 58.68; H, 7.66; N, 7.60. Found: C, 58.59; H, 7.82; N, 7.53.

(1*S*,6*S*)-2-(2,3-*O*-Isopropylidene-β-D-ribofuranosyl)-7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (9b) MS *m/z*: 368 (M^+). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 1.03, 1.04, 1.08, 1.24 (3H each, s, CCH_3), 1.35, 1.52 (3H each, s, isopropylidene), 2.98 (1H, d, 6-H, J=10.0 Hz), 3.20 (1H, br, 5′-OH), 3.71—3.95 (2H, m, 5′-H), 3.86 (1H, d, 1-H, J=10.0 Hz), 4.16 (1H, dd, 4′-H, J=3.3, 6.3 Hz), 4.80 (1H, d, 1′-H, J=4.0 Hz), 4.95 (1H, dd, 3′-H, J=3.3, 6.3 Hz), 5.27 (1H, dd, 2′-H, J=4.0, 6.3 Hz), 7.44 (1H, br, NH). *Anal.* Calcd for $C_{18}H_{28}N_2O_6$: C, 58.68; H, 7.66; N, 7.60. Found: C, 58.42; H, 7.90; N, 7.37.

X-Ray Crystallographic Analysis of 9a A crystal of **9a** with the dimensions of 0.3×0.4×0.4 mm^3 was used for the analysis. The cell dimensions and diffraction intensities were measured on a Rigaku four-circle diffractometer, using graphite-monochromated Cu K_α radiation (λ=1.5479 Å).

Crystal Data: $C_{18}H_{28}N_2O_6$, orthorhombic, space group $P2_12_12_1$, a=10.871(2) Å, b=23.802(5) Å, c=7.365(1) Å, V=1905.7 Å^3, Z=4, D_c=1.284 g·cm^{-3}. One thousand four hundred and eighty three independent reflections in the range of $2\theta<150°$ were collected by the use of the 2θ–ω scan mode with a scanning rate of 8° (2θ) min^{-1}. A total of 1375 independent reflections with $|F_O|>3\sigma(|F_O|)$ were obtained and corrected for Lorentz and polarization factors but not for absorption. The structure was elucidated by a direct method using MULTAN.[19] The E-map of the phase set with the highest figure of merit showed the skeleton of the molecule, whose structure was refined by a block-diagonal least squares method with anisotropic temperature factors. A difference Fourier synthesis was then calculated and the positions of all hydrogen atoms except those of methyl groups were found. The positions of the 15 hydrogen atoms in methyl groups were calculated and inculded in the final stage of refinement. The atomic scattering factors were those given by the International Tables for X-Ray Crystallography.[20] The final R value was 8.9%, where $R=\sum||F_O|-|F_C||/\sum|F_C|$.

The final atomic parameters are listed in Table IV. Bond lengths and angles are shown in Tables V and VI. No abnormal lengths or angles were found in the structure.

General Procedure for the Photoaddition of 11—13 to 3 A solution of one of **11—13** (2 mmol) and **3** (1.68 g, 20 mmol) in dry acetone (600 ml) was irradiated with a 400 W high-pressure mercury lamp through a Pyrex filter under a nitrogen atmosphere for 72 h. After evaporation of the solvent, the residue was subjected to column chromatography on silica gel with $CHCl_3$–EtOH (10:1), and the products were recrystallized from appropriate solvents; yields, melting points, MS data, and combustion values are listed in Table VII.

(1*R*,6*R*)-4,7,7,8,8-Pentamethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (14a) and (1*S*,6*S*)-4,7,7,8,8-Pentamethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (15a) The ratio of **14a** and **15a** was 1.2:1 as determined from the isolated yields.

14a: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.89, 0.91, 0.93, 1.01 (3H each, s, CCH_3), 2.93 (1H, d, 6-H, J=10.2 Hz, 3.17 (3H, s, NCH_3), 3.94 (1H, d, 1-H, J=10.2 Hz), 4.53—4.77 (3H, m, 4′-H, 5′-H), 5.86 (1H, t, 2′-H, J=6.0 Hz), 5.89 (1H, dd, 3′-H, J=4.0, 6.0 Hz), 6.21 (1H, d, 1′-H,

TABLE VII. Photocycloaddition Reactions of **11**—**13** with **3** in Acetone at Room Temperature

Starting material	Product	Product			*Anal.* Calcd (%)			Found (%)		
		Yield (%)	mp (°C)	MS (*m/z*)	C	H	N	C	H	N
12a	**14a**	35	140—141[a]	654	67.87	5.85	4.28	67.61	6.03	4.07
	15a	29	71—73[a]	654	67.87	5.85	4.28	67.79	5.98	4.11
12b	**14b, 15b**	91	Foam	668	68.25	6.03	4.19	68.15	6.16	3.99
12c	**14c, 15c**	93	Foam	730	70.67	5.79	3.83	70.53	5.91	3.65
11	**16a**	66	116—118[a]	658	65.65	5.32	4.26	65.37	5.52	4.20
	17a	26	88—90[a]	658	65.65	5.32	4.26	65.43	5.41	4.08
13a	**16b, 17b**	99	Foam	672	66.07	5.51	4.17	65.87	5.72	3.90
13b	**16c, 17c**	96	Foam	686	66.46	5.72	4.07	66.25	5.86	3.95
13c	**16d, 17d**	92	Foam	748	68.97	5.51	3.74	68.81	5.73	3.49

a) Recrystallized from benzene–hexane (1 : 1).

TABLE VIII. Debenzoylations of **14**—**17** with NaOMe

Starting material	Product			*Anal.* Calcd (%)			Found (%)		
	Yield (%)	mp (°C)	MS (*m/z*)	C	H	N	C	H	N
14a	90	123—124[a]	342	56.12	7.65	8.18	55.88	7.85	8.11
15a	92	Foam	342	56.12	7.65	8.18	56.07	7.72	8.09
14b, 15b	91	Foam	356	57.29	7.92	7.86	57.00	8.19	7.65
14c, 15c	96	Foam	418	63.14	7.23	6.69	63.36	7.43	6.42
16a	61	127—128[a]	346	52.01	6.69	8.08	51.92	6.77	7.98
17a	69	121—122[a]	346	52.01	6.69	8.08	51.89	6.81	8.02
16b, 17b	75	Foam	360	53.32	6.99	7.77	53.10	7.18	7.56
16c, 17c	90	Foam	374	54.53	7.26	7.48	54.43	7.39	7.45
16d, 17d	78	Foam	436	60.53	6.69	6.41	60.43	6.53	6.13

a) Recrystallized from EtOH.

J=6.0 Hz), 7.31—7.63, 7.92—8.15 (15H, m, $C_6\underline{H}_5\times3$).

15a: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.91, 0.92, 0.96, 1.10 (3H each, s, CCH_3), 2.95 (1H, d, 6-H, J=10.2 Hz), 3.19 (3H, s, NCH_3), 3.89 (1H, d, 1-H, J=10.2 Hz), 4.50—4.89 (3H, m, 4′-H, 5′-H), 5.56 (1H, dd, 2′-H, J=5.0, 6.0 Hz), 5.87 (1H, d, 1′-H, J=5.0 Hz), 5.98 (1H, t, 3′-H, J=6.0 Hz), 7.26—7.60, 7.87—8.14 (15H, m, $C_6\underline{H}_5\times3$).

(1*R*,6*R*)-4-Ethyl-7,7,8,8-tetramethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (14b) and (1*S*,6*S*)-4-Ethyl-7,7,8,8-tetramethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (15b) The ratio of **14b** and **15b** was 3 : 2 as determined from the ^{1}H-NMR spectra.

14b: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.88, 0.91, 0.93, 0.98 (3H each, s, CCH_3), 1.10 (3H, t, $CH_2C\underline{H}_3$, J=7.0 Hz), 2.91 (1H, d, 6-H, J=10.2 Hz), 3.85 (2H, q, $C\underline{H}_2CH_3$, J=7.0 Hz), 3.92 (1H, d, 1-H, J=10.2 Hz), 4.53—4.77 (3H, m, 4′-H, 5′-H), 5.84 (1H, t, 2′-H, J=6.0 Hz), 5.89 (1H, dd, 3′-H, J=4.0, 6.0 Hz), 6.25 (1H, d, 1′-H, J=6.0 Hz), 7.30—7.61, 7.85—8.13 (15H, m, $C_6\underline{H}_5\times3$).

15b: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.92, 0.93, 0.95, 1.09 (3H each, s, CCH_3), 1.14 (3H, t, $CH_2C\underline{H}_3$, J=7.0 Hz), 2.93 (1H, d, 6-H, J=10.2 Hz), 3.82—3.94 (2H, m, $C\underline{H}_2CH_3$), 3.88 (1H, d, 1-H, J=10.2 Hz), 4.51—4.89 (3H, m, 4′-H, 5′-H), 5.55 (1H, dd, 2′-H, J=5.3, 6.0 Hz), 5.90 (1H, d, 1′-H, J=5.3 Hz), 5.98 (1H, t, 3′-H, J=6.0 Hz), 7.28—7.60, 7.88—8.15 (15H, m, $C_6\underline{H}_5\times3$).

(1*R*,6*R*)-4-Benzyl-7,7,8,8-tetramethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (14c) and (1*S*,6*S*)-4-Benzyl-7,7,8,8-tetramethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (15c) The ratio of **14c** and **15c** was 3 : 2 as determined from the ^{1}H-NMR spectra.

14c: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.80, 0.86, 0.87, 0.94 (3H each, s, CCH_3), 2.93 (1H, d, 6-H, J=9.8 Hz), 3.93 (1H, d, 1-H, J=9.8 Hz), 4.53—4.76 (3H, m, 4′-H, 5′-H), 5.01 (2H, br, $C\underline{H}_2C_6H_5$), 5.80 (1H, t, 2′-H, J=6.5 Hz), 5.86 (1H, dd, 3′-H, J=3.0, 6.5 Hz), 6.37 (1H, d, 1′-H, J=6.5 Hz), 7.20—7.62, 7.88—8.15 (20H, m, $C_6\underline{H}_5\times4$).

15c: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.84, 0.88, 0.92, 1.06 (3H each, s, CCH_3), 2.95 (1H, d, 6-H, J=9.8 Hz), 3.90 (1H, d, 1-H, J=9.8 Hz), 4.50—4.88 (3H, m, 4′-H, 5′-H), 4.96 (2H, br, $C\underline{H}_2C_6H_5$), 5.50 (1H, t, 2′-H, J=5.5 Hz), 5.96 (1H, d, 1′-H, J=5.5 Hz), 5.98 (1H, t, 3′-H, J=5.5 Hz), 7.20—7.62, 7.88—8.15 (20H, m, $C_6\underline{H}_5\times4$).

(1*S*,6*S*)-6-Fluoro-7,7,8,8-tetramethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (16a) and (1*R*,6*R*)-6-Fluoro-7,7,8,8-tetramethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (17a) The ratio of **16a** and **17a** was 5 : 2 as determined from the isolated yields.

16a: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.96, 0.96, 0.98 (3H each, s, CCH_3), 0.89 (3H, d, CCH_3, J=4.0 Hz), 4.06 (1H, d, 1-H, J=21.0 Hz), 4.57—4.75 (3H, m, 4′-H, 5′-H), 5.70 (1H, dd, 2′-H, J=6.5, 7.5 Hz), 5.83 (1H, dd, 3′-H, J=3.0, 6.5 Hz), 6.42 (1H, d, 1′-H, J=7.5 Hz), 7.32—7.64, 7.93—8.16 (15H, m, $C_6\underline{H}_5\times3$), 7.78 (1H, br, NH).

17a: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.94, 1.02, 1.09 (3H each, s, CCH_3), 1.08 (3H, d, CCH_3, J=4.0 Hz), 4.05 (1H, d, 1-H, J=21.0 Hz), 4.54—4.90 (3H, m, 4′-H, 5′-H), 5.58 (1H, dd, 2′-H, J=5.5, 6.0 Hz), 5.89 (1H, d, 1′-H, J=5.5 Hz), 5.92 (1H, dd, 3′-H, J=6.0, 8.0 Hz), 7.28—7.60, 7.84—8.13 (15H, m, $C_6\underline{H}_5\times3$), 7.81 (1H, br, NH).

(1*S*,6*S*)-6-Fluoro-4,7,7,8,8-pentamethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (16b) and (1*R*,6*R*)-6-Fluoro-4,7,7,8,8-pentamethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (17b) The ratio of **16b** and **17b** was 5 : 2 as determined from the ^{1}H-NMR spectra.

16b: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.86, 0.93, 0.96 (3H each, s, CCH_3), 0.91 (3H, d, CCH_3, J=4.0 Hz), 3.20 (3H, s, NCH_3), 4.03 (1H, d, 1-H, J=21.5 Hz), 4.56—4.75 (3H, m, 4′-H, 5′-H), 5.74 (1H, dd, 2′-H, J=6.5, 7.0 Hz), 5.85 (1H, dd, 3′-H, J=3.0, 7.0 Hz), 6.37 (1H, d, 1′-H, J=6.5 Hz), 7.33—7.64, 7.94—8.17 (15H, m, $C_6\underline{H}_5\times3$).

17b: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.83, 0.97 (3H each, s, CCH_3), 1.08, 1.10 (3H each, d, CCH_3, J=4.0 Hz), 3.21 (3H, s, NCH_3), 3.98 (1H, d, 1-H, J=22.0 Hz), 4.53—4.88 (3H, m, 4′-H, 5′-H), 5.65 (1H, dd, 2′-H, J=5.0, 6.0 Hz), 5.81 (1H, d, 1′-H, J=5.0 Hz), 5.98 (1H, t, 3′-H, J=6.0 Hz), 7.27—7.60, 7.84—8.16 (15H, m, $C_6H_5\times3$).

(1*S*,6*S*)-4-Ethyl-6-fluoro-7,7,8,8-tetramethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (16c) and (1*R*,6*R*)-4-Ethyl-6-fluoro-7,7,8,8-tetramethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (17c) The ratio of **16c** and **17c** was 3 : 1 as determined from the ^{1}H-NMR spectra.

16c: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.87, 0.94, 0.96 (3H each, s, CCH_3), 0.90 (3H, d, CCH_3, J=4.0 Hz), 1.15 (3H, t, $CH_2C\underline{H}_3$, J=7.0 Hz), 3.89 (2H, q, $C\underline{H}_2CH_3$, J=7.0 Hz), 4.01 (1H, d, 1-H, J=22.0 Hz), 4.57—4.75

(3H, m, 4′-H, 5′-H), 5.72 (1H, dd, 2′-H, J=6.0, 7.0 Hz), 5.85 (1H, dd, 3′-H, J=3.0, 6.0 Hz), 6.39 (1H, d, 1′-H, J=7.0 Hz), 7.33—7.63, 7.94—8.16 (15H, m, $C_6H_5 \times 3$).

17c: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.85, 0.97 (3H each, s, CCH_3), 1.08, 1.10 (3H, d, CCH_3, J=4.0 Hz), 1.15 (3H, t, $CH_2C\underline{H}_3$, J=7.0 Hz), 3.86—3.94 (2H, m, $C\underline{H}_2CH_3$), 3.96 (1H, d, 1-H, J=22.0 Hz), 4.53—4.88 (3H, m, 4′-H, 5′-H), 5.64 (1H, dd, 2′-H, J=4.5, 6.0 Hz), 5.83 (1H, d, 1′-H, J=4.5 Hz), 5.98 (1H, t, 3′-H, J=6.0 Hz), 7.26—7.60, 7.82—8.12 (15H, m, $C_6H_5 \times 3$).

(1*S*,6*S*)-4-Benzyl-6-fluoro-7,7,8,8-tetramethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (16d) and (1*R*,6*R*)-4-Benzyl-6-fluoro-7,7,8,8-tetramethyl-2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (17d) The ratio of **16d** and **17d** was 3 : 1 as determined from the ^{1}H-NMR spectra.

16d: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.63, 0.81, 0.90 (3H each, s, CCH_3), 0.85 (3H, d, CCH_3, J=4.0 Hz), 4.00 (1H, d, 1-H, J=21.5 Hz), 4.57—4.74 (3H, m, 4′-H, 5′-H), 5.01 (2H, br s, $C\underline{H}_2C_6H_5$), 5.71 (1H, dd, 2′-H, J=6.5, 7.0 Hz), 5.84 (1H, dd, 3′-H, J=3.0, 6.5 Hz), 6.47 (1H, d, 1′-H, J=7.0 Hz), 7.18—7.62, 7.84—8.16 (20H, m, $C_6\underline{H}_5 \times 4$).

17d: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 0.63, 1.03, 1.32 (3H each, s, CCH_3), 1.04 (3H, d, CCH_3, J=4.0 Hz), 3.98 (1H, d, 1-H, J=21.5 Hz), 4.52—4.88 (3H, m, 4′-H, 5′-H), 4.98 (2H, br s, $C\underline{H}_2C_6H_5$), 5.59 (1H, dd, 2′-H, J=5.0, 6.0 Hz), 5.92 (1H, d, 1′-H, J=5.0 Hz), 5.96 (1H, t, 3′-H, J=6.0 Hz), 7.20—7.61, 7.84—8.15 (20H, m, $C_6\underline{H}_5 \times 4$).

General Procedure for the Debenzoylation of 14—17 A solution of one of **14**—**17** (2 mmol) in anhydrous MeOH (24 ml) was treated with 1 N NaOMe in MeOH (0.46 ml) and then heated at 50—60 °C for 3 h. The reaction mixture was neutralized carefully with Dowex 50 (H^+-form) resin to pH 6.0. The resin was removed by filtration and washed well with MeOH. The filtrates and washings were combined and evaporated *in vacuo*. The residue was subjected to column chromatography on silica gel with $CHCl_3$–MeOH (5 : 1). The eluate was evaporated *in vacuo*, and the residue was recrystallized from an appropriate solvent; yields, melting points, MS data, and combustion values are listed in Table VIII.

(1*R*,6*R*)-4,7,7,8,8-Pentamethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (18a) ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.80, 0.84, 0.94, 1.19 (3H each, s, CCH_3), 2.93 (1H, d, 6-H, J=10.0 Hz), 3.04 (3H, s, NCH_3), 3.45—3.71 (3H, m, 4′-H, 5′-H), 3.82 (1H, br t, 3′-H, J=5.0 Hz), 3.97 (1H, br t, 2′-H, J=6.5 Hz), 4.00 (1H, d, 1-H, J=10.0 Hz), 5.56 (1H, d, 1′-H, J=6.5 Hz).

(1*S*,6*S*)-4,7,7,8,8-Pentamethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (19a) ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.85, 0.88, 0.99, 1.19 (3H each, s, CCH_3), 2.89 (1H, d, 6-H, J=10.0 Hz), 3.04 (3H, s, NCH_3), 3.46—3.72 (3H, m, 4′-H, 5′-H), 3.79 (1H, dd, 2′-H, J=5.5, 7.5 Hz), 3.89 (1H, dd, 3′-H, J=2.0, 5.5 Hz), 4.23 (1H, d, 1-H, J=10.0 Hz), 5.74 (1H, d, 1′-H, J=7.5 Hz).

(1*R*,6*R*)-4-Ethyl-7,7,8,8-tetramethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (18b) and (1*S*,6*S*)-4-Ethyl-7,7,8,8-tetramethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (19b) 18b: ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.84, 0.86, 0.93, 1.19 (3H each, s, CCH_3), 1.13 (3H, t, $CH_2C\underline{H}_3$, J=7.0 Hz), 2.92 (1H, d, 6-H, J=10.0 Hz), 3.45—3.71 (3H, m, 4′-H, 5′-H), 3.74 (2H, q, $C\underline{H}_2CH_3$, J=7.0 Hz), 3.82 (1H, dd, 3′-H, J=4.0, 6.0 Hz), 3.97 (1H, t, 2′-H, J=6.0 Hz), 3.99 (1H, d, 1-H, J=10.0 Hz), 5.57 (1H, d, 1′-H, J=6.0 Hz).

19b: ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.81, 0.89, 0.99, 1.19 (3H each, s, CCH_3), 1.02 (3H, t, $CH_2C\underline{H}_3$, J=7.0 Hz), 2.88 (1H, d, 6-H, J=10.0 Hz), 3.45—3.71 (3H, m, 4′-H, 5′-H), 3.75 (2H, q, $C\underline{H}_2CH_3$, J=7.0 Hz), 3.79 (1H, dd, 2′-H, J=5.0, 7.5 Hz), 3.89 (1H, dd, 3′-H, J=2.0, 5.0 Hz), 4.21 (1H, d, 1-H, J=10.0 Hz), 5.77 (1H, d, 1′-H, J=7.5 Hz).

(1*R*,6*R*)-4-Benzyl-7,7,8,8-tetramethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (18c) and (1*S*,6*S*)-4-Benzyl-7,7,8,8-tetramethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (19c) 18c: ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.68. 0.77, 0.92, 1.18 (3H each, s, CCH_3), 2.98 (1H, d, 6-H, J=10.0 Hz), 3.42—3.72 (3H, m, 4′-H, 5′-H), 3.81 (1H, dd, 3′-H, J=4.0, 6.0 Hz), 3.98 (1H, t, 2′-H, J=6.0 Hz), 4.03 (1H, d, 1-H, J=10.0 Hz), 4.89 (2H, s, $C\underline{H}_2C_6H_5$), 5.57 (1H, d, 1′-H, J=6.0 Hz), 7.20—7.33 (5H, m, $C_6\underline{H}_5$).

19c: ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.78, 0.82, 0.98, 1.18 (3H each, s, CCH_3), 2.96 (1H, d, 6-H, J=10.0 Hz), 3.42—3.72 (3H, m, 4′-H, 5′-H), 3.78 (1H, dd, 2′-H, J=5.0, 7.5 Hz), 3.90 (1H, dd, 3′-H, J=2.0, 5.0 Hz), 4.26 (1H, d, 1-H, J=10.0 Hz), 4.89 (2H, s, $C\underline{H}_2C_6H_5$), 5.78 (1H, d, 1′-H, J=7.5 Hz), 7.20—7.33 (5H, m, $C_6\underline{H}_5$).

(1*S*,6*S*)-6-Fluoro-7,7,8,8-tetramethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (20a) ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.81, 0.91, 1.05 (3H each, s, CCH_3), 1.14 (3H, d, CCH_3, J=3.6 Hz), 3.39—3.75 (3H, m, 4′-H, 5′-H), 3.83 (1H, dd, 3′-H, J=3.0, 6.0 Hz), 3.92 (1H, dd, 2′-H, J=6.0, 6.5 Hz), 4.23 (1H, d, 1-H, J=22.4 Hz), 5.56 (1H, d, 1′-H, J=6.5 Hz).

(1*R*,6*R*)-6-Fluoro-7,7,8,8-tetramethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (21a) ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.89, 0.93, 1.10 (3H each, s, CCH_3), 1.13 (3H, d, CCH_3, J=3.2 Hz), 3.47—3.75 (3H, m, 4′-H, 5′-H), 3.80 (1H, dd, 2′-H, J=5.0, 7.5 Hz), 3.90 (1H, dd, 3′-H, J=2.0, 5.0 Hz), 4.47 (1H, d, 1-H, J=22.4 Hz), 5.72 (1H, d, 1′-H, J=7.5 Hz).

(1*S*,6*S*)-6-Fluoro-4,7,7,8,8-pentamethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (20b) and (1*R*,6*R*)-6-Fluoro-4,7,7,8,8-pentamethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (21b) 20b: ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.73, 0.88, 1.05 (3H each, s, CCH_3), 1.15 (3H, d, CCH_3, J=3.3 Hz), 3.10 (3H, s, NCH_3), 3.25—3.77 (3H, m, 4′-H, 5′-H), 3.80—4.00 (2H, m, 2′-H, 3′-H), 4.34 (1H, d, 1-H, J=22.4 Hz), 5.62 (1H, d, 1′-H, J=6.5 Hz),

21b: ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.82, 0.91, 1.10 (3H each, s, CCH_3), 0.93 (3H, d, CCH_3, J=3.0 Hz), 3.16 (3H, s, NCH_3), 3.25—3.77 (3H, m, 4′-H, 5′-H), 3.80—4.00 (2H, m, 2′-H, 3′-H), 4.52 (1H, d, 1-H, J=22.4 Hz), 5.76 (1H, d, 1′-H, J=7.0 Hz).

(1*S*,6*S*)-4-Ethyl-6-fluoro-7,7,8,8-tetramethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (20c) and (1*R*,6*R*)-4-Ethyl-6-fluoro-7,7,8,8-tetramethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]-octane-3,5-dione (21c) 20c: ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.75, 0.89, 1.05 (3H each, s, CCH_3), 1.16 (3H, d, CCH_3, J=3.5 Hz), 1.17 (3H, t, $CH_2C\underline{H}_3$, J=7.0 Hz), 3.48—3.55 (2H, m, 5′-H), 3.69—3.82 (1H, m, 4′-H), 3.83—3.98 (2H, m, 2′-H, 3′-H), 4.03 (2H, q, $C\underline{H}_2CH_3$, J=7.0 Hz), 4.32 (1H, d, 1-H, J=22.4 Hz), 5.62 (1H, d, 1′-H, J=6.5 Hz).

21c: ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.83, 0.92, 1.08 (3H each, s, CCH_3), 1.10 (3H, d, CCH_3, J=2.5 Hz), 1.15 (3H, t, $CH_2C\underline{H}_3$, J=7.0 Hz), 3.48—3.55 (2H, m, 5′-H), 3.67—3.82 (3H, m, 4′-H, $C\underline{H}_2CH_3$), 3.82—3.95 (2H, m, 2′-H, 3′-H), 4.50 (1H, d, 1-H, J=22.4 Hz), 5.78 (1H, d, 1′-H, J=7.5 Hz).

(1*S*,6*S*)-4-Benzyl-6-fluoro-7,7,8,8-tetramethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione (20d) and (1*R*,6*R*)-4-Benzyl-6-fluoro-7,7,8,8-tetramethyl-2-(β-D-ribofuranosyl)-*cis*-2,4-diazabicyclo-[4.2.0]octane-3,5-dione (21d) 20d: ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.57, 0.79, 1.02 (3H each, s, CCH_3), 1.14 (3H, d, CCH_3, J=3.5 Hz), 3.46—3.56 (2H, m, 5′-H), 3.70—3.77 (1H, m, 4′-H), 3.82—3.99 (2H, m, 2′-H, 3′-H), 4.35 (1H, d, 1-H, J=23.0 Hz), 4.93 (2H, br s, $C\underline{H}_2C_6H_5$), 5.62 (1H, d, 1′-H, J=6.5 Hz), 7.21—7.98 (5H, m, $C_6\underline{H}_5$).

21d: ^{1}H-NMR [DMSO-d_6 (added D_2O)] δ: 0.67, 0.86, 1.08 (3H each, s, CCH_3), 0.95 (3H, d, CCH_3, J=3.0 Hz), 3.46—3.56 (2H, m, 5′-H), 3.70—3.77 (1H, m, 4′-H), 3.82—3.99 (2H, m, 2′-H, 3′-H), 4.54 (1H, d, 1-H, J=23.0 Hz), 4.98 (2H, br s, $C\underline{H}_2C_6H_5$), 5.89 (1H, d, 1′-H, J=7.5 Hz), 7.21—7.98 (5H, m, $C_6\underline{H}_5$).

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References and Notes

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