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Articles

Ceric Ammonium Nitrate on Silica Gel for Efficient and Selective Removal of Trityl and Silyl Groups

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Silica gel-supported ceric ammonium nitrate ($CAN-SiO_2$) was found effective for rapid and selective cleavage of trityl (Tr), monomethoxytrityl (MMTr), and dimethoxytrityl (DMTr) groups from protected nucleosides and nucleotides under mild conditions. Efficiency of deprotections depended upon the stability of the resultant carbocationic species: $DMTr^+ > MMTr^+ > Tr^+$. Use of a catalytic amount of this solid-supported reagent can also efficiently and selectively remove the *tert*-butyldimethylsilyl or the triisopropylsilyl group from a primary hydroxyl functionality in di- or trisilyl ethers of ribonucleosides. A comparative study of deprotection reactions by utilization of CAN alone or $CAN-SiO_2$ indicates a remarkable increase in the rate of the reactions involving a solid support. The mechanism of electron-transfer processes is proposed for the use of $CAN-SiO_2$ in the removal of these protective groups from organic molecules.

Introduction

The concept of utilization of reagents adsorbed on inert inorganic supports has been applied in organic synthesis.[1] For example, chromic acid adsorbed on silica gel can oxidize alcohols efficiently.[2] Sodium borohydride impregnated on alumina reduces carbonyl compounds in aprotic solvents.[3]

Efficiency resulting from inorganic material-supported reagents may come from the combination of three factors: (i) an increase in the effective surface area for reactions; (ii) the presence of pores which constrain both substrates and catalysts and thus lower the entropy of activation of reactions; and (iii) the acceleration of the reaction resulting from bringing substrates and reagents into proximity.[1,4−7]

Recently ceric ammonium nitrate ($Ce(NH_4)_2(NO_3)_6$, CAN) has been reported as a one-electron-transfer catalyst for removal of triphenylmethyl (Tr), monomethoxytrityl (MMTr), and *tert*-butoxycarbonyl (*t*-BOC) groups from organic compounds.[8,9] Under the neutral conditions

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(1) Butters, M. In *Solid Supports and Catalysts in Organic Synthesis*; Smith, K., Ed.; Ellis Horwood: New York, 1992; pp 65−188.
(2) Santaniello, E.; Ponti, F.; Manzocchi, A. *Synthesis* **1978**, 534.
(3) Santaniello, E.; Ponti, F.; Manzocchi, A. *Synthesis* **1978**, 891.
(4) McKillop, A.; Young, D. W. *Synthesis* **1979**, 401; *ibid.* 481.
(5) Cornelis, A.; Laszlo, P. *Synthesis* **1985**, 909.
(6) Laszlo, P. *Acc. Chem. Res.* **1986**, *19*, 121.
(7) Diddams, P. In *Solid Supports and Catalysts in Organic Synthesis*; Smith, K., Ed.; Ellis Horwood: New York, 1992; Chapter 1.

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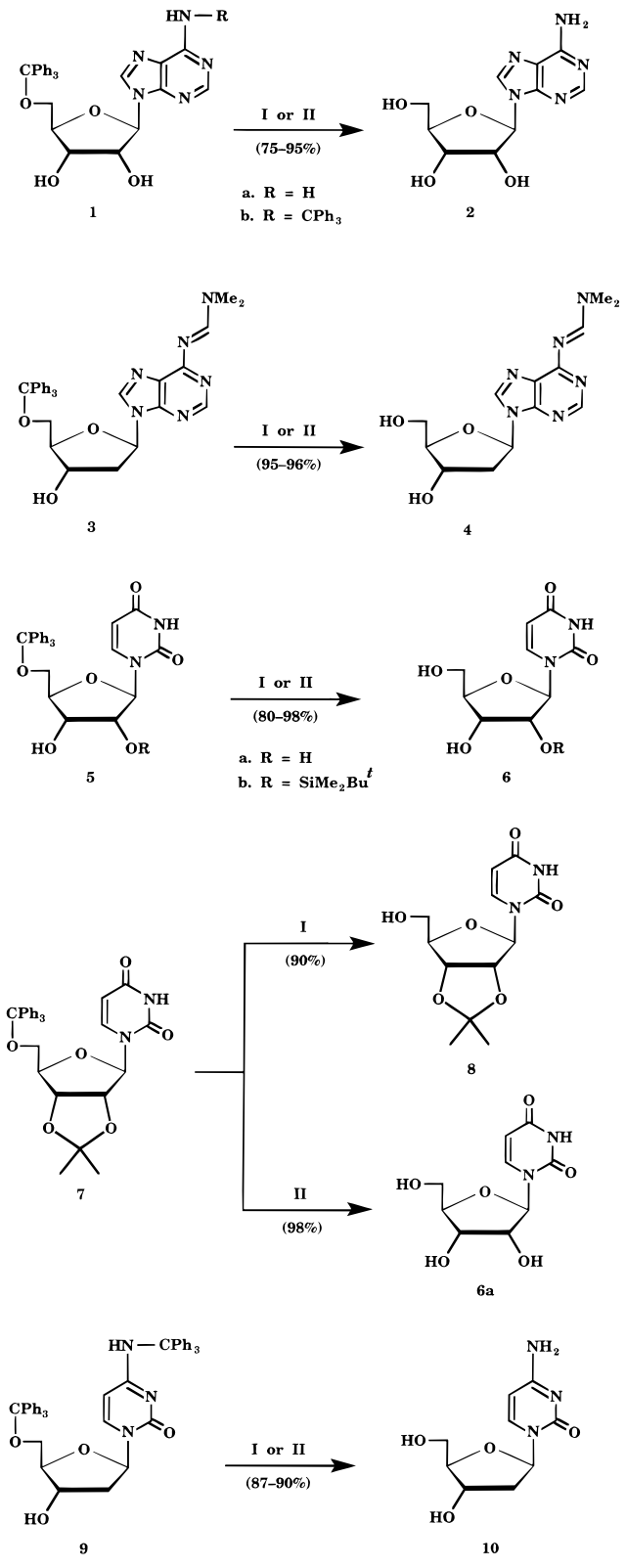
applied, several acid-sensitive groups survive, including isopropylidene, (dimethylamino)methylidene, *tert*-butyldimethylsilyl, and acyl functionalities.[8] Furthermore, indole, pyrimidine, and phthalimide nuclei remain intact and the undesired racemization does not occur in amino esters.[9]

The *tert*-butyldimethylsilyl (TBDMS) and triisopropylsilyl (TIPS) groups are among the most commonly used moieties for protection of the hydroxyl functionality in organic synthesis.[10,11] Reagents applied for their removal include aqueous acids (e.g., HF in aqueous MeCN)[11−15] and fluoride ion (e.g., Bu_4NF in THF).[11,16] The TBDMS group can also be removed by use of clay in aqueous MeOH[17] and CAN in MeOH.[18] Furthermore, use of the mixture of MeOH and CCl_4 as the solvents under sonication was reported[19] for the selective deprotection of the TBDMS group on the primary hydroxyl functionality in 1,3-bis(*tert*-butyldimethylsiloxy)butane.

We found that those methods were not applicable for the selective removal of a TBDMS group from silyl ethers with different steric environment in nucleosides, nor for the TIPS group. For example, separate treatment of bis-silylated adenosine derivatives **27a** and **27b**, individually, with 0.85 equiv of CAN in MeOH for 16 h gave the completely desilylated adenosine in 84−88% yields. Sonication of the mixture of **27a** in MeOH/CCl_4 for 30 h led to its recovery in >97% yield. These sonochemical conditions were too mild to remove the 5′-TBDMS group from nucleosides because its steric environment is more crowded than "normal" primary *tert*-butyldimethylsilyl ethers.

We believe that the adsorption of organic compounds containing a trityl or a silyl group onto the CAN-silica gel reagent could bring substrates and the catalysts into proximity.[1,7] This facilitates the electron-transfer process between reactants and thus may cause the deprotection process to proceed much faster under mild conditions.[20−22] Herein we report our new findings that CAN adsorbed on silica gel functioned as an effective reagent for removal of the Tr, MMTr, DMTr, TBDMS, and TIPS functionalities from a variety of ribonucleoside substrates. Being rapid and selective, this new procedure converted the substrates to the parent alcohols or amines in good to excellent yields. These outcomes broaden the applicability of the trityl and the silyl groups, especially in the field of nucleoside chemistry.

Scheme 1

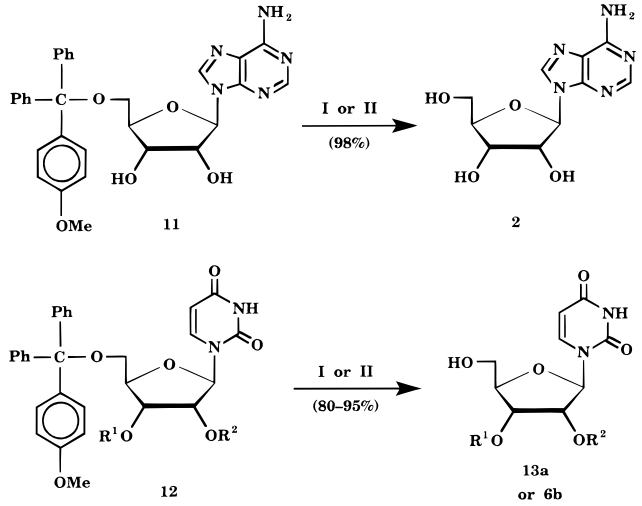


Results and Discussion

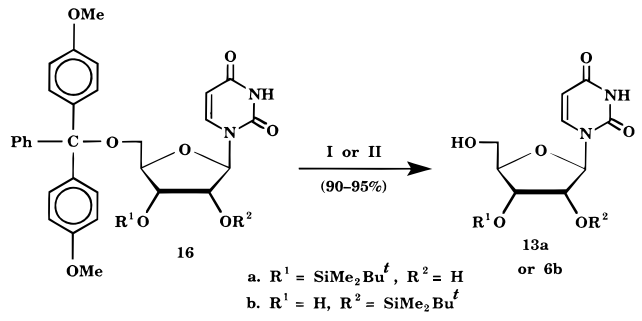
Removal of the Trityl, Monomethoxytrityl, and Dimethoxytrityl Groups from Protected Nucleosides (Schemes 1−3 and Table 1). The Tr, MMTr, and DMTr (dimethoxytrityl) groups are often used to protect

(8) Hwu, J. R.; Jain, M. L.; Tsay, S.-C.; Hakimelahi, G. H. *J. Chem. Soc., Chem. Commun.* **1996**, 545.
(9) Hwu, J. R.; Jain, M. L.; Tsay, S.-C.; Hakimelahi, G. H. *Tetrahedron Lett.* **1996**, *37*, 2035.
(10) Lalonde, M.; Chan, T. H. *Synthesis* **1985**, 817.
(11) Rücker, C. *Chem. Rev.* **1995**, *95*, 1009, and references therein.
(12) Nelson, T. D.; Crouch, R. D. *Synthesis* **1996**, 1031.
(13) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
(14) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley: New York, 1991; pp 77−83.
(15) Newton, R. F.; Reynolds, D. P.; Finch, M. A. W.; Kelly, D. R.; Roberts, S. M. *Tetrahedron Lett.* **1979**, *20*, 3981.
(16) Kocie'nski, P. J. *Protective Groups*; Georg Thieme Verlag Stuttgart: New York, 1994; pp 33−37.
(17) Asakura, J.; Robins, M. J.; Asaka, Y.; Kim, T. H. *J. Org. Chem.* **1996**, *61*, 9026.
(18) Gupta, A. D.; Singh, R.; Singh, V. K. *Synlett* **1996**, 69.
(19) Lee, A. S.-Y.; Yeh, H.-C.; Tsai, M.-H. *Tetrahedron Lett.* **1995**, *36*, 6891.
(20) Keinan, E.; Mazur, Y. *J. Org. Chem.* **1978**, *43*, 1020.
(21) Hudlicky, M. *J. Org. Chem.* **1974**, *39*, 3460.
(22) Taylor, E. C.; Chiang, C. S.; McKillop, A.; White, J. F. *J. Am. Chem. Soc.* **1976**, *98*, 6750.

Scheme 2



Scheme 3



the 5′-hydroxyl group in nucleosides.[23] Reagents used for removal of these groups include hydrogen chloride, hydrogen bromide, acetic acid, and trifluoroacetic acid.[24]

(23) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley: New York, 1991; pp 60−61.
(24) MacCoss, M.; Cameron, D. J. *Carbohydr. Res.* **1978**, *60*, 206 and references therein.

Table 1. Comparison of the Efficiency for Detritylation of Protected Nucleosides by Use of CAN (0.10 Equiv) in MeCN or Silica Gel-Supported CAN (0.10 Equiv) in CH_2Cl_2 at 25 °C

starting material	time (h)		yield (%) by isolation		
	CAN	CAN−SiO_2	CAN	CAN−SiO_2	product
1a	13	1.5	92[a]	95	**2**
1b	15	2.0	75	92	**2**
3	8.0	1.0	96	95	**4**
5a	11	1.5	88	98	**6a**
5b	12	2.0	80	90	**6b**
7	10	−	90	−	**8**
7	−	1.5	−	98	**6a**
9	15	2.0	87	90	**10**
11	1.0	0.10	98[a]	98	**2**
12a	1.5	0.10	80	90	**13a**
12b	1.25	0.10	85	95	**6b**
14a	1.5	0.10	80	90	**15a**
14b	1.2	0.10	75	95	**15b**
16a	0.15	0.01	90	92	**13a**
16b	0.10	0.01	90	95	**6b**

[a] A mixture of MeCN and DMF (3:1) was used as the solvent.

Acidic conditions, however, may cause cleavage of nucleobases in nucleosides and nucleotides.[25]

We found that use of CAN−SiO_2 (containing 0.10 equiv of CAN) can efficiently detritylate several nucleosides bearing a tritylated hydroxyl group (i.e., **1**, **3**, **5**, **7**, and **9**)[8] or amino group (i.e., **1b** and **9**) in CH_2Cl_2 at 25 °C (Scheme 1). To understand the efficiency of using CAN−SiO_2, we compared the results obtained from detritylations in the presence and absence of silica gel as the solid support. Complete detritylation by use of 0.10 equiv of CAN in acetonitrile (i.e., Method I) took 8.0−15 h at 25 °C; yields of the isolated products ranged from 75 to 96% (see Table 1). The above reactions went much faster (1.0−2.0 h) and produced the same products in higher yields (90−98%) when the CAN−silica gel reagent was utilized (i.e., Method II). The only different results in these two methods came from the conversions of **7** → **8** by CAN and **7** → **6a** by CAN−SiO_2; in the latter reaction, the isopropylidene group in **7** was removed (Scheme 1 and Table 1).

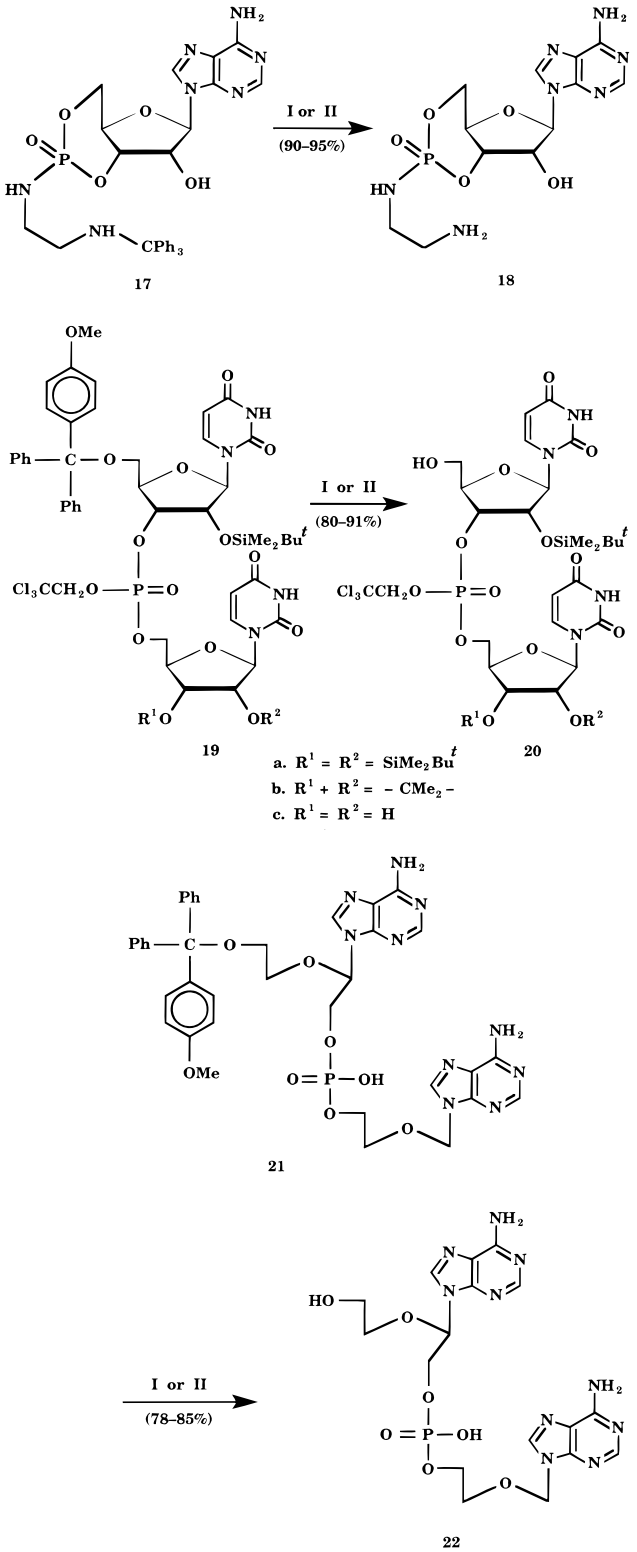
Furthermore, we applied these two methods to monomethoxytritylated nucleosides **11**,[8] **12a**,**b**,[26] and **14a**,**b**[26,27] (Scheme 2 and Table 1). Removal of the 5′-*O*-monomethoxytrityl group from those substrates gave the parent alcohols **2**,[8] **13a**, **6b**[26] and **15a**,**b**,[26,27] respectively. Similarly, removal of the 5′-*O*-dimethoxytrityl group from protected nucleosides **16a**,**b**[28] by use of CAN in acetonitrile or CAN−SiO_2 in CH_2Cl_2 afforded the parent alcohols **13a**[26] and **6b**,[26] respectively (Scheme 3 and Table 1).

Cleavage of the MMTr group by use of CAN in acetonitrile took 1.0−1.5 h and yields ranged from 75 to 98% for the isolated products. Use of CAN−SiO_2 took only 6.0 min. On the other hand, removal of the DMTr functionality by CAN took 6.0−9.0 min and the yields were 90%. Utilization of CAN−SiO_2 required <60 s and produced the desired product in 92−95% yields (see Table 1).

Efficiency of deprotections by use of CAN depended upon stability of the resultant carbocationic species:

(25) Krecmerova, M.; Seela, F. *Nucleosides, Nucleotides* **1992**, *11*, 1393.
(26) Ogilvie, K. K.; Beaucage, S. L.; Schifman, A. L.; Theriault, N. Y.; Sadana, K. L. *Can. J. Chem.* **1978**, *56*, 2768.
(27) Ogilvie, K. K.; Nemer, M. J. *Can. J. Chem.* **1980**, *58*, 1389.
(28) Hakimelahi, G. H.; Proba, Z. A.; Ogilvie, K. K. *Can. J. Chem.* **1982**, *60*, 1106.

Scheme 4



$DMTr^+ > MMTr^+ > Tr^+$. Under the same conditions, the deprotection of 5′-*O*-DMTr nucleosides proceeded about 10 times faster than the deprotection of 5′-*O*-MMTr nucleosides (Table 1). Moreover, the deprotection of 5′-*O*-MMTr nucleosides proceeded about 10−20 times faster than deprotection of 5′-*O*-Tr nucleosides.

Table 2. Comparison of the Efficiency for Detritylation of Protected Nucleotides by Use of CAN (0.10 Equiv) in MeCN or Silica Gel-Supported CAN (0.10 Equiv) in CH_2Cl_2 at 25 °C

starting material	time (h)		yield (%) by isolation		
	CAN	CAN−SiO_2	CAN	CAN−SiO_2	product
17	10	1.5	90[a]	95	**18**
19a	1.0	0.10	91	90	**20a**
19b	1.0	0.10	80	90	**20b**
19b	2.0	–	85	–	**20b**
19b	–	2.0	–	88	**20c**
21	1.0	0.10	78	85	**22**

[a] A mixture of MeCN and DMF (3:1) was used as the solvent.

Removal of the Trityl and Monomethoxytrityl Groups from Protected Nucleotides (Scheme 4 and Table 2). We compared the efficiency of detritylation of nucleotides by CAN in the presence and absence of the SiO_2-solid support. Tritylated phosphoramidate **17**[29] in a wet mixture of acetonitrile and DMF (3:1) was treated with a catalytic amount of CAN (0.10 equiv) at 25 °C to afford detritylated nucleotide **18**[8] in 90% yield after 10 h. When the above reaction was performed by use of CAN−SiO_2 (containing 0.10 equiv of CAN) in CH_2Cl_2 at 25 °C, **18** was obtained in 95% yield after 1.5 h (Table 2).

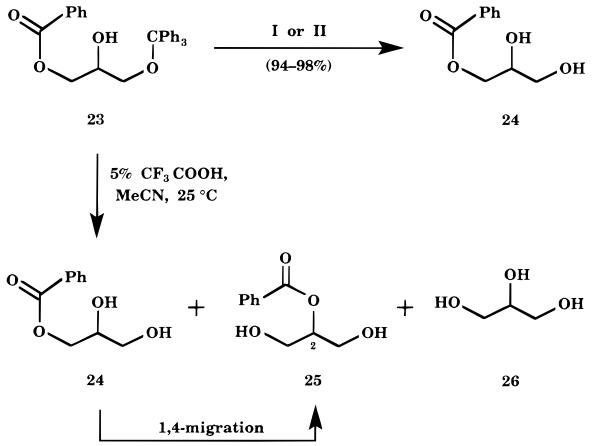
We also compared the efficiency of the two methods for the removal of the MMTr group from the nucleotides possessing acid labile functionalities. Those functionalities include the *tert*-butyldimethylsilyl group in **19a**,**b**[26] and the isopropylidene group in **19b**.[26] Treatment of 5′-*O*-MMTr dinucleotides **19a** or **19b** with CAN in acetonitrile at 25 °C for 1.0 h produced dinucleotides **20a**[26] (91% yield) and **20b**[26] (80% yield), respectively. By using CAN−SiO_2 in CH_2Cl_2, we detritylated **19a**,**b** to the corresponding dinucleotides **20a**,**b** in 90% yield after 6.0 min. These results as well as those presented in Tables 1 and 2 indicate that reactions involving solid support reagents proceeded ∼10 times faster than the corresponding detritylation reactions without solid support.

By prolonging the reaction time for 5′-*O*-MMTr dinucleotide **19b** to 2.0 h, we obtained dinucleotide derivative **20b** in 85% yield by using CAN alone in acetonitrile. The isopropylidene unit in **19b**, however, was removed by use of CAN−SiO_2 in CH_2Cl_2. Thus after 2.0 h, dinucleotide **19b** was converted to triol **20c** in 88% yield. These results are similar to those for the conversions of **7** → **8** and **7** → **6a** under comparable conditions (see Scheme 1). Furthermore, we removed the MMTr group from acyclic nucleotide **21**[30] to give **22** in 78% yield using CAN in acetonitrile after 1.0 h. The same conversion took only 6.0 min and gave 85% yield of **22** by use of CAN−SiO_2 in CH_2Cl_2 (Scheme 4 and Table 2).

Detritylation of 1-Benzoyl-3-(triphenylmethyl)-glycerol (Scheme 5). We found that the detritylation of 1-benzoyl-3-(triphenylmethyl)glycerol (**23**) by using CAN (0.10 equiv) in acetonitrile at 25 °C gave 1-benzoylglycerol (**24**) in 94% yield after 9.0 h (Scheme 5).[8] Performance of the same transformation in the presence of CAN−SiO_2 (0.10 equiv of CAN) in CH_2Cl_2 at 25 °C afforded detritylated product **24** in 98% yield after 45

(29) Hakimelahi, G. H.; Kunju, K.; Lin, L. C.; Tsay, S.-C. *Bull. Inst. Chem. Acad. Sin.* **1993**, *40*, 11.
(30) Hakimelahi, G. H.; Zarrinehzad, M.; Jarrahpour, A. A.; Sharghi, H. *Helv. Chim. Acta* **1987**, *70*, 219.

Scheme 5



I. CAN (0.10 equiv), MeCN, 25 °C
II. CAN (0.10 equiv)–silica gel, CH_2Cl_2, 25 °C

min. The acyl group in **23** survived and resided at its original position during detritylation by both methods.

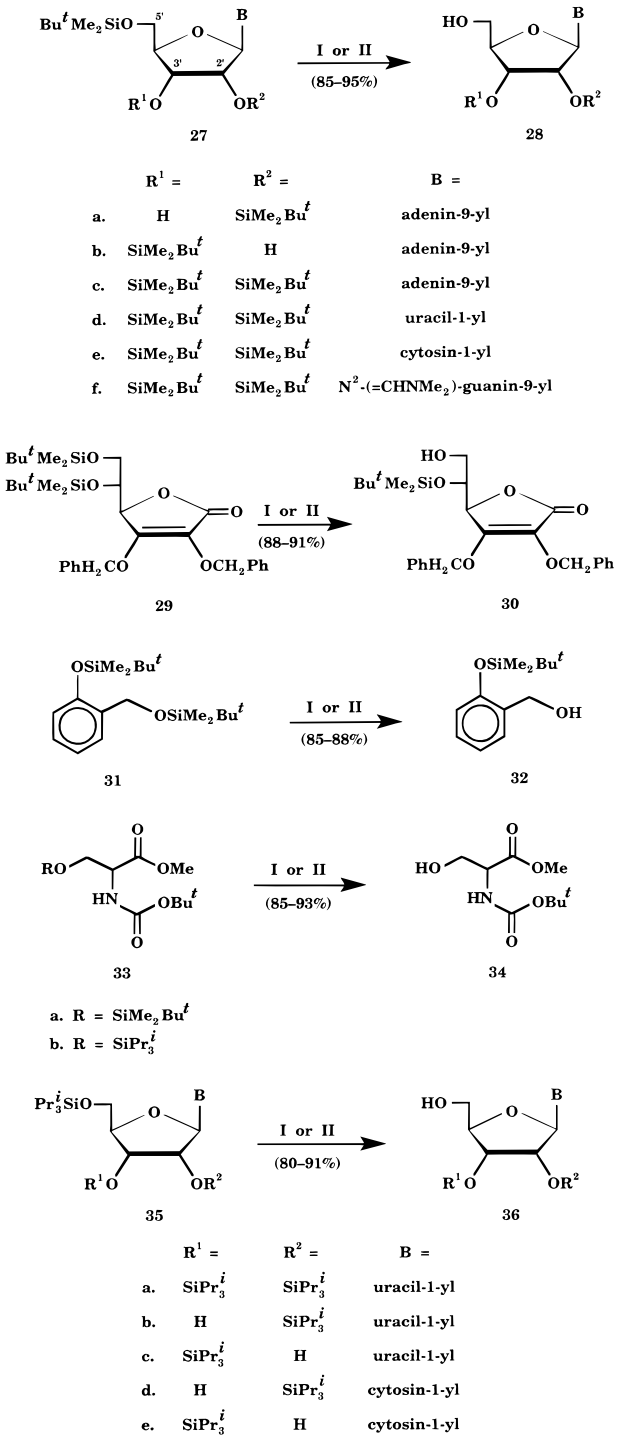
In contrast, treatment of **23** with 5% CF_3CO_2H in acetonitrile gave a mixture of **24**−**26**[8] in a ratio of 1.5:1:2.5. Isomerization of 1-benzoylglycerol (**24**) to 2-benzoylglycerol (**25**) was evidenced by ^{1}H NMR spectrometry of the above mixture. The C-2 proton appeared at lower field (δ 5.49 ppm) in 2-benzoylglycerol (**25**) in comparison with that of the corresponding regioisomer **24** with δ 4.00 ppm.[8]

Desilylations by Use of Ceric Ammonium Nitrate (Scheme 6 and Table 3). We treated a compound containing TBDMS groups (i.e., **27a**−**f**, **29**, **31**, and **33a**) in 2-propanol with 0.85 equiv of CAN (Scheme 6). After the solution was stirred at 25 °C for 2.0−26 h, the solvent was removed and the residue was purified by chromatography to give the deprotected products (i.e., **28a**−**f**, **30**, **32**, and **34**, individually) in 85−95% yields (see Table 3). This deprotection procedure was applicable to 2′,5′-disilylated, 3′,5′-disilylated, and 2′,3′,5′-trisilylated nucleosides (i.e., **27a**−**f**), disilylated ascorbic acid **29**, siloxymethyl phenol ether **31**, and silylated amino ester derivative **33a**. Furthermore, the same deprotection also proceeded in the presence of 0.20 equiv of CAN, yet much longer reaction time (e.g., ∼72 h for **27a**) was required.

The TBDMS group in a secondary ether was found virtually remained intact under the conditions involving CAN (Table 3). Although the adjacent migration of the 2′- and 3′-*O*-TBDMS groups of ribonucleosides was reported in MeOH or pyridine,[31] such a migration was not observed in **28a**, **28b**, **30**, and **32** under the conditions we applied. Furthermore, we found that the TBDMS group can also be removed selectively in the presence of a *tert*-butoxycarbonyl functionality (see Table 3 for **33a** → **34**). Use of methanol, ethanol, or 1-propanol as the solvent, however, resulted in the deprotection of all TBDMS groups. Thus, selective deprotection can be accomplished upon proper choice of the reaction media.

Silica Gel Impregnated Ceric Ammonium Nitrate in Desilylations (Scheme 6 and Table 3). In comparison with the TBDMS group, several advantages[32] are associated with the TIPS group for its use in synthetic

Scheme 6



	R^1 =	R^2 =	B =
a.	H	$SiMe_2Bu^t$	adenin-9-yl
b.	$SiMe_2Bu^t$	H	adenin-9-yl
c.	$SiMe_2Bu^t$	$SiMe_2Bu^t$	adenin-9-yl
d.	$SiMe_2Bu^t$	$SiMe_2Bu^t$	uracil-1-yl
e.	$SiMe_2Bu^t$	$SiMe_2Bu^t$	cytosin-1-yl
f.	$SiMe_2Bu^t$	$SiMe_2Bu^t$	N^2-(=CHNMe$_2$)-guanin-9-yl

	R^1 =	R^2 =	B =
a.	$SiPr_3^i$	$SiPr_3^i$	uracil-1-yl
b.	H	$SiPr_3^i$	uracil-1-yl
c.	$SiPr_3^i$	H	uracil-1-yl
d.	H	$SiPr_3^i$	cytosin-1-yl
e.	$SiPr_3^i$	H	cytosin-1-yl

I. CAN (0.85 equiv), 2-propanol, 25 °C
II. CAN (0.45 equiv)–silica gel, 2-propanol/CCl_4 (1:1), 65 °C

chemistry. The advantages include low cost and ready availability of pure triisopropylsilyl chloride (TIPSCl), greater stability of TIPS over TBDMS ethers, more facile deprotection of TIPS over TBDMS derivatives under acidic conditions, and relatively high volatility of TIPS ethers for the purpose of gas chromatography and mass spectral analysis.

Consequently, we intended to apply our newly developed conditions to the selective removal of a TIPS group from di- or tri-silyl ethers. We found that the above reaction conditions involving the use of CAN alone,

(31) Beaucage, S. L.; Iyer, R. P. *Tetrahedron* **1992**, *48*, 2223.
(32) Cunico, R. F.; Bedell, L. *J. Org. Chem.* **1980**, *45*, 4797.

Table 3. Comparison of the Efficiency for Selective Desilylation of Di- or Tri-*tert*-butyldimethylsilyl or Triisopropylsilyl Ethers by Use of CAN (0.85 Equiv) in 2-Propanol at 25 °C or Silica Gel-Supported CAN (0.45 Equiv) in a Mixture of 2-Propanol and CCl_4 (1:1) at 65 °C

	time (h)		yield (%) by isolation		
substrate	CAN	CAN−SiO_2	CAN	CAN−SiO_2	product
27a	26	7.0	87	90	**28a**
27b	24	9.0	85	88	**28b**
27c	24	8.0	85	88	**28c**
27d	24	8.0	93	95	**28d**
27e	25	12	95	95	**28e**
27f	26	13	85	89	**28f**
29	20	7.0	88	91	**30**
31	2.0	1.5	85	88	**32**
33a	10	4.0	85	93	**34**
35a	60	12	0	87	**36a**
35b	60	15	0	91	**36b**
35c	60	17	0	85	**36c**
35d	60	21	0	80	**36d**
35e	60	28	0	83	**36e**

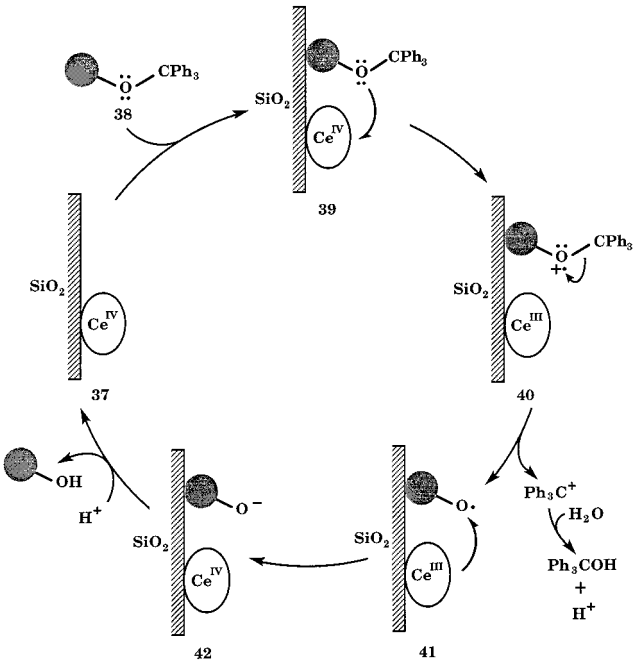
unfortunately, were not applicable directly for the removal of the TIPS group and nucleosides **35a**−**e** were recovered (see Table 3). Thus, we decided to apply solid support strategy involving the use of CAN−SiO_2 for removal of the TBDMS and the TIPS groups. Various silylated compounds **27a**−**f**, **29**, **31**, **33a**, and **35a**−**e** were treated with 0.45 equiv of silica gel supported CAN in a mixture of 2-propanol and CCl_4 (1:1) at 65 °C for 1.5−28 h. The desired products **28a**−**f**, **30**, **32**, **34**, and **36a**−**e** were generated in 80−95% yields (see Scheme 6 and Table 3).

Our results indicate that the TBDMS group in primary silyl ethers **27a**−**f**, **29**, **31**, and **33a** were selectively removed from multisilyl ethers by CAN−SiO_2; the yields were comparable with those of the reactions involving CAN alone. The amount of CAN required was less than that in the reactions involving CAN−SiO_2 and the reaction time was shorter. Moreover, the TIPS group in primary silyl ethers **35a**−**e** was also selectively removed by use of CAN−SiO_2. Furthermore, we found that the desilylating rates did not change by using the reagent CAN or CAN−SiO_2 when 2-propanol was applied as the exclusive solvent (see Table 3). This could be due to the easy removal of CAN from CAN−SiO_2 by 2-propanol; as a result, the concept of the solid support strategy was no longer applicable.

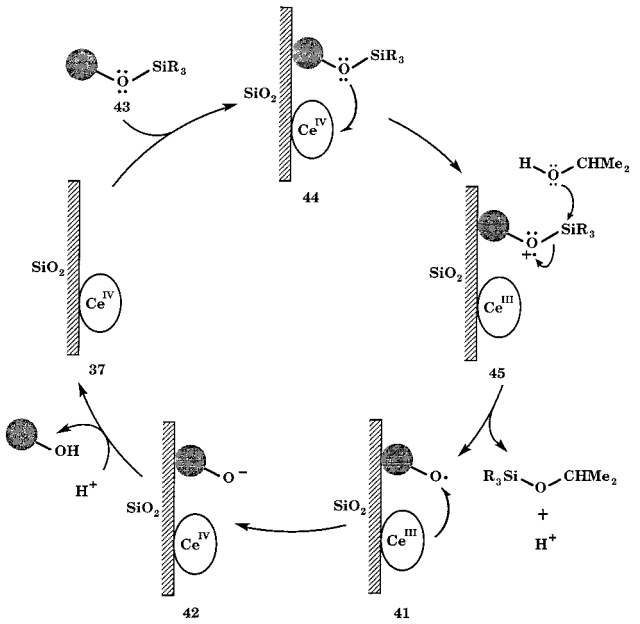
The newly developed method by use of CAN alone or silica gel supported CAN are applicable to silylated adenosine, uridine, guanosine, and cytidine. Their nucleobases did not interfere the electron-transfer processes between cerium species and the substrates. Acidic deprotection of the TIPS group is much easier than the TBDMS group;[32] yet by use of the CAN or CAN−SiO_2 strategy allowed removal of the TBDMS functionality faster than removal of the TIPS group (Table 3). For example, *tert*-butyldimethylsilyl derivative **33a** was readily converted to desilylated product **34** in an excellent yield by use of CAN or CAN−SiO_2, yet triisopropylsilyl derivative **33b** failed to produce **34** under the same reaction conditions (see Table 3 and Scheme 6).

Mechanism for Detritylations and Desilylations of Protected Nucleosides and Nucleotides (Schemes 7 and 8). We found that the pK_a (cf. pH) values of the solutions remained constant during removal of the trityl or silyl groups from compounds listed in Tables 1−3. Thus, the possibility may be ruled out for the formation of nitric acid from CAN by moisture during the course of the reactions.

Scheme 7



Scheme 8



These newly developed deprotection reactions could involve electron-transfer processes.[8,9,33,34] We propose a mechanism in Scheme 7 for removal of the trityl group from organic molecules by using CAN−SiO_2 (**37**). The trityl-containing compounds **38** was adsorbed on **37** to afford **39**. The proximity of **38** to CAN in **39** results in a favorable entropy of activation and, consequently, a rate enhancement of the reaction.

An essential step in detritylation reactions involves oxidation of trityl ethers in **39** to give the corresponding radical cations in **40**, while the reduction of Ce^{IV} to Ce^{III}

(33) Ho, T. L. In *Organic Syntheses by Oxidation with Metal Compounds*; Mijs, W. J., de Jonge, C. R. H. I., Eds.; Plenum Press: New York, 1986; Chapter 11, pp 569−631.

(34) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29.

takes place.[33] Radical cations then undergo fragmentation to give trityl cations and alkoxy radicals as shown in **41**. The trityl cation reacts with water to generate the byproduct triphenylmethanol. Meanwhile, reduction of alkoxy radicals in **41** to alkoxides in **42** allows regeneration of Ce^{IV} from Ce^{III}. Consequently, only a catalytic amount of CAN is required for detritylations. Finally, protonation of alkoxides in **42** by water produces the free alcohols.

Removal of the silyl groups from silyl ethers by CAN−SiO_2 could go through a similar mechanism as shown in Scheme 8. The first step involves oxidation of silyl ethers **43** after it was attached to CAN−SiO_2 (see **44**).[33] The resultant radical cations in **45** could then undergo an S_N2 reaction with 2-propanol to give alkoxy radicals in **41** and the byproduct silyl ethers $R_3SiOCHMe_2$. These byproducts were isolated in 80−90% yields. Regeneration of Ce(IV)−SiO_2 from Ce(III)−SiO_2 during reduction of alkoxy radicals in **41** to alkoxides in **42** allows the use of CAN−SiO_2 in a small amount for completion of the entire deprotection process. Finally, protonation of **42** gives the free primary alcohols.

The selective removal of the TBDMS or the TIPS moiety from a primary, in the presence of a secondary, silyl ether possibly comes from two steps: The first involves the steric congestion between the bulky reagent CAN and the secondary silyl ether moiety in **44** during the electron-transfer process. The second involves an unfavorable nucleophilic attack of 2-propanol on the secondary silyl ether radical cations in **45**.

To support our proposed mechanism, the reactions for **27a**, **27d**, **27e**, **35a**, and **35c** were carried out in the presence of 2,6-di-*tert*-butyl-4-methylphenol (0.45 equiv) as a radical inhibitor.[35] As predicted, desilylation reactions did not proceed and the starting materials were recovered. In the absence of radical inhibitors, but in the presence of $NaHCO_3$ (0.45 equiv), the above reactions produced the desired products **28a**, **28d**, **28e**, **36a**, and **36c**, respectively, in comparable yields with those reactions involving CAN−SiO_2. Thus, our desilylation reactions were accomplished through an electron-transfer pathway rather than an acid-catalyzed cleavage.

Conclusions

Ceric ammonium nitrate adsorbed on silica gel functioned as an effective catalyst for removal of the Tr, MMTr, and DMTr functionalities from a variety of protected nucleosides and nucleotides. Some protecting groups sensitive to acids survived under our newly developed conditions; they include (dimethylamino)-methylidene, *tert*-butyldimethylsilyl, and isopropylidene groups. The ester group did not migrate to the adjacent hydroxyl group and the *N*-glycosidic bond of nucleosides and nucleotides as well as the phosphoramidate linkage remained intact.

Reagent CAN−SiO_2 was also found to act as an efficient catalyst for selective deprotection of the primary TBDMS and TIPS ethers in ribonucleosides and other organic compounds in a mixture of 2-propanol and CCl_4 (1:1). The compatible nucleobases towards the catalytic deprotection conditions include adenine, cytosine, guanine, and uracil.

Use of silica gel supported CAN allowed the deprotection reactions to proceed much faster and, often, to give the desired products in a higher yield. In addition to chemoselectivity, advantages associated with this CAN-silica gel reagent include mild reaction conditions, very short reaction time, and only a catalytic amount of the reagent required.

Experimental Section

General Methods. Dry ether was obtained by distillation from the sodium kettle of benzophenone under nitrogen. Other solvents, including chloroform, dichloromethane, ethyl acetate, and hexanes were distilled over CaH_2 under nitrogen. All other reagents and chemicals were purchased from commercial sources and used without further purification.

Products were purified by use of gravity column chromatography (Merck silica gel 60, particle size 70−230 or 230−400 mesh ASTM). Thin-layer chromatography (TLC) was carried out on glass plates (20 cm × 20 cm) coated with a 1-mm thick layer of silica gel DSF-5 (Terrochem Laboratories). Analytical TLC was performed on precoated plates purchased from Merck (Silica Gel $60F_{254}$). Compounds were visualized by use of UV light, I_2 vapor, or 2.5% phosphomolybdic acid in ethanol with heating.

Preparation of Silica Gel-Supported Ceric Ammonium Nitrate. Neutral silica gel (9.01 g, Merck Kieselgel 60, particle size 0.063−0.200 mm, 70−230 mesh) was mixed with a solution of CAN (1.02 g) in water (2.0 mL). Evaporation of water under reduced pressure (0.1 Torr) for 4.0 h gave a dry yellowish powder, which contained 10% (by weight) of CAN. This reagent was found active for at least six months by storage in a well-capped bottle. The similar reagent containing 20% of CAN in silica gel was prepared by use of the same silica gel (8.02 g) and CAN (2.01 g).

Standard Procedure for Detritylation by Use of Ceric Ammonium Nitrate (Method I). To a solution of tritylated compound (1.0 equiv) in wet acetonitrile was added a catalytic amount of CAN (0.10 equiv). The reaction mixture was stirred at 25 °C until the TLC did not show any starting material. The solvent was then removed under reduced pressure and the residue was purified either by crystallization or column chromatography to afford the desired product with purity >99.9%.

Standard Procedure for Detritylation by Use of Silica Gel-Supported Ceric Ammonium Nitrate (Method II). A suspension of tritylated compound (1.0 equiv) in CH_2Cl_2 was treated with CAN−SiO_2 (containing 0.10 equiv of CAN). It was stirred at 25 °C until the reaction was completed, as monitored by TLC. The reaction mixture was then filtered to remove triphenylmethanol, and the silica gel containing product was washed with hot methanol. The filtrate was evaporated, and the residue was purified to afford the desired product with purity >99.9%.

Adenosine (2): From 5′-*O*-(Triphenylmethyl)adenosine (1a) by Method I. The standard procedure was followed by use of **1a** (407 mg, 0.801 mmol, 1.0 equiv), CAN (43.8 mg, 0.0798 mmol, 0.10 equiv), MeCN (9.0 mL), and DMF (3.0 mL). After the reaction mixture was stirred for 13 h, the solvent was removed under reduced pressure. The residue was washed with ether to remove triphenylmethanol and the product was recrystallized from MeOH to afford **2** (196 mg, 0.734 mmol) in 92% yield: mp 234−236 °C. Its physical properties and spectroscopic characteristics are consistent with those of an authentic sample.[36]

From 5′-*O*-(Triphenylmethyl)adenosine (1a) by Method II. The standard procedure was followed by use of **1a** (364 mg, 0.715 mmol, 1.0 equiv), CAN−SiO_2 (392 mg, containing 39.2 mg of CAN, 0.0718 mmol, 0.10 equiv), and CH_2Cl_2 (10 mL). After the reaction mixture was stirred for 1.5 h, it was worked

(35) Janzen, E. G.; Wilcox, A. L.; Manoharan, V. *J. Org. Chem.* **1993**, *58*, 3597, and references therein.

(36) Compounds are available from Aldrich or Sigma Chemical Co.

up and the residue was recrystallized from MeOH to afford **2** (180 mg, 0.674 mmol) in 95% yield.

From 6-*N*-5′-*O*-Di(triphenylmethyl)adenosine (1b) by Method I. The standard procedure was followed by use of **1b** (295 mg, 0.392 mmol, 1.0 equiv), CAN (21.8 mg, 0.0397 mmol, 0.10 equiv), and MeCN (10 mL). After the reaction mixture was stirred for 15 h, the solvent was removed under reduced pressure. The residue was washed with ether to remove triphenylmethanol and the product was recrystallized from MeOH to afford **2** (78.6 mg, 0.294 mmol) in 75% yield.

From 6-*N*-5′-*O*-Di(triphenylmethyl)adenosine (1b) by Method II. The standard procedure was followed by use of **1b** (410 mg, 0.545 mmol, 1.0 equiv), CAN−SiO_2 (0.300 g, containing 30.0 mg of CAN, 0.0547 mmol, 0.10 equiv), and CH_2Cl_2 (10 mL). After the reaction mixture was stirred for 2.0 h, it was worked up and the residue was recrystallized from MeOH to afford **2** (134 mg, 0.502 mmol) in 92% yield.

From 5′-*O*-(*p*-Methoxyphenyldiphenylmethyl)adenosine (11) by Method I. The standard procedure was followed by use of **11** (342 mg, 0.634 mmol, 1.0 equiv), CAN (34.8 mg, 0.0636 mmol, 0.10 equiv), MeCN (9.0 mL), and DMF (3.0 mL). After the reaction mixture was stirred for 1.0 h, the solvent was removed under reduced pressure. The residue was washed with ether to remove triphenylmethanol and the product was recrystallized from MeOH to afford **2** (167 mg, 0.625 mmol) in 98% yield.

From 5′-*O*-(*p*-Methoxyphenyldiphenylmethyl)adenosine (11) by Method II. The standard procedure was followed by use of **11** (586 mg, 1.09 mmol, 1.0 equiv), CAN−SiO_2 (570 mg, containing 57.0 mg of CAN, 0.10 mmol, 0.10 equiv), and CH_2Cl_2 (10 mL). After the reaction mixture was stirred for 0.10 h, it was worked up and the residue was recrystallized from MeOH to afford **2** (285 mg, 1.06 mmol) in 98% yield.

6-*N*-[(Dimethylamino)methylene]-2′-deoxyadenosine (4): Method I. The standard procedure was followed by use of 6-*N*-[(dimethylamino)methylene]-5′-*O*-triphenylmethyl-2′-deoxyadenosine (**3**, 584 mg, 1.06 mmol, 1.0 equiv), CAN (58.6 mg, 0.107 mmol, 0.10 equiv), and MeCN (15 mL). After the reaction mixture was stirred for 8.0 h, the solvent was removed under reduced pressure and the residue was purified by column chromatography (10% MeOH in EtOAc as eluant) to afford **4** (312 mg, 1.02 mmol) in 96% yield: mp 236−238 °C (EtOH, lit.[37] mp 235−238 °C); R_f = 0.60 (30% MeOH in EtOAc); ^{1}H NMR (DMSO-d_6) δ 2.24−2.32 (m, 1 H), 2.74−2.82 (m, 1 H), 3.11 (s, 3 H), 3.16 (s, 3 H), 3.55−3.68 (m, 2 H), 4.38−4.46 (m, 2 H), 5.12 (br s, 1 H), 5.31 (br s, 1 H), 6.39 (t, J = 7.2 Hz, 1 H), 8.39 (s, 1 H), 8.43 (s, 1 H), 8.89 (s, 1 H). Its spectroscopic characteristics are consistent with those of the same compound reported.[37]

Method II. The standard procedure was followed by use of **3** (326 mg, 0.593 mmol, 1.0 equiv), CAN−SiO_2 (330 mg, containing 33.0 mg of CAN, 0.0601 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 1.0 h, it was worked up and the residue was purified by column chromatography (EtOAc as eluant) to afford **4** (173 mg, 0.563 mmol) in 95% yield.

Uridine (6a): From 5′-*O*-(Triphenylmethyl)uridine (5a) by Method I. The standard procedure was followed by use of **5a** (404 mg, 0.831 mmol, 1.0 equiv), CAN (51.2 mg, 0.0933 mmol, 0.10 equiv), and MeCN (8.0 mL). After the reaction mixture was stirred for 11 h, it was concentrated under reduced pressure and the residue was purified by column chromatography (20% MeOH in EtOAc as eluant) to afford **6a** (178 mg, 0.729 mmol) in 88% yield: mp 165−166 °C (EtOH). Its physical properties and spectroscopic characteristics are consistent with those of an authentic sample.[36]

From 5′-*O*-(Triphenylmethyl)uridine (5a) by Method II. The standard procedure was followed by use of **5a** (442 mg, 0.909 mmol, 1.0 equiv), CAN−SiO_2 (502 mg, containing 50.2 mg of CAN, 0.0915 mmol, 0.10 equiv), and CH_2Cl_2 (10 mL). After the reaction mixture was stirred for 1.5 h, it was worked up and the residue was recrystallized from EtOH to afford **6a** (216 mg, 0.885 mmol) in 98% yield.

From 2′,3′-*O*-(Isopropylidene)-5′-*O*-(triphenylmethyl)-uridine (7) by Method II. The standard procedure was followed by use of **7** (484 mg, 0.920 mmol, 1.0 equiv), CAN−SiO_2 (510 mg, containing 51.0 mg of CAN, 0.0930 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 1.5 h, it was worked up and the residue was recrystallized from EtOH to afford **6a** (219 mg, 0.897 mmol) in 98% yield.

2′-*O*-(*tert*-Butyldimethylsilyl)uridine (6b): From 2′-*O*-(*tert*-Butyl-dimethylsilyl)-5′-*O*-(triphenylmethyl)uridine (5b) by Method I. The standard procedure was followed by use of **5b** (364 mg, 0.606 mmol, 1.0 equiv), CAN (34.2 mg, 0.0623 mmol, 0.10 equiv), and MeCN (10 mL). After the reaction mixture was stirred for 12 h, it was concentrated under reduced pressure and the residue was purified by column chromatography (40% EtOAc in hexanes as eluant) to afford **6b** (174 mg, 0.486 mmol) in 80% yield: mp 192−194 °C (EtOAc/hexanes, lit.[26] mp 189−194 °C); R_f = 0.27 (EtOAc); ^{1}H NMR ($CDCl_3$) δ 0.13 (s, 6 H), 0.91 (s, 9 H), 1.56 (br s, 1 H), 2.58 (br s, 1 H), 3.65−3.92 (m, 2 H), 3.98−4.01 (m, 1 H), 4.32−4.37 (m, 1 H), 4.43−4.46 (m, 1 H), 5.50−5.52 (d, J = 4.5 Hz, 1 H), 5.70 (d, J = 8.0 Hz, 1 H), 7.44 (d, J = 8.0 Hz, 1 H), 8.43 (s, 1 H). Its spectroscopic characteristics are consistent with those of the same compound reported.[26]

From 2′-*O*-(*tert*-Butyldimethylsilyl)-5′-*O*-(triphenylmethyl)uridine (5b) by Method II. The standard procedure was followed by use of **5b** (312 mg, 0.520 mmol, 1.0 equiv), CAN−SiO_2 (286 mg, containing 28.6 mg of CAN, 0.0521 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 2.0 h, it was worked up and the residue was purified by column chromatography (40% EtOAc in hexanes as eluant) to afford **6b** (167 mg, 0.466 mmol) in 90% yield.

From 2′-*O*-(*tert*-Butyldimethylsilyl)-5′-*O*-(*p*-methoxyphenyldiphenylmethyl)uridine (12b) by Method I. The standard procedure was followed by use of **12b** (342 mg, 0.540 mmol, 1.0 equiv), CAN (30.0 mg, 0.0547 mmol, 0.10 equiv), and MeCN (10 mL). After the reaction mixture was stirred for 1.25 h, it was concentrated under reduced pressure and the residue was purified by column chromatography (40% EtOAc in hexanes as eluant) to afford **6b** (165 mg, 0.460 mmol) in 85% yield.

From 2′-*O*-(*tert*-Butyldimethylsilyl)-5′-*O*-(*p*-methoxyphenyldiphenylmethyl)uridine (12b) by Method II. The standard procedure was followed by use of **12b** (270 mg, 0.428 mmol, 1.0 equiv), CAN−SiO_2 (235 mg, containing 23.5 mg of CAN, 0.0428 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 0.10 h, it was worked up and the residue was purified by column chromatography (40% EtOAc in hexanes as eluant) to afford **6b** (145 mg, 0.405 mmol) in 95% yield.

From 2′-*O*-(*tert*-Butyldimethylsilyl)-5′-*O*-[di(*p*-methoxyphenyl)phenylmethyl]uridine (16b) by Method I. The standard procedure was followed by use of **16b** (426 mg, 0.646 mmol, 1.0 equiv), CAN (35.5 mg, 0.0647 mmol, 0.10 equiv), and MeCN (10 mL). After the reaction mixture was stirred for 0.10 h, it was concentrated under reduced pressure and the residue was purified by column chromatography (40% EtOAc in hexanes as eluant) to afford **6b** (208 mg, 0.581 mmol) in 90% yield.

From 2′-*O*-(*tert*-Butyldimethylsilyl)-5′-*O*-[di(*p*-methoxyphenyl)phenylmethyl]uridine (16b) by Method II. The standard procedure was followed by use of **16b**, (383 mg, 0.580 mmol, 1.0 equiv), CAN−SiO_2 (325 mg, containing 32.5 mg of CAN, 0.0590 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for <1 min, it was worked up and the residue was purified by column chromatography (40% EtOAc in hexanes as eluant) to afford **6b** (197 mg, 0.550 mmol) in 95% yield.

2′,3′-*O*-(Isopropylidene)uridine (8): Method I. The standard procedure was followed by use of 2′,3′-*O*-(isopropylidene)-5′-*O*-(triphenylmethyl)uridine (**7**, 286 mg, 0.543 mmol, 1.0 equiv), CAN (30.2 mg, 0.0550 mmol, 0.10 equiv), and MeCN (10 mL). After the reaction mixture was stirred for 10 h, it

(37) Zemlicka, J.; Chladek, S.; Holy, A.; Smrt, J. *Collect. Czech. Chem. Commun.* **1966**, *31*, 3198.

was concentrated under reduced pressure and the residue was purified by column chromatography (30% EtOAc in hexanes as eluant) to afford **8** (138 mg, 0.485 mmol) in 90% yield: mp 172−174 °C (EtOAc/hexanes). Its physical properties and spectroscopic characteristics are consistent with those of an authentic sample.[36]

2′-Deoxycytidine (10): Method I. The standard procedure was followed by use of 4-*N*-,5′-*O*-di(triphenylmethyl)-2′-deoxycytidine (**9**, 554 mg, 0.784 mmol, 1.0 equiv), CAN (43.6 mg, 0.0795 mmol, 0.10 equiv), and MeCN (10 mL). After the reaction mixture was stirred for 15 h, it was concentrated under reduced pressure and the residue was purified by column chromatography (40% MeOH in EtOAc as eluant) to afford **10** (154 mg, 0.678 mmol) in 87% yield: mp 207−210 °C (EtOH). Its physical properties and spectroscopic characteristics are consistent with that of an authentic sample.[36]

Method II. The standard procedure was followed by use of **9** (305 mg, 0.428 mmol, 1.0 equiv), CAN−SiO_2 (230 mg, containing 23.0 mg of CAN, 0.0419 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 2.0 h, it was worked up and the residue was purified by column chromatography (40% MeOH in EtOAc as eluant) to afford **10** (87.6 mg, 0.385 mmol) in 90% yield.

3′-*O*-(*tert*-Butyldimethylsilyl)uridine (13a): From 3′-*O*-(*tert*-Butyldimethylsilyl)-5′-*O*-(*p*-methoxyphenyldiphenylmethyl)uridine (12a) by Method I. The standard procedure was followed by use of **12a** (330 mg, 0.520 mmol, 1.0 equiv), CAN (29.0 mg, 0.0529 mmol, 0.10 equiv), and MeCN (10 mL). After the reaction mixture was stirred for 1.5 h, it was concentrated under reduced pressure and the residue was purified by column chromatography (40% EtOAc in hexanes as eluant) to afford **13a** (150 mg, 0.418 mmol) in 80% yield: mp 204−206 °C (EtOAc/hexanes, mp 203−206 °C[26]); R_f = 0.25 (EtOAc); ^{1}H NMR ($CDCl_3$) δ 0.15 (s, 6 H), 1.01 (s, 9 H), 1.99 (br s, 1 H), 2.08 (br s, 1 H), 3.59−3.98 (m, 2 H), 4.02−4.15 (m, 2 H), 4.44−4.48 (m, 1 H), 5.50 (d, J = 4.5 Hz, 1 H), 5.72 (d, J = 8.0 Hz, 1 H), 7.45 (d, J = 8.0 Hz, 1 H), 8.50 (br s, 1 H). Its spectroscopic characteristics are consistent with those of the same compound reported.[26]

From 3′-*O*-(*tert*-Butyldimethylsilyl)-5′-*O*-(*p*-methoxyphenyldiphenylmethyl)uridine (12a) by Method II. The standard procedure was followed by use of **12a** (350 mg, 0.555 mmol, 1.0 equiv), CAN−SiO_2 (305 mg, containing 30.5 mg of CAN, 0.0556 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 0.10 h, it was worked up and the residue was purified by column chromatography (40% EtOAc in hexanes as eluant) to afford **13a** (179 mg, 0.500 mmol) in 90% yield.

From 3′-*O*-(*tert*-Butyldimethylsilyl)-5′-*O*-[di(*p*-methoxyphenyl)phenylmethyl]uridine (16a) by Method I. The standard procedure was followed by use of **16a** (492 mg, 0.745 mmol, 1.0 equiv), CAN (44.1 mg, 0.0804 mmol, 0.10 equiv), and MeCN (12 mL). After the reaction mixture was stirred for 0.15 h, it was concentrated under reduced pressure and the residue was purified by column chromatography (40% EtOAc in hexanes as eluant) to afford **13a** (240 mg, 0.670 mmol) in 90% yield.

From 3′-*O*-(*tert*-Butyldimethylsilyl)-5′-*O*-[di(*p*-methoxyphenyl)phenylmethyl]uridine (16a) by Method II. The standard procedure was followed by use of **16a** (287 mg, 0.434 mmol, 1.0 equiv), CAN−SiO_2 (240 mg, containing 24.0 mg of CAN, 0.0437 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 0.010 h, it was worked up and the residue was purified by column chromatography (40% EtOAc in hexanes as eluant) to afford **13a** (143 mg, 0.398 mmol) in 92% yield.

2′-*O*-(*tert*-Butyldimethylsilyl)-3′-*O*-levulinoyl-2-*N*-benzoylguanosine (15a): Method I. The standard procedure was followed by use of 2′-*O*-(*tert*-butyldimethylsilyl)-3′-*O*-levulinoyl-5′-*O*-(*p*-methoxyphenyldiphenylmethyl)-2-*N*-benzoylguanosine (**14a**, 347 mg, 0.398 mmol, 1.0 equiv), CAN (22.0 mg, 0.0401 mmol, 0.10 equiv), and MeCN (10 mL). After the reaction mixture was stirred for 1.5 h, it was concentrated under reduced pressure and washed with ether to remove *p*-methoxytriphenylmethanol. The residue was purified by TLC plates (Et_2O/$CHCl_3$/EtOH = 1.0:0.9:0.1 as eluant) to afford **15a** (0.190 g, 0.317 mmol) in 80% yield: mp 194−196 °C (EtOH, lit.[27] mp 192−196 °C); R_f = 0.45 ($CHCl_3$/EtOH = 9:1); ^{1}H NMR (DMSO-d_6) δ −0.23 (s, 3 H), 0.40 (s, 3 H), 0.60 (s, 9 H), 2.12 (s, 3 H), 2.29 (t, J = 6.0 Hz, 2 H), 2.72 (t, J = 6.0 Hz, 2 H), 4.30−4.75 (m, 3 H), 3.85−4.30 (m, 3 H), 5.62 (d, J = 8.0 Hz, 1 H), 7.48−8.03 (m, 5 H), 8.09 (s, 1 H), 9.20 (br s, 1 H), 9.35 (br s, 1 H). Its spectroscopic characteristics are consistent with those of the same compound reported.[27]

Method II. The standard procedure was followed by use of **14a** (276 mg, 0.317 mmol, 1.0 equiv), CAN−SiO_2 (173 mg, containing 17.3 mg of CAN, 0.0315 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 0.10 h, it was worked up and the residue was purified by TLC plates (Et_2O/$CHCl_3$/EtOH = 1.0:0.9:0.1 as eluant) to afford **15a** (171 mg, 0.285 mmol) as a white solid in 90% yield.

3′-*O*-(*tert*-Butyldimethylsilyl)-2′-*O*-levulinoyl-2-*N*-benzoylguanosine (15b): Method I. The standard procedure was followed by use of 3′-*O*-(*tert*-butyldimethylsilyl)-2′-*O*-levulinoyl-5′-*O*-(*p*-methoxyphenyldiphenylmethyl)-2-*N*-benzoylguanosine (**14b**, 282 mg, 0.323 mmol, 1.0 equiv), CAN (17.8 mg, 0.0324 mmol, 0.10 equiv), and MeCN (10 mL). After the reaction mixture was stirred for 1.2 h, it was concentrated under reduced pressure and washed with ether to remove *p*-methoxytriphenylmethanol. The residue was purified by TLC plates (Et_2O/$CHCl_3$/EtOH = 1.0:0.9:0.1 as eluant) to afford **15b** (145 mg, 0.242 mmol) in 75% yield: mp 200−202 °C (EtOH, lit.[27] mp 201−202 °C); R_f = 0.40 ($CHCl_3$/EtOH = 9:1); ^{1}H NMR (DMSO-d_6) δ −0.01 (s, 6 H), 0.71 (s, 9 H), 2.05 (s, 3 H), 2.25 (t, J = 6.5 Hz, 2 H), 2.73 (t, J = 6.5 Hz, 2 H), 4.23−4.72 (m, 3 H), 3.80−4.20 (m, 3 H), 5.82 (d, J = 6.5 Hz, 1 H), 7.50−8.05 (m, 5 H), 8.15 (s, 1 H), 9.10 (br s, 1 H), 9.30 (br s, 1 H). Its spectroscopic characteristics are consistent with those of the same compound reported.[27]

Method II. The standard procedure was followed by use of **14b** (307 mg, 0.352 mmol, 1.0 equiv), CAN−SiO_2 (196 mg, containing 19.6 mg of CAN, 0.0357 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 0.10 h, it was worked up and the residue was purified by TLC plates (Et_2O/$CHCl_3$/EtOH = 1.0:0.9:0.1 as eluant) to afford **15b** (201 mg, 0.335 mmol) in 95% yield.

2-Aminoethyl (Adenosine)-3′,5′-cyclic Phosphoramide (18): Method I. The standard procedure was followed by use of 2-(*N*-trimethylphenyl)aminoethyl (adenosine)-3′,5′-cyclic phosphoramide (**17**, 725 mg, 1.18 mmol, 1.0 equiv), CAN (64.6 mg, 0.0117 mmol, 0.10 equiv), MeCN (30 mL), and DMF (10 mL). After the reaction mixture was stirred for 10 h, it was concentrated under reduced pressure and the residue was washed with ether to remove triphenylmethanol. The product was recrystallized from methanol to afford **18** (395 mg, 1.06 mmol) as a white crystal in 90% yield: mp 103−104 °C (lit.[8] mp 103−104 °C); R_f = 0.40 (MeOH/EtOAc = 1.5:1); UV (EtOH): λ_{max} (ϵ) = 260 nm (15 300); ^{1}H NMR (DMSO-d_6) δ 2.71 (br s, 2 H), 2.87 (br s, 2 H), 3.03 (br s, 2 H), 4.36−4.61 (m, 5 H), 4.83 (br s, 1 H, OH), 6.07 (s, 1 H), 7.84 (br s, 1 H), 7.93 (br s, 2 H), 8.03 (s, 1 H), 8.11 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 27.54, 35.76, 69.22, 71.94, 72.11, 76.53, 92.01, 118.24, 140.21, 147.73, 151.42, 154.97. Its spectroscopic characteristics are consistent with those of the same compound reported.[8]

Method II. The standard procedure was followed by use of **17** (485 mg, 0.791 mmol, 1.0 equiv), CAN−SiO_2 (438 mg, containing 43.8 mg of CAN, 0.0798 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 1.5 h, it was worked up and the residue was recrystallized from MeOH to afford **18** (279 mg, 0.752 mmol) in 95% yield.

Trichloroethyl 3′-[2′-*O*-(*tert*-Butyldimethylsilyl)uridyl] 5′-[2′,3′-*O*-(bis-*tert*-Butyldimethylsilyl)uridyl] Phosphate (20a): Method I. The standard procedure was followed by use of trichloroethyl 3′-[2′-*O*-(*tert*-butyldimethylsilyl)-5′-*O*-(*p*-methoxyphenyldiphenylmethyl)uridyl] 5′-[2′,3′-*O*-(bis-*tert*-butyldimethylsilyl)uridyl] phosphate (**19a**, 356 mg, 0.275 mmol, 1.0 equiv), CAN (15.0 mg, 0.0273 mmol, 0.10 equiv), and MeCN (8.0 mL). After the reaction mixture was stirred for 1.0 h, it was concentrated under reduced pressure and the residue was purified by column chromatography (10% MeOH in EtOAc as

eluant) to afford **20a** (256 mg, 0.250 mmol) in 91% yield: mp 126−128 °C (EtOAc/hexanes, lit.[26] mp 121−127 °C); R_f = 0.13 (EtOAc); ^{1}H NMR ($CDCl_3$) δ 0.13 (s, 6 H), 0.15 (s, 6 H), 0.19 (s, 6 H), 0.92 (s, 9 H), 1.02 (s, 18 H), 2.50 (br s, 1 H), 3.58−3.96 (m, 4 H), 3.98−4.36 (m, 4 H), 4.45−4.49 (m, 2 H), 4.53 (d, J = 12 Hz, 2 H), 5.71 (d, J = 8.0 Hz, 2 H), 5.76 (d, J = 4.0 Hz, 1 H), 5.78 (d, J = 4.0 Hz, 1 H), 7.54 (d, J = 8.0 Hz, 1 H), 7.58 (d, J = 8.0 Hz, 1 H), 8.40 (br s, 1 H), 8.60 (br s, 1 H). Its spectroscopic characteristics are consistent with those of the same compound reported.[26]

Method II. The standard procedure was followed by use of **19a** (296 mg, 0.228 mmol, 1.0 equiv), CAN−SiO_2 (125 mg, containing 12.5 mg of CAN, 0.0230 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 0.10 h, it was worked up and the residue was purified by column chromatography (10% MeOH in EtOAc as eluant) to afford **20a** (210 mg, 0.205 mmol) in 90% yield.

Trichloroethyl 3′-[2′-*O*-(*tert*-Butyldimethylsilyl)uridyl] 5′-[2′,3′-*O*-(Isopropylidene)uridyl] Phosphate (20b): Method I. The standard procedure was followed by use of trichloroethyl 3′-[2′-*O*-(*tert*-butyldimethylsilyl)-5′-*O*-(*p*-methoxyphenyldiphenylmethyl)uridyl] 5′-[2′,3′-*O*-(isopropylidene)uridyl] phosphate (**19b**, 524 mg, 0.473 mmol, 1.0 equiv), CAN (26.0 mg, 0.0479 mmol, 0.10 equiv), and MeCN (10 mL). After the reaction mixture was stirred for 1.0 h, it was concentrated under reduced pressure and the residue was purified by column chromatography (10% MeOH in EtOAc) to afford **20b** (319 mg, 0.382 mmol) in 80% yield: mp 134−135 °C (EtOAc/hexanes); R_f = 0.10 (EtOAc); ^{1}H NMR ($CDCl_3$) δ 0.17 (br s, 6 H), 0.99 (s, 9 H), 1.33 (s, 3 H), 1.52 (s, 3 H), 2.35 (br s, 1 H), 3.57−3.97 (m, 4 H), 3.98−4.38 (m, 4 H), 4.44−4.53 (m, 2 H), 4.56 (d, J = 12 Hz, 2 H), 5.60 (d, J = 8.0 Hz, 1 H), 5.82 (d, J = 8.0 Hz, 1 H), 5.80 (d, J = 4.0 Hz, 1 H), 5.93 (d, J = 4.0 Hz, 1 H), 7.60 (d, J = 8.0 Hz, 1 H), 7.72 (d, J = 8.0 Hz, 1 H), 8.48 (br s, 1 H), 8.90 (br s, 1 H). Anal. Calcd for $C_{29}H_{42}Cl_3N_4O_{14}PSi$: C, 41.66; H, 5.06; N, 6.70. Found: C, 41.48; H, 4.98; N, 6.82.

Method II. The standard procedure was followed by use of **19b** (314 mg, 0.283 mmol, 1.0 equiv), CAN−SiO_2 (155 mg, containing 15.5 mg of CAN, 0.0280 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 0.10 h, it was worked up and the residue was purified by column chromatography (10% MeOH in EtOAc as eluant) to afford **20b** (213 mg, 0.255 mmol) in 90% yield.

Trichloroethyl 3′-[2′-*O*-(*tert*-Butyldimethylsilyl)uridyl] 5′-Uridyl Phosphate (20c): Method II. The standard procedure was followed by use of **19b** (350 mg, 0.316 mmol, 1.0 equiv), CAN−SiO_2 (174 mg, containing 17.4 mg of CAN, 0.0318 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 2.0 h, it was worked up and the residue was purified by column chromatography (10% MeOH in EtOAc as eluant) to afford **20c** (220 mg, 0.277 mmol) as solids in 88% yield: mp 161−163 °C (EtOAc/hexanes); R_f = 0.040 (EtOAc); ^{1}H NMR (DMSO-d_6) δ 0.10 (br s, 6 H), 1.20 (s, 9 H), 2.30−2.50 (br, 3 H), 3.49−3.88 (m, 4 H), 3.89−4.32 (m, 4 H), 5.25−5.38 (m, 2 H), 4.56 (d, J = 11 Hz, 2 H), 5.62 (d, J = 7.5 Hz, 1 H), 5.81 (d, J = 7.5 Hz, 1 H), 5.81 (d, J = 4.0 Hz, 1 H), 5.92 (d, J = 4.0 Hz, 1 H), 7.80 (d, J = 7.5 Hz, 1 H), 7.98 (d, J = 7.5 Hz, 1 H), 11.20 (br s, 2 H). Anal. Calcd for $C_{26}H_{38}Cl_3N_4O_{14}PSi$: C, 39.23; H, 4.81; N, 7.04. Found: C, 39.44; H, 4.75; N 7.12.

2-[1-(Adenin-9-yl)methoxy]ethyl 2-(Adenin-9-yl)-2-(2-hydroxyethoxy)ethyl Phosphate (22): Method I. The standard procedure was followed by use of 2-[1-(adenin-9-yl)-methoxy]ethyl 2-(adenin-9-yl)-2-[2-(*p*-methoxyphenyldiphenylmethyl)ethoxy]ethyl phosphate (**21**, 378 mg, 0.483 mmol, 1.0 equiv), CAN (26.3 mg, 0.0480 mmol, 0.10 equiv), and MeCN (10.0 mL). After the reaction mixture was stirred for 1.0 h, it was concentrated under reduced pressure and the residue was purified by column chromatography (20% MeOH in $CHCl_3$ as eluant) and followed by recrystallization with EtOH to afford **22** (192 mg, 0.376 mmol) in 78% yield: mp >250 °C dec; R_f = 0.49 (*i*-PrOH/NH_4OH/H_2O = 7:1:2); ^{1}H NMR (DMSO-d_6/D_2O) δ 3.70−4.14 (m, 10 H), 5.48−5.68 (m, 3 H), 7.98 (s, 1 H), 8.17 (s, 1 H), 8.61 (s, 1 H), 8.80 (s, 1 H). Its spectroscopic characteristics are consistent with those of the same compound reported.[30]

Method II. The standard procedure was followed by use of **21** (414 mg, 0.529 mmol, 1.0 equiv), CAN−SiO_2 (290 mg, containing 29.0 mg of CAN, 0.0520 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 0.10 h, it was worked up and the residue was purified by column chromatography (20% MeOH in $CHCl_3$ as eluant) to afford **22** (230 mg, 0.450 mmol) in 85% yield.

1-*O*-Benzoylglycerol (24): Method I. The standard procedure was followed by use of 1-*O*-benzoyl-3-*O*-(triphenylmethyl)glycerol (**23**, 727 mg, 1.66 mmol, 1.0 equiv), CAN (91.0 mg, 0.165 mmol, 0.10 equiv), and MeCN (10 mL). After the reaction mixture was stirred for 9.0 h, it was concentrated under reduced pressure and the residue was purified by column chromatography (Et_2O as eluant) to afford **24** (305 mg, 1.56 mmol) as an oil in 94% yield: R_f = 0.46 (ether); ^{1}H NMR ($CDCl_3$) δ −2.45 (br s, 1 H), 3.59−3.74 (m, 2 H), 3.95 (d, J = 6.2 Hz, 1 H), 4.00−4.23 (m, 1 H), 4.36−4.40 (m, 2 H), 7.36−8.01 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 63.42, 65.79, 70.39, 128.48, 129.74, 133.36, 166.99. Its spectroscopic characteristics are consistent with those of the same compound reported.[8]

Method II. The standard procedure was followed by use of **23** (648 mg, 1.48 mmol, 1.0 equiv), CAN−SiO_2 (812 mg, containing 81.2 mg of CAN, 0.148 mmol, 0.10 equiv), and CH_2Cl_2 (8.0 mL). After the reaction mixture was stirred for 45 min, it was worked up and the residue was purified by chromatography on silica gel (Et_2O as eluant) to afford **24** (284 mg, 1.45 mmol) as an oil in 98% yield.

Standard Procedure for Desilylation by Use of Ceric Ammonium Nitrate (Method III). A solution of a silylated compound (1.0 equiv) in 2-propanol (10 mL/mmol) was treated with CAN (0.85 equiv). It was stirred at 25 °C until no starting material was left as shown by TLC. The reaction mixture was concentrated under reduced pressure and the residue was purified by use of gravity column chromatography packed with silica gel to provide the desired product with purity >99.9%.

Standard Procedure for Desilylation by Use of Ceric Ammonium Nitrate Adsorbed on Silica Gel (Method IV). A solution of a silylated compound (1.0 equiv) in a mixture of 2-propanol and CCl_4 (1:1, 10 mL/mmol) was treated with CAN−SiO_2 (containing 0.45 equiv of CAN). It was heated at reflux until no starting material was left as shown by TLC. The reaction mixture was concentrated under reduced pressure and the residue was purified by use of gravity column chromatography packed with silica gel to provide the desired product with purity >99.9%.

2′-*O*-(*tert*-Butyldimethylsilyl)adenosine (28a). Method III. The standard procedure was followed by use of **27a** (98.5 mg, 0.199 mmol, 1.0 equiv), CAN (92.7 mg, 0.169 mmol, 0.85 equiv), and 2-PrOH (2.0 mL). After the reaction mixture was stirred for 26 h, it was worked up and the residue was purified by use of column chromatography (EtOAc as the eluant) to afford **28a** (65.9 mg, 0.173 mmol) as white solids in 87% yield. Its physical properties and spectroscopic characteristics are consistent with those of the same compound reported.[26]

Method IV. The standard procedure was followed by use of **27a** (131 mg, 0.264 mmol, 1.0 equiv), CAN−SiO_2 (130 mg, containing 65.1 mg of CAN, 0.119 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 2.7 mL). After the reaction mixture was stirred for 7.0 h, it was worked up and the residue was purified by use of column chromatography (EtOAc as the eluant) to afford **28a** (90.7 mg, 0.238 mmol) as white solids in 90% yield.

3′-*O*-(*tert*-Butyldimethylsilyl)adenosine (28b). Method III. The standard procedure was followed by use of **27b** (101 mg, 0.204 mmol, 1.0 equiv), CAN (94.9 mg, 0.173 mmol, 0.85 equiv), and 2-PrOH (2.0 mL). After the reaction mixture was stirred for 24 h, it was worked up and the residue was purified by use of column chromatography (EtOAc as the eluant) to afford **28b** (66.2 mg, 0.173 mmol) as white solids in 85% yield. Its physical properties and spectroscopic characteristics are consistent with those of the same compound reported.[26]

Method IV. The standard procedure was followed by use of **27b** (179 mg, 0.361 mmol, 1.0 equiv), CAN−SiO_2 (178 mg,

containing 89.1 mg of CAN, 0.162 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 3.6 mL). After the reaction mixture was stirred for 9.0 h, it was worked up and the residue was purified by use of column chromatography (EtOAc as the eluant) to afford **28b** (121 mg, 0.318 mmol) as white solids in 88% yield.

2′,3′-*O*-Bis(*tert*-butyldimethylsilyl)adenosine (28c). Method III. The standard procedure was followed by use of **27c** (165 mg, 0.271 mmol, 1.0 equiv), CAN (126 mg, 0.230 mmol, 0.85 equiv), and 2-PrOH (2.7 mL). After the reaction mixture was stirred for 24 h, it was worked up and the residue was purified by use of column chromatography (50% EtOAc in hexanes as the eluant) to afford **28c** (114 mg, 0.230 mmol) as white solids in 85% yield. Its physical properties and spectroscopic characteristics are consistent with those of the same compound reported.[26]

Method IV. The standard procedure was followed by use of **27c** (112 mg, 0.184 mmol, 1.0 equiv), CAN−SiO_2 (90.6 mg, containing 45.3 mg of CAN, 0.0831 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 1.8 mL). After the reaction mixture was stirred for 8.0 h, it was worked up and the residue was purified by use of column chromatography (50% EtOAc in hexanes as the eluant) to afford **28c** (80.3 mg, 0.162 mmol) as white solids in 88% yield.

2′,3′-*O*-Bis(*tert*-butyldimethylsilyl)uridine (28d). Method III. The standard procedure was followed by use of **27d** (151 mg, 0.258 mmol, 1.0 equiv), CAN (120 mg, 0.219 mmol, 0.85 equiv), and 2-PrOH (2.6 mL). After the reaction mixture was stirred for 24 h, it was worked up and the residue was purified by use of column chromatography (50% EtOAc in hexanes as the eluant) to afford **28d** (113 mg, 0.240 mmol) as white solids in 93% yield. Its physical properties and spectroscopic characteristics are consistent with those of the same compound reported.[26]

Method IV. The standard procedure was followed by use of **27d** (105 mg, 0.179 mmol, 1.0 equiv), CAN−SiO_2 (88.4 mg, containing 44.2 mg of CAN, 0.0806 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 1.8 mL). After the reaction mixture was stirred for 8.0 h, it was worked up and the residue was purified by use of column chromatography (50% EtOAc in hexanes as the eluant) to afford **28d** (80.3 mg, 0.170 mmol) as white solids in 95% yield.

2′,3′-*O*-Bis(*tert*-butyldimethylsilyl)cytidine (28e). Method III. The standard procedure was followed by use of **27e** (115 mg, 0.197 mmol, 1.0 equiv), CAN (91.6 mg, 0.167 mmol, 0.85 equiv), and 2-PrOH (2.0 mL). After the reaction mixture was stirred for 25 h, it was worked up and the residue was purified by use of column chromatography (5% MeOH in EtOAc as the eluant) to afford **28e** (88.3 mg, 0.187 mmol) as white solids in 95% yield. Its physical properties and spectroscopic characteristics are consistent with those of the same compound reported.[38]

Method IV. The standard procedure was followed by use of **27e** (191 mg, 0.326 mmol, 1.0 equiv), CAN−SiO_2 (161 mg, containing 80.4 mg of CAN, 0.147 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 3.3 mL). After the reaction mixture was stirred for 12 h, it was worked up and the residue was purified by use of column chromatography (5% MeOH in EtOAc as the eluant) to afford **28e** (146 mg, 0.310 mmol) as white solids in 95% yield.

2-*N*-(*N*,*N*-Dimethylformamidyl)-2′,3′-*O*-bis(*tert*-butyldimethylsilyl)guanosine (28f). Method III. The standard procedure was followed by use of **27f** (241 mg, 0.354 mmol, 1.0 equiv), CAN (165 mg, 0.301 mmol, 0.85 equiv), and 2-PrOH (3.5 mL). After the reaction mixture was stirred for 26 h, it was worked up and the residue was purified by use of column chromatography (5% MeOH in EtOAc as the eluant) to afford **28f** (171 mg, 0.301 mmol) as white solids in 85% yield: mp (EtOAc) 143−145 °C; R_f = 0.30 (EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.46 (s, 3 H), −0.16 (s, 3 H), 0.080 (s, 3 H), 0.090 (s, 3 H), 0.76 (s, 9 H), 0.92 (s, 9 H), 3.10 (s, 3 H), 3.16 (s, 3 H), 3.50−3.65 (m, 2 H), 4.07−4.11 (m, 1 H), 4.21−4.25 (m, 1 H), 4.81−4.89 (m, 1 H), 5.48 (br s, 1 H), 5.62 (d, J = 7.47 Hz, 1 H), 7.52 (s, 1 H), 8.16 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.58, −4.59, 17.84, 18.03, 25.74, 30.14, 34.97, 62.69, 73.85, 76.33, 88.17, 90.37, 119.83 138.95, 146.78, 156.93, 157.43, 157.88; IR (KBr) 3230, 1684, 1626, 1459, 1106, 831 cm^{-1}; MS m/z (%) 567 (100, $M^+ + 1$). Anal. Calcd for $C_{25}H_{46}N_6O_5Si_2$: C, 52.97; H, 8.18; N, 14.83. Found: C, 52.90; H, 8.21; N, 14.91.

Method IV. The standard procedure was followed by use of **27f** (204 mg, 0.300 mmol, 1.0 equiv), CAN−SiO_2 (148 mg, containing 74.0 mg of CAN, 0.135 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 3.0 mL). After the reaction mixture was stirred for 13 h, it was worked up and the residue was purified by use of column chromatography (5% MeOH in EtOAc as the eluant) to afford **28f** (151 mg, 0.267 mmol) as white solids in 89% yield.

2′,3′-*O*-Dibenzyl-5′-*O*-(*tert*-butyldimethylsilyl)ascorbic Acid (30). Method III. The standard procedure was followed by use of **29** (217 mg, 0.371 mmol, 1.0 equiv), CAN (173 mg, 0.315 mmol, 0.85 equiv), and 2-PrOH (3.7 mL). After the reaction mixture was stirred for 20 h, it was worked up and the residue was purified by use of column chromatography (20% EtOAc in hexanes as the eluant) to afford **30** (154 mg, 0.326 mmol) as a colorless oil in 88% yield: R_f = 0.29 (20% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.12 (s, 3 H), −0.09 (s, 3 H), 0.72 (s, 9 H), 3.53−3.62 (m, 2 H), 3.81−3.85 (m, 1 H), 4.67 (d, J = 1.38 Hz, 1 H), 4.98−5.15 (m, 4 H), 7.08−7.24 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.16, −4.54, 17.88, 25.56, 62.96, 70.09, 73.49, 73.67, 75.26, 121.40, 127.70, 128.05, 128.60, 135.10, 136.09, 156.57, 169.80; IR (neat) 3254, 1747, 1673, 1156, 1042, 839 cm^{-1}; MS m/z (%) 413 (2, $M^{\bullet+} - {}^{\bullet}C_4H_9$), 121 (22), 91 (100); HRMS calcd for $C_{22}H_{25}O_6Si$ ($M^{\bullet+} - {}^{\bullet}C_4H_9$) 413.1420, found 413.1410. Anal. Calcd for $C_{26}H_{34}O_6Si$: C, 66.35; H, 7.28. Found: C, 66.05; H, 7.31.

Method IV. The standard procedure was followed by use of **29** (179 mg, 0.306 mmol, 1.0 equiv), CAN−SiO_2 (151 mg, containing 75.5 mg of CAN, 0.138 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 3.1 mL). After the reaction mixture was stirred for 7.0 h, it was worked up and the residue was purified by use of column chromatography (20% EtOAc in hexanes as the eluant) to afford **30** (131 mg, 0.279 mmol) as a colorless oil in 91% yield.

2-(*tert*-Butyldimethylsiloxy)benzyl Alcohol (32). Method III. The standard procedure was followed by use of **31** (242 mg, 0.686 mmol, 1.0 equiv), CAN (320 mg, 0.583 mmol, 0.85 equiv), and 2-PrOH (6.9 mL). After the reaction mixture was stirred for 2.0 h, it was worked up and the residue was purified by use of column chromatography (15% EtOAc in hexanes as the eluant) to afford **32** (139 mg, 0.583 mmol) as a colorless oil in 85% yield. Its physical properties and spectroscopic characteristics are consistent with those of the same compound reported.[39]

Method IV. The standard procedure was followed by use of **31** (371 mg, 1.05 mmol, 1.0 equiv), CAN−SiO_2 (520 mg, containing 260 mg of CAN, 0.473 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 10.5 mL). After the reaction mixture was stirred for 1.5 h, it was worked up and the residue was purified by use of column chromatography (15% EtOAc in hexanes as the eluant) to afford **32** (220 mg, 0.924 mmol) as a colorless oil in 88% yield.

***N*-(*tert*-Butoxycarbonyl)-L-serine Methyl Ester (34). Method III.** The standard procedure was followed by use of **33a** (341 mg, 1.02 mmol, 1.0 equiv), CAN (475 mg, 0.867 mmol, 0.85 equiv), and 2-PrOH (10 mL). After the reaction mixture was stirred for 10 h, it was worked up and the residue was purified by use of column chromatography (25% EtOAc in hexanes as the eluant) to afford ester **34** (191 mg, 0.867 mmol) as a colorless oil in 85% yield. Its physical properties and spectroscopic characteristics are consistent with those of an authentic sample.[36]

Method IV. The standard procedure was followed by use of **33a** (214 mg, 0.642 mmol, 1.0 equiv), CAN−SiO_2 (316 mg,

(38) Ogilvie, K. K.; Schifman, A. L.; Penney, C. L. *Can. J. Chem.* **1979**, *57*, 2230.

(39) Heslin, J. C.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1417.

containing 158 mg of CAN, 0.289 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 6.4 mL). After the reaction mixture was stirred for 4.0 h, it was worked up and the residue was purified by use of column chromatography (25% EtOAc in hexanes as the eluant) to afford **34** (131 mg, 0.597 mmol) as a colorless oil in 93% yield.

2′,3′-*O*-Bis(triisopropylsilyl)uridine (36a). Method IV. The standard procedure was followed by use of **35a** (210 mg, 0.295 mmol, 1.0 equiv), CAN−SiO_2 (146 mg, containing 73.0 mg of CAN, 0.133 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 3.0 mL). After the reaction mixture was stirred for 12 h, it was worked up and the residue was purified by use of column chromatography (50% EtOAc in hexanes as the eluant) to afford **36a** (143 mg, 0.257 mmol) as white solids in 87% yield: mp (50% EtOAc in hexanes) 224−226 °C; R_f = 0.56 (EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92−1.17 (m, 42 H), 3.02 (br s, 1 H), 3.71 (dd, J = 12.8, 2.4 Hz, 1 H), 3.88 (dd, J = 12.8, 2.4 Hz, 1 H), 4.08−4.12 (m, 1 H), 4.36−4.40 (m, 1 H), 4.83−4.86 (m, 1 H), 5.50 (d, J = 6.4 Hz, 1 H), 5.72 (d, J = 8.0 Hz, 1 H), 7.55 (d, J = 8.0 Hz, 1 H), 9.12 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.65, 12.95, 17.88, 18.00, 18.10, 18.15, 62.34, 73.63, 73.94, 86.12, 93.89, 102.31, 143.66, 150.41, 163.08; IR (KBr) 3455, 1695, 1089, 882 cm^{-1}; MS m/z 513 (100, $M^{\bullet+} - {}^{\bullet}C_3H_7$), 225 (81), 75 (32); HRMS calcd for $C_{24}H_{45}N_2O_6Si_2$ ($M^{\bullet+} - {}^{\bullet}C_3H_7$) 513.2816, found 513.2805. Anal. Calcd for $C_{27}H_{52}N_2O_6Si_2$: C, 58.23; H, 9.41; N, 5.03. Found: C, 58.05; H, 9.42; N, 4.98.

2′-*O*-(Triisopropylsilyl)uridine (36b). Method IV. The standard procedure was followed by use of **35b** (179 mg, 0.322 mmol, 1.0 equiv), CAN−SiO_2 (159 mg, containing 79.3 mg of CAN, 0.145 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 3.2 mL). After the reaction mixture was stirred for 15 h, it was worked up and the residue was purified by use of column chromatography (10% MeOH in EtOAc as the eluant) to afford **36b** (117 mg, 0.293 mmol) as white solids in 91% yield: mp (EtOAc) 155−156 °C (lit.[40] mp 154−155 °C); R_f = 0.30 (ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99−1.10 (m, 21 H), 2.81 (br s, 1 H), 3.07 (br s, 1 H), 3.73 (dd, J = 12.4, 2.4 Hz, 1 H), 3.90 (dd, J = 12.4, 2.4 Hz, 1 H), 4.15−4.19 (m, 1 H), 4.21−4.25 (m, 1 H), 4.83−4.86 (m, 1 H), 5.54 (d, J = 6.4 Hz, 1 H), 5.74 (d, J = 8.0 Hz, 1 H), 7.47 (d, J = 8.0 Hz, 1 H), 8.67 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.04, 17.63, 17.72, 62.71, 71.72, 73.78, 85.51, 93.69, 102.87, 142.94, 150.33, 163.00; IR (KBr) 3575, 1675, 1087, 872 cm^{-1}; MS m/z (%) 357 (54, $M^{\bullet+} - {}^{\bullet}C_3H_7$), 225 (100), 75 (32); HRMS calcd for $C_{15}H_{25}N_2O_6Si$ ($M^{\bullet+} - {}^{\bullet}C_3H_7$) 357.1482, found 357.1466. Anal. Calcd for $C_{18}H_{32}N_2O_6Si$: C, 53.98; H, 8.05; N, 6.99. Found: C, 53.87; H, 8.10; N, 6.89.

3′-*O*-(Triisopropylsilyl)uridine (36c). Method IV. The standard procedure was followed by use of **35c** (161 mg, 0.290 mmol, 1.0 equiv), CAN−SiO_2 (143 mg, containing 71.5 mg of CAN, 0.131 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 2.9 mL). After the reaction mixture was stirred for 17 h, it was worked up and the residue was purified by use of column chromatography (EtOAc as the eluant) to afford **36c** (98.7 mg, 0.247 mmol) as white solids in 85% yield: mp (EtOAc) 176−177 °C; R_f = 0.22 (EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08−1.11 (m, 21 H), 2.78 (br s, 1 H), 3.01 (br s, 1 H), 3.76 (dd, J = 12.4, 2.4 Hz, 1 H), 3.94 (dd, J = 12.4, 2.4 Hz, 1 H), 4.05−4.08 (m, 1 H), 4.40−4.46 (m, 1 H), 4.59−4.61 (m, 1 H), 5.51 (d, J = 4.4 Hz, 1 H), 5.71 (d, J = 8.0 Hz, 1 H), 7.46 (d, J = 8.0 Hz, 1 H), 8.58 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.20, 17.86, 61.81, 71.31, 73.79, 85.68, 94.28, 102.60, 142.51, 150.22, 162.78; IR (KBr) 3445, 1686, 1084, 880 cm^{-1}; MS m/z (%) 357 (38, $M^{\bullet+} - {}^{\bullet}C_3H_7$), 225 (74), 185 (100), 173 (78), 75 (57); HRMS calcd for $C_{15}H_{25}N_2O_6Si$ ($M^{\bullet+} - {}^{\bullet}C_3H_7$) 357.1482, found 357.1476. Anal. Calcd for $C_{18}H_{32}N_2O_6Si$: C, 53.98; H, 8.05; N, 6.99. Found: C, 53.79; H, 8.09; N, 6.92.

2′-*O*-(Triisopropylsilyl)cytidine (36d). Method IV. The standard procedure was followed by use of **35d** (164 mg, 0.296 mmol, 1.0 equiv), CAN−SiO_2 (146 mg, containing 73.0 mg of CAN, 0.133 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 3.0 mL). After the reaction mixture was stirred for 21 h, it was worked up and the residue was purified by use of column chromatography (10% MeOH in EtOAc as the eluant) to afford **36d** (94.6 mg, 0.237 mmol) as white solids in 80% yield: mp (EtOAc) 210−212 °C; R_f = 0.15 (EtOAc); ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.99−1.16 (m, 21 H), 3.61 (dd, J = 12.4, 2.4 Hz, 1 H), 3.72 (dd, J = 12.4, 2.4 Hz, 1 H), 3.95−4.05 (m, 2 H), 4.31−4.35 (m, 1 H), 5.22 (br s, 1 H), 5.41 (br s, 1 H), 5.70 (d, J = 4.0 Hz, 1 H), 6.20 (d, J = 8.0 Hz, 1 H), 8.38 (d, J = 8.0 Hz, 1 H), 9.96 (br s, 2 H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 11.88, 12.19, 17.97, 62.60, 69.54, 76.85, 84.39, 89.57, 94.28, 141.81, 155.74, 164.86; IR (KBr) 3345, 1665, 1102, 823 cm^{-1}; MS m/z (%) 356 (36, $M^{\bullet+} - {}^{\bullet}C_3H_7$), 224 (100), 185 (67), 112 (24); HRMS calcd for $C_{15}H_{26}N_3O_5Si$ ($M^{\bullet+} - {}^{\bullet}C_3H_7$) 356.1642, found 356.1648. Anal. Calcd for $C_{18}H_{33}N_3O_5Si$: C, 54.11; H, 8.32; N, 10.52. Found: C, 54.28; H, 8.29; N, 10.66.

3′-*O*-(Triisopropylsilyl)cytidine (36e). Method IV. The standard procedure was followed by use of **35e** (144 mg, 0.259 mmol, 1.0 equiv), CAN−SiO_2 (128 mg, containing 64.1 mg of CAN, 0.117 mmol, 0.45 equiv), and 2-PrOH/CCl_4 (1:1, 2.6 mL). After the reaction mixture was stirred for 28 h, it was worked up and the residue was purified by use of column chromatography (10% MeOH in EtOAc as the eluant) to afford **36e** (85.8 mg, 0.215 mmol) as white solids in 83% yield: mp (EtOAc) 114−115 °C; R_f = 0.14 (EtOAc); ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.97−1.11 (m, 21 H), 3.53 (dd, J = 10.8, 2.0 Hz, 1 H), 3.66 (dd, J = 10.8, 2.0 Hz, 1 H), 3.70−3.95 (m, 1 H), 4.04−4.10 (m, 1 H), 4.20−4.22 (m, 1 H), 5.26 (br s, 1 H), 5.31 (br s, 1 H), 5.77 (d, J = 5.2 Hz, 1 H), 5.97 (d, J = 7.2 Hz, 1 H), 8.05 (d, J = 7.2 Hz, 1 H), 8.66 (br s, 2 H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 12.31, 18.26, 18.34, 60.57, 69.85, 76.48, 85.61, 89.91, 94.71, 144.89, 155.90, 159.91; IR (KBr) 3395, 1664, 1092, 822 cm^{-1}; MS m/z (%) 356 (36, $M^{\bullet+} - {}^{\bullet}C_3H_7$), 224 (74), 185 (68), 112 (100); HRMS calcd for $C_{15}H_{26}N_3O_5Si$ ($M^{\bullet+} - {}^{\bullet}C_3H_7$) 356.1642, found 356.1641. Anal. Calcd for $C_{18}H_{33}N_3O_5Si$: C, 54.11; H, 8.32; N, 10.52. Found: C, 54.35; H, 8.36; N, 10.55.

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(40) Ogilvie, K. K.; Sadna, K. L.; Thompson, E. A.; Quilliam, M. A.; Westmore, J. B. *Tetrahedron Lett.* **1974**, *33*, 2861.