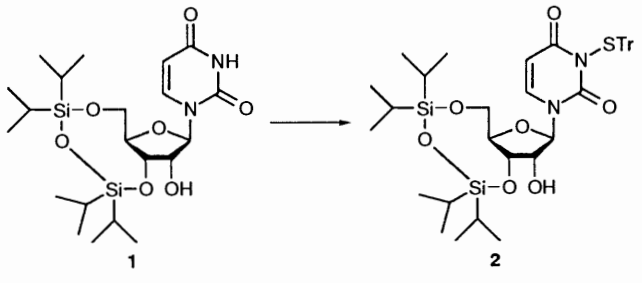
Synthesis and Properties of *N*-Tritylthio Nucleoside Derivatives and Reductive Removal of the Tritylthio Group by Use of Tributyltin Hydride and Tris(trimethylsilyl)silane

Mitsuo Sekine* and Kohji Seio
Department of Life Science, Tokyo Institute of Technology, Nagatsuta, Midoriku, Yokohama 227, Japan

N-Sulfenylations of ribo- and deoxyribo-nucleoside derivatives have been studied by the use of triphenylmethanesulfenyl chloride as a sulfenylating reagent under a variety of conditions. A two-phase system using 0.2 mol dm^{-3} Na_2CO_3–CH_2Cl_2 was found to be effective for *N*-sulfenylation of deoxycytidine, deoxyadenosine and guanosine derivatives (**7b**, **9b**, **9c** and **11d**), which were partially or fully protected at the hydroxy functions. In the case of adenosine **9c**, the N^1-sulfenylated deoxyadenosine derivative **10f** was also formed. For the *N*-sulfenylation of the 5'-protected thymidine derivative **7a**, phase-transfer catalysis was successfully used. It was found that the *N*-TrS group could be removed by reductive C–S bond cleavage using Bu_3SnH or $(Me_3Si)_3SiH$ in toluene in the presence of AIBN under reflux for 5 min. In several cases, the Bu_3SnH-mediated deprotection occurred in the absence of AIBN. When triethylborane or sonication was used as a radical initiator, the cleavage reaction could be carried out at room temperature. The stability of the TrS group attached to these nucleoside bases was examined under several acidic and basic conditions.

In chemical conversion of nucleosides directed towards the synthesis of anticancer and antiviral drugs[1–3] as well as oligonucleotides,[4–14] the reactive amino and imido groups on the base moieties have been appropriately protected. For example, *N*-acylnucleoside derivatives have been prepared as typical synthetic intermediates by peracylation of nucleosides followed by selective hydrolysis of the resulting *O*-ester functions.[15,16] Recently, transient protection procedures developed originally by Jones,[17] which involved the selective *O*-trimethylsilylation followed by *N*-protection, have proved to be useful for the synthesis of such *N*-protected nucleosides.[18–21] The selective *N*-protection has been achieved only in the case of cytidine and deoxycytidine[22–28] among the eight common deoxyribonucleosides and ribonucleosides except for a few examples.[29–33]

The tritylthio (TrS) group[34,35] has recently been reported as the protecting group of the imido function of uridine in the synthesis of oligouridylates by Takaku.[36] This group was introduced selectively to the uracil imido function of a 2'-unprotected 3',5'-cyclic silyl ether derivative **1** of uridine by



1 **2**

treatment with triphenylmethanesulfenyl chloride (TrSCl) (2 mol equiv.) in the presence of triethylamine in CH_2Cl_2 to give the *N*-STr derivative **2** in 81% yield.[36] Later, we reported that compound **2** could be obtained quantitatively from compound **1** by the use of phase-transfer catalysis.[37]

It is known that the 2'-hydroxy group of 3',5'-cyclic silyl ether derivatives such as **1** was extremely unreactive to phosphorylating reagents because of the neighbouring isopropyl group on the 3'-silicon atom.[38] Therefore, it seemed that the high regioselectivity observed in the phase-transfer catalysis could be explained in terms of the steric effect of the 3'-protecting group. However, there was another possibility, that the inherent property of the reagent led to such a high selectivity towards the amido function without affecting the 2'-hydroxy group of compound **1**. Quite recently, Netscher[39] has reported that 2,2,2-trifluoro-1,1-diphenylethanesulfenyl chloride, a reagent similar to TrSCl, reacted with several amino alcohols to give the corresponding sulfenamides selectively without sulfenation of the hydroxy groups. Zervas[34] originally reported that amino acid derivatives could be *N*-sulfenylated by treatment with TrSCl in tetrahydrofuran (THF) solutions containing 5% Na_2CO_3. These results strongly suggested that hydroxy groups of nucleosides would remain intact if TrSCl were to be employed as a sulfenylating reagent for *N*-sulfenylation. This expectation led us to study the selective protection of the amino and imido group of multifunctional nucleosides by the use of TrSCl.

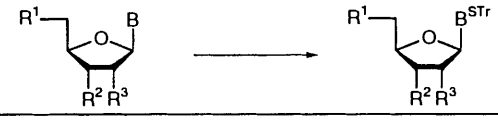
The TrS group was first used as the *N*-protecting group of amino acids.[34] The presence of this group can be easily detected on TLC by the colour of a trityl cation which is generated by heating. The great lipophilicity of the TrS group is helpful for chromatographic separation of TrS-containing products. This unique protecting group has been removed by the use of HCl,[34] $CuCl_2$,[35] HI,[35] trimethylsilyl iodide,[35] and iodine.[36]

In this paper, we report several interesting aspects of TrSCl in the selective introduction of the TrS group into the imido and amino groups of various nucleoside derivatives, and we also describe a new method for its removal by the use of Bu_3SnH and $(Me_3Si)_3SiH$.

Results and Discussion

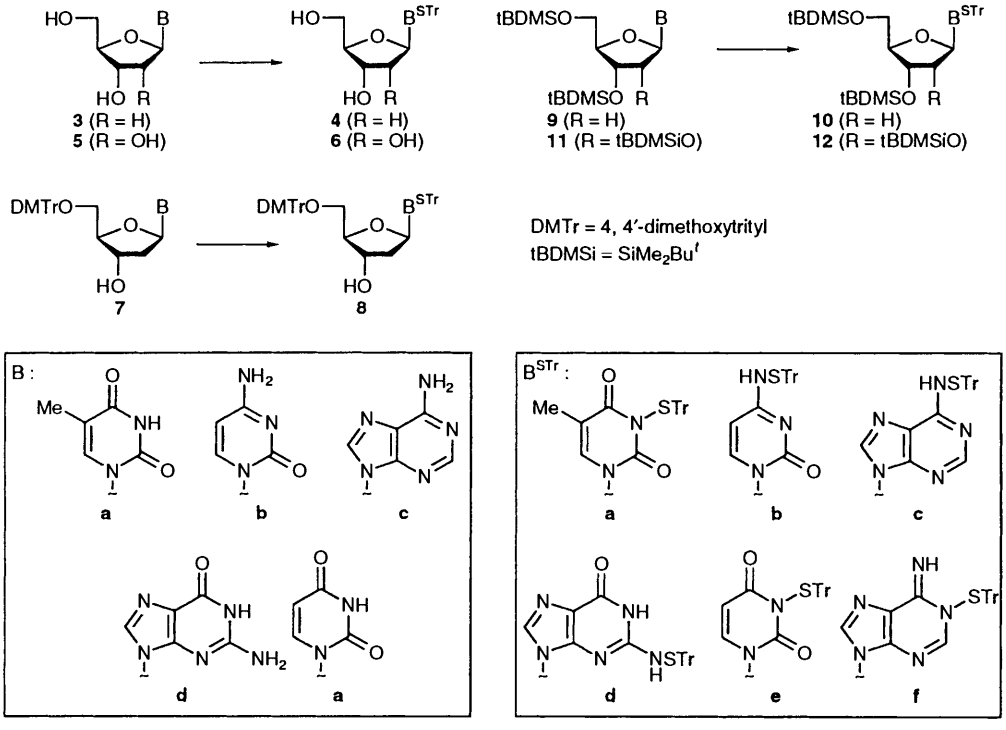
First, the reaction of unprotected deoxycytidine **3b** with TrSCl was conducted under a variety of conditions using Na_2CO_3[34] as a base. When deoxycytidine was allowed to react with 5 mol equiv. of TrSCl in aq. THF in the presence of 3 mol equiv. of Na_2CO_3 (Method A), N^3-(triphenylmethylsulfenyl)deoxycytidine **4b** was isolated in 72% yield as shown in Table 1 and Scheme 1. *O*-Sulfenylation was not observed in this reaction. The use of a lesser amount of reagent led to a poorer yield of compound **4b**. This was mainly because of competitive

Table 1 *N*-Sulfenylation of deoxyribonucleoside and ribonucleoside derivatives with triphenylmethanesulfenyl chloride



Compound	R^1	R^2	R^3	B	Method[a]	TrSCl (mol equiv.)	Bu_4NBr (mol equiv.)	Time (*t*/h)	Product	Yield (%)
3a	OH	OH	H	Thy	A	1.1		24	**4a**	trace
3b	OH	OH	H	Cyt	A	1.1		1	**4b**	10
3b	OH	OH	H	Cyt	A	5.0		1	**4b**	72
5e	OH	OH	OH	Ura	A	1.1		9.5	**6e**	21
7a	DMTrO	OH	H	Thy	B	1.2	0.02	8	**8a**	95
7b	DMTrO	OH	H	Cyt	C	2.0		2	**8b**	90
7c	DMTrO	OH	H	Ade	C	2.0		6	**8c** / **8f** (1:1)	75
9b	tBDMSiO	tBDMSiO	H	Cyt	B	1.0	0.04	14	**10b**	53
9b	tBDMSiO	tBDMSiO	H	Cyt	B	2.0	0.04	2	**10b**	93
9b	tBDMSiO	tBDMSiO	H	Cyt	C	2.0		1.5 6	**10b**	90
9b	tBDMSiO	tBDMSiO	H	Cyt	D	2.0		6	**10b**	43
9b	tBDMSiO	tBDMSiO	H	Cyt	E	2.0		2	**10b**	61
9c	tBDMSiO	tBDMSiO	H	Ade	C	2.0		2	**10c** / **10f**	34 / 49 (83)
11d	tBDMSiO	tBDMSiO	tBDM-SiO	Gua	C	2.0		2	**12d**	84

[a] Method A: 6.5% aq. Na_2CO_3–THF (1:1); Method B: Bu_4NBr–0.2 mol dm^{-3} Na_2CO_3–CH_2Cl_2 (2:1); Method C: 0.2 mol dm^{-3} aq. Na_2CO_3–CH_2Cl_2 (2:1); Method D: pyridine–CH_2Cl_2; Method E: Et_3N–CH_2Cl_2. All reactions were carried out at room temperature.



Scheme 1

decomposition of TrSCl during the reaction. Deoxyadenosine **3c** and deoxyguanosine **3d** did not react smoothly with TrSCl under similar conditions. However, treatment of uridine **5e** with TrSCl using Method A gave N^3-(triphenylmethylsulfenyl)-uridine **6e** as the sole product in 21% yield selectively without formation of *O*-sulfenylated products. Contrary to this result, thymidine **3a** exhibited an extremely poor reactivity towards this reagent under similar conditions. The presence of the 5-methyl group of compound **3a** affected considerably the N^3-sulfenylation.

Since these reactions proceeded slowly and did not go to completion, we have studied an alternative *N*-sulfenylation of protected deoxyribonucleoside derivatives by the use of phase-transfer catalysis, which has proved to be effective for *N*-sulfenylation of the imido group of a protected lipophilic uridine derivative.[37] When a two-phase system using Bu_4NBr as phase-transfer catalyst was employed (Method B), 5′-*O*-(4,4′-dimethoxytrityl)thymidine **7a** was successfully converted into the *N*-sulfenylated product **8a** in 95% yield. The 3′-hydroxy group was not sulfenylated at all although this hydroxy group was not sterically hindered as in compound **1**. Therefore, it is now clear that the selective *N*-sulfenylation is essentially attributable to the inherent inactivity of the reagent towards hydroxy groups. A similar reaction of 3′,5′-*O*-bis-(*tert*-butyldimethylsilyl)de-

Table 2 Reactions of NH-containing compounds with TrSCl by the use of Method A

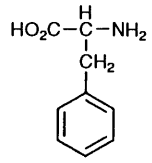
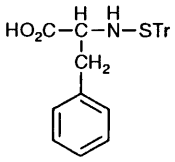
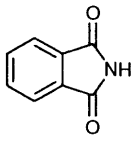
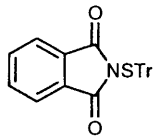
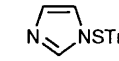
Substrate		TrSCl (mol equiv.)	Time (*t*/min)	Yield (%)	Product	
	**13**	1.1	30	95		**14**
	**15**	1.1	60	86		**16**
	**17**	1.3	5	84		**18**

Table 3 Removal of the TrS group from *N*-sulfenylated products by means of Bu_3SnH and $(Me_3Si)_3SiH$

Substrate	Reagent	(mol equiv.)	Additive	(mol equiv.)[a]	Time (*t*/min)	Temp. (*T*/°C)	Product	Yield (%)
2	Bu_3SnH	1.0			5	115	**1**	53
2	Bu_3SnH	2.5			5	115	**1**	86
2	Bu_3SnH	2.5	AIBN	0.1	210	70	**1**	82
2	Bu_3SnH	5.0	BEt_3	0.6	120	r.t.[b]	**1**	84
2	Bu_3SnH	2.5	AIBN	2.0 ((((	540	r.t.[b]	**1**	62
2	Bu_3SnH	10.0	AIBN	1.8 ((((	540	r.t.[b]	**1**	76
2	$(Me_3Si)_3SiH$	2.2	AIBN	0.01	90	115	**1**	48
8a	Bu_3SnH	2.5			5	115	**7a**	82
10b	Bu_3SnH	2.5			5	115	**9b**	93
10b	$(Me_3Si)_3SiH$	2.2	AIBN	0.01	180	115	**9b**	63
12d	Bu_3SnH	2.5			5	115	**11d**	83
12d	$(Me_3Si)_3SiH$	2.2	AIBN	0.01	120	115	**11d**	81
14	Bu_3SnH	2.5			5	115	**13**	82

[a] ((((= Ultrasonic wave. [b] r.t. is room temperature.

oxycytidine **9b** gave the 4-*N*-blocked product **10b** in 93% yield. Interestingly, it was found that when the phase-transfer catalyst was eliminated from the reaction (Method C), a similar reaction occurred to give compound **10b** in high yield, as shown in Table 1. This result suggested that the amino group of compound **9b** had a sufficient nucleophilicity in the two-phase system. On the other hand, the usual reaction of compound **9b** with TrSCl in the presence of pyridine (Method D) or triethylamine (Method E) in dichloromethane gave compound **10b** in a lower yield. The two-phase reaction has also proved to be useful for the *N*-sulfenylation of 5′-*O*-(4,4′-dimethoxytrityl)-deoxycytidine **7b**, which gave the *N*-sulfenylated product **8b** in 90% yield.

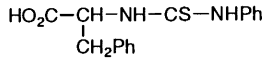
Next, the two-phase reaction was applied to the *N*-sulfenylation of 3′,5′-*O*-bis-(*tert*-butyldimethylsilyl)deoxyadenosine **9c**. This reaction proceeded as usual but gave two products. The two products could be separated by silica gel column chromatography to afford the 6-*N*-sulfenylated product **10c** having a higher R_f-value and the N^1-sulfenylated isomer **10f**. Since the separation of these products was tedious, we attempted to isolate desilylated materials **4c** and **4f** after treatment of the mixture containing isomers **10c** and **10f** with Bu_4NF (TBAF). The fluoride ion-mediated desilylation afforded diol **4f** in 45% yield from compound **9c** along with deoxyadenosine **3c**. The latter product was probably formed *via* fluoride ion-promoted detritylthiolation of compound **10c**. A great difference in stability of the TrS–N linkage toward fluoride ion between isomers **10c** and **10f** was observed.

In the case of 5′-*O*-(4,4′-dimethoxytrityl)deoxyadenosine **7c**, a similar reaction gave a mixture of the 6-*N*-sulfenylated product **8c** and the N^1-sulfenylated isomer **8f** which could not be separated by silica gel column chromatography. A similar two-phase reaction of 2′,3′,5′-*O*-tris-(*tert*-butyldimethylsilyl)-guanosine **11d** with TrSCl gave 2-*N*-sulfenylated product **12d** in 84% yield.

In connection with the function-selective *N*-sulfenylation using TrSCl, we also examined the *N*-sulfenylation of several simpler substrates as summarized in Table 2. When reaction of phenylalanine **13** with TrSCl was carried out under the conventional conditions (Method A), the *N*-STr product **14** was selectively obtained in 95% yield without the carboxy group being affected. Under these conditions, phthalimide **15** and imidazole **17** reacted smoothly with TrSCl to give the products **16** and **18** in 86 and 84% yield, respectively.

Next, removal of the TrS group from *N*-sulfenylated nucleoside derivatives was studied. As an alternative method for removal of this protecting group, we chose reductive desulfenylation using Bu_3SnH.[40–42] When the *N*-sulfenylated uridine derivative **2** was refluxed with 2.5 mol equiv. of Bu_3SnH in toluene for a short time (5 min), the TrS group was quantitatively removed and the parent compound **1** was isolated in 86% yield. In a similar manner, 5′-*O*-(4,4′-dimethoxytrityl)-N^3-(triphenylmethylsulfenyl)thymidine **8a**, 3′,5′-*O*-bis-(*tert*-butyldimethylsilyl)-4-*N*-(triphenylmethylsulfenyl)deoxycytidine **10b**, 2′,3′,5′-*O*-tris-(*tert*-butyldimethylsilyl)-2-*N*-(triphenylmethylsulfenyl)deoxyguanosine **12d** and *N*-(triphenylmethylsulfenyl)-

phenylalanine **14** were deprotected to give the parent compounds **7a**, **9b**, **11d** and **13** in high yield as shown in Table 3. In the case of phenylalanine **13**, the product was characterized by further conversion into a thiourea derivative **19**.



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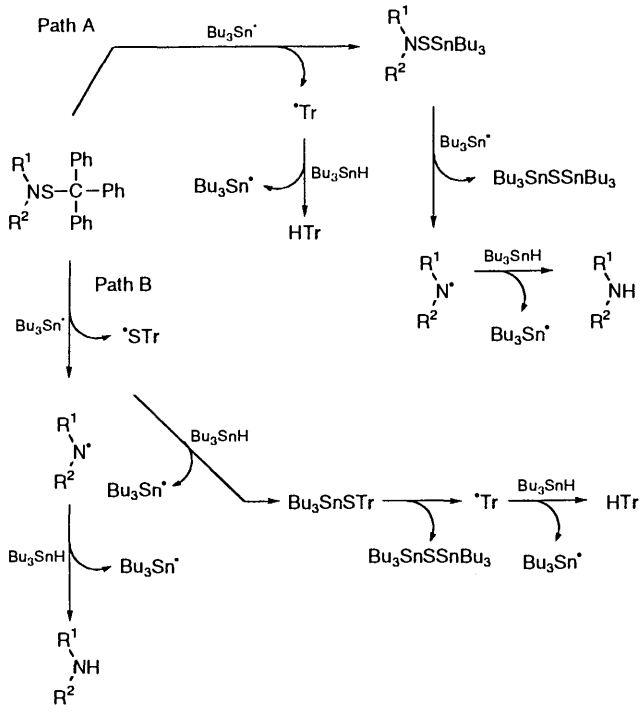
To clarify the mechanism of reductive removal of the TrS group, Bu_3SnH (1 mol equiv.) was employed in the case of substrate **2**. This reaction was not completed and about half of the starting material remained unchanged. Compound **1** was obtained in 53% yield. This result implies that both C–S and N–S bonds of compound **2** were simultaneously cleaved during the whole reaction. Probably, the reductive elimination of the TrS group proceeded *via* the initial cleavage of the S–C bond between the Tr group and the sulfur atom (Path A) as shown in Scheme 2. Then, the N–$SSnBu_3$ derivative once generated was rapidly desulfurized by another reducing reagent. Otherwise, the initial cleavage between the N–S bond and then 1 mol equiv. of Bu_2SnH was consumed by the predominant reaction with the resulting TrS–$SnBu_3$ over the initial reaction (Path B).

It is interesting to note that Netscher[39] reported that 2,2,2-trifluoro-1,1-diphenylethanesulfenylamide derivatives were almost totally recovered when treated with Bu_3SnH. Under conditions similar to those described by Netscher, compound **2** was converted into compound **1** although a longer period of time was required. These facts supported the mechanism *via* Path A and implied that the easy removal of the TrS group encountered in our cases was probably attributed to easy formation of the stable trityl radical which would be the rate-determining step in the present reaction, while the 2,2,2-trifluoro-1,1-diphenylethyl radical would be less stabilized than the trityl radical.

We also found that the TrS group could be removed at room temperature by using Bu_3SnH in the presence of BEt_3[43] or by ultrasonic irradiation.[44] These results are summarized in Table 3. These conditions would be useful for chemical conversion of nucleic acid derivatives.



Scheme 2

Next, we studied a new procedure for removal of the TrS group by use of a less toxic reducing reagent, namely $(Me_3Si)_3SiH$.[45,46] When this reagent (2.2 mol equiv.) was used for removal from compound **2**, the reaction was completed in 1.5 h, the parent uridine derivative being obtained in 48% yield. A more lipophilic by-product was formed to a considerable extent. In the case of 3′,5′-*O*-bis-(*tert*-butyldimethylsilyl)-4-*N*-(triphenylmethylsulfenyl)deoxycytidine **10b**, the deprotected product **9b** was obtained in 63% yield. In this reaction, the competitive formation of a more polar by-product was detected. However, similar treatment of 2′,3′,5′,*O*-tris-(*tert*-butyldimethylsilyl)-2-*N*-(triphenylmethylsulfenyl)deoxyguanosine **12d** with $(Me_3Si)_3SiH$ gave compound **11d** in satisfactory yield (81%) as shown in Table 3. No significant side-reactions were observed in this case. It is concluded that this reagent is not suitable for pyrimidine nucleosides and should be limited to purine nucleosides.

Finally, the stability of *N*-tritylthionucleoside derivatives **6e**, **4b**, **10c**, **10f**, and **12d** under acidic and basic conditions has been examined. These results are summarized in Table 4. Under both acidic and basic conditions, the TrS group of these compounds was found to be eliminated slowly but considerably in some cases. In particular, the N–S bond of substrates **6e** and **10c** was cleaved completely by treatment with conc. NH_3–pyridine (2:3, v/v) in 10 and 8 h, respectively. This result suggested that, when the TrS group was employed as the *N*-protecting group of uridine for oligoribonucleotide synthesis where conc. NH_3 was used for removal of *N*-acyl groups at the final stage, the previous treatment with iodine[36] was unnecessary. The TrS group of substrates **4b** and **10c** was more resistant to 80% acetic acid than were those of substrates **6e** and **12d**. Among those compounds tested, 4-*N*-(tritylthio)deoxycytidine **4b** was most stable toward conc. NH_3, Et_3N–pyridine–water, and 80% acetic acid.

Compared with other protecting groups for amino functions of nucleosides, the TrS group would be used as a semi-stable protecting group for chemical transformation of other functional groups. In the case of guanosine, especially a new route to 6-*O*-modified guanosine derivatives would be developed *via* *N*-(tritylthio)guanosine derivatives such as compound **12d**. The TrS group would be developed *via* *N*-(tritylthio)guanosine derivatives such as compound **12d**. The TrS group would be compatible with more base- or acid-labile hydroxy-protecting groups such as phenoxyacetyl or 4,4′-dimethoxytrityl, since the TrS group was sufficiently stable under basic or acidic conditions required for removal of these hydroxy-protecting groups. However, the TrS group has a lack of general utility as an *N*-protecting group since it is difficult to introduce this protecting group selectively to the 6-*N*-position of adenosine.

We are now studying further applications of these findings to the synthesis of base-cyclized uridylyl (3′–5′) uridine derivatives.

Experimental

M.p.s were obtained on a Mitamura Melt-Temp apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were measured at 270 MHz and 67.8 MHz, respectively, on a JEOL-EX 270 spectrometer with $SiMe_4$ as the internal standard. *J* Values are given in Hz. UV spectra were taken on a Hitachi U-2000 spectrophotometer. TLC was performed by the use of Merck-Kieselgel 60-F-254 (0.25 mm) with a developing solvent of CH_2Cl_2–MeOH (9:1, v/v). Column chromatography was performed with silica gel C-200 purchased from Waco Co. Ltd., and a minipump for a goldfish bowl was conveniently used to attain sufficient pressure for rapid chromatographic separation.

Table 4 Stability of *N*-(tritylthio)nucleoside derivatives under acidic and basic conditions

Conditions	$t_{\frac{1}{2}}$ Compound 6e	4b	10c	10f	12d
Conc. NH_3–pyridine (2:3), 25 °C	1 h	60% stable after 20 h	45 min	7 h	3 h
	10 h ($t_{comp.}$)[a]		8 h ($t_{comp.}$)[a]		
Et_3N–water–pyridine (1:4:5), 25 °C	40 h	70% stable after 40 h	3 h	20 h	20 h
80% AcOH	3 h	24 h	24 h	24 h	3 h

[a] $t_{comp.}$ is the time taken for the reaction to go to completion.

Method A: Typical Procedure.—4-N-(*Triphenylmethylsulfenyl*)*deoxycytidine* **4b**. To a solution of deoxycytidine (66 mg, 0.25 mmol) in THF (2.5 cm^3)–6.5% aq. Na_2CO_3 (1 cm^3, 0.75 mmol) was added a THF solution (4 cm^3) of TrSCl (777 mg, 2.5 mmol) over a period of 5 min. The resulting solution was stirred for 1 h. The mixture was partitioned between diethyl ether and water. The ethereal layer was collected and the aqueous layer was further extracted with diethyl ether. The combined organic phase was washed twice with water, dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was chromatographed on a column of silica gel with CH_2Cl_2–MeOH to give *compound* **4b** as foam (125 mg, 72%) (Found: C, 64.8; H, 5.5; N, 7.6. $C_{28}H_{27}N_3O_4S{\cdot}H_2O$ requires C, 64.7; H, 5.6; N, 8.1%); $\delta_H(CDCl_3)$ 2.20 (1 H, m, 2'-H^a), 2.40 (1 H, m, 2'-H^b), 3.78 (2 H, br, 5'-H), 3.94 (1 H, br, 4'-H), 4.42 (1 H, dd, $J_{2'a,3'}$ 5.4 and $J_{2'b,3'}$ 12.3, 3'-H), 5.68 (1 H, d, $J_{5,6}$ 7.3, 5-H), 6.01 (1 H, t, $J_{1',2'}$ 6.1, 1'-H), 7.20–7.37 (15 H, m, ArH) and 7.27 (1 H, d, $J_{5,6}$ 7.3, 6-H); $\delta_C(CDCl_3)$ 169.15, 155.18, 142.43, 141.82, 129.63, 128.25, 127.44, 92.58, 87.46, 72.41, 69.76, 61.35 and 40.70.

N^3-(*Triphenylmethylsulfenyl*)*uridine* **6e** (Found: C, 60.7; H, 4.9; N, 5.0. $C_{28}H_{26}N_2O_6S{\cdot}2H_2O$ requires C, 60.6; H, 4.7; N, 5.1%); $\delta_H(CDCl_3)$ 3.73 (1 H, br, 5'-H^a), 3.85–4.02 (2 H, m, 4'-H and 5'-H^b), 4.12 (1 H, m, 3'-H), 4.20 (1 H, m, 2'-H), 5.26 (1 H, d, $J_{1',2'}$ 3.5, 1'-H), 5.56 (1 H, d, $J_{5,6}$ 9, 5-H), 7.20 (10 H, s, ArH) and 7.40 (2 H, m, ArH and 6-H); $\delta_C(CDCl_3)$ 60.54, 68.97, 74.90, 75.46, 84.77, 92.42, 100.65, 127.80, 130.98, 139.36, 142.64, 152.76 and 164.12.

Method B: Typical Procedure.—5'-O-(4,4'-*Dimethoxytrityl*)-N^3-(*triphenylmethylsulfenyl*)*thymidine* **8a**. To a two-phase solution of compound **7a** (273 mg, 0.5 mmol) in CH_2Cl_2 (10 cm^3)–0.2 mol dm^{-3} Na_2CO_3 (20 cm^3) were added TrSCl (187 mg, 0.6 mmol) and Bu_4NBr (32 mg, 0.1 mmol). The resulting mixture was vigorously stirred at room temperature for 6 h. The organic phase was collected and washed twice with saturated aq. $NaHCO_3$. The organic layers were combined, dried over Na_2SO_4, and filtered. The filtrate was evaporated under reduced pressure. The residue was chromatographed on a silica gel column with hexane–CH_2Cl_2 (2:3) to give *compound* **8a** (389 mg, 95%) (Found: C, 72.5; H, 5.8; N, 3.2. $C_{50}H_{46}N_2O_7S$ requires C, 73.2; H, 5.7; N, 3.4%); $\delta_H(CDCl_3)$ 1.36 (3 H, s, Me), 1.96–2.27 (2 H, m, 2'-H_2), 3.30 (1 H, dd, $J_{4',5'a}$ 3.3, J_{gem} 10.6, 5'-H^a), 3.42 (1 H, dd, $J_{4',5'a}$ 3.3, J_{gem} 10.6, 5'-H^b), 3.77 (1 H, m, 4'-H), 4.42 (1 H, m, 3'-H), 6.02 (1 H, t, $J_{1',2'}$ 6.9, 1'-H) and 6.75–7.45 (29 H, m, ArH and 6-H); $\delta_C(CDCl_3)$ 163.88, 158.63, 151.93, 144.26, 142.44, 135.31, 133.21, 130.78, 128.00, 127.89, 127.30, 127.12, 113.17, 109.49, 86.79, 86.15, 85.88, 74.88, 71.88, 63.27, 55.17, 53.37 and 13.12.

Method C: Typical Procedure.—3',5'-O-(*Bis*-(tert-*butyldimethylsilyl*)-4-N-(*triphenylmethylsulfenyl*)*deoxycytidine* **10b**. To a two-phase solution of compound **9c** (273 mg, 0.45 mmol) in CH_2Cl_2 (9 cm^3)–0.2 mol dm^{-3} Na_2CO_3 (18 cm^3) was added TrSCl (280 mg, 0.9 mmol). The resulting mixture was vigorously stirred at room temp. for 2 h. Extraction was performed with CH_2Cl_2. The organic extracts were combined, washed with water, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was chromatographed on a column of silica gel with CH_2Cl_2–MeOH to give *compound* **10b** (304 mg, 90%) (Found: C, 65.6; H, 7.4; N, 5.7. $C_{40}H_{55}N_3O_4SSi_2$ requires C, 65.8; H, 7.6; N, 5.8%); $\delta_H(CDCl_3)$ 0.15 (12 H, m, SiMe), 0.97 (18 H, m, Bu^t), 1.99 (1 H, m, 2'-H^a), 2.40 (1 H, m, 2'-H^b), 3.73 (1 H, d, J_{gem} 9.2, 5'-H^a), 3.85–3.92 (2 H, m, 5'-H^b and 4'-H), 4.32 (1 H, dd, $J_{2',3'}$ 5.9 and 10.9, 3'-H), 5.61 (1 H, d, $J_{5,6}$ 7.6, 5-H), 6.18 (1 H, dd, $J_{1',2'}$ 2.7 and 6.3, 1'-H), 7.20–7.37 (15 H, m, ArH) and 7.77 (1 H, d, $J_{5,6}$ 7.6, 6-H); $\delta_C(CDCl_3)$ 154.73, 142.01, 141.58, 129.61, 128.29, 127.35, 91.63, 87.14, 85.88, 76.53, 72.20, 69.76, 61.67, 42.10, 25.93, 25.68, 18.34, 17.94, −4.62, −4.96, −5.46 and −5.51.

3',5'-O-*Bis*(tert-*butyldimethylsilyl*)-6-N-(*triphenylmethylsulfenyl*)*deoxyadenosine* **10c** (Found: C, 64.6; H, 7.5; N, 8.7. $C_{41}H_{55}N_5O_3SSi_2{\cdot}\frac{1}{2}H_2O$ requires C, 64.5; H, 7.4; N, 9.2%); $\delta_H(CDCl_3)$ 0.09 (12 H, m, Me), 0.90 (18 H, s, Bu^t), 2.42 (1 H, m, 2'-H^a), 2.62 (1 H, m, 2'-H^b), 3.75 (1 H, dd, $J_{4',5'}$ 3.3, J_{gem} 11.2, 5'-H^a), 3.87 (1 H, dd, $J_{4',5'}$ 4.3, J_{gem} 11.2, 5'-H^b), 4.00 (1 H, m, 4'-H), 4.60 (1 H, m, 3'-H), 6.42 (1 H, t, $J_{1',2'}$ 6.2, 1'-H), 7.20–7.44 (15 H, m, ArH), 8.16 (1 H, s, 2-H) and 8.53 (1 H, s, 8-H); $\delta_C(CDCl_3)$ 153.96, 152.45, 149.90, 143.70, 130.10, 127.94, 127.22, 122.46, 87.80, 84.48, 72.38, 71.70, 62.63, 40.92, 25.91, 25.70, 18.35, 17.94, −4.71, −4.84, −5.44 and −5.53.

3',5'-O-*Bis*(tert-*butyldimethylsilyl*)-N'-(*triphenylmethylsulfenyl*)*deoxyadenosine* **10f** (Found: C, 64.6; H, 7.5; N, 8.7. $C_{41}H_{55}N_5O_3SSi_2{\cdot}\frac{1}{2}H_2O$ requires C, 64.5; H, 7.4; N, 9.2%); $\delta_H(CDCl_3)$ 0.13 (12 H, m, Me), 0.97 (18 H, s, Bu^t), 2.42 (1 H, m, 2'-H^a), 2.62 (1 H, m, 2'-H^b), 3.82 (1 H, dd, $J_{4',5'}$ 3.3, J_{gem} 11.2, 5'-H^a), 3.90 (1 H, dd, $J_{4',5'}$ 4.3, J_{gem} 11.2, 5'-H^b), 4.07 (1 H, m, 4'-H), 4.66 (1 H, m, 3'-H), 6.47 (1 H, t, $J_{1',2'}$ 6.7, 1'-H), 6.55 (1 H, br, NH), 7.52–7.58 (6 H, m, ArH), 7.21–7.36 (9 H, m, ArH), 8.09 (1 H, s, 2-H) and 8.46 (1 H, s, 8-H); $\delta_C(CDCl_3)$ 155.16, 152.43, 149.43, 139.43, 129.88, 127.98, 127.01, 122.50, 87.91, 84.33, 73.23, 71.99, 62.80, 41.13, 25.93, 25.73, 18.39, 17.99, −4.69, −4.82, −5.41 and −5.50.

2',3',5'-O-*Tris*(tert-*butyldimethylsilyl*)-2-N-(*triphenylmethylsulfenyl*)*guanosine* **12d** (Found: C, 62.5; H, 7.6; N, 7.4. $C_{47}H_{69}N_5O_5SSi_3$ requires C, 62.7; H, 7.7; N, 7.8%); $\delta_H(CDCl_3)$ 0.11 and 0.93 (45 H, s, TBDMS), 3.75 (1 H, dd, J_{gem} 11.6, $J_{4',5'a}$ 2.3, 5'-H^a), 3.92 (1 H, dd, J_{gem} 11.6, $J_{4',5'a}$ 3.0, 5'-H^b), 4.06 (1 H, br, 4'-H), 4.24 (2 H, br, 2'- and 3'-H), 5.23 (1 H, br, 1'-H), 5.70 (1 H, br, N'-H), 7.23–7.42 (15 H, m, ArH) and 7.76 (1 H, s, 8-H); $\delta_C(CDCl_3)$ 156.59, 156.26, 147.67, 141.87, 135.53, 130,48, 127.78, 127.64, 87.58, 84.57, 84.19, 75.74, 71.24, 62.09, 26.09, 25.82, 25.72, 18.53, 18.04, 17.90, −4.35, −4.58, −4.09, −4.80, −5.37 and −5.42.

5'-O-(4,4'-*Dimethoxytrityl*)-4-N-(*triphenylmethylsulfenyl*)-

deoxycytidine **8b** (Found: C, 71.0; H, 5.8; N, 4.6. $C_{49}H_{45}N_3O_6S\cdot\frac{3}{2}H_2O$ requires C, 71.2; H, 5.9; N, 5.1%); $\delta_H(CDCl_3)$ 2.20 (1 H, m, 2'-H[a]), 2.50 (1 H, m, 2'-H[b]), 3.40 (1 H, dd, $J_{4',5'}$ 3.3, J_{gem} 10.5, 5'-H[a]), 3.53 (1 H, dd, J_{gem} 10.5, and $J_{4',5'}$ 3.3, 5'-H[b]), 3.78 (6 H, s, OMe), 3.95 (1 H, m, 4'-H), 4.40 (1 H, m, 3'-H), 5.44 (1 H, d, $J_{5,6}$ 7.3, 5-H), 6.18 (1 H, dd, $J_{1',2'}$ 4.6 and 5.9, 1'-H), 6.83–7.40 (28 H, m, ArH) and 7.72 (1 H, d, $J_{5,6}$ 7.3, 6-H); $\delta_C(CDCl_3)$ 168.85, 158.68, 155.09, 144.38, 142.06, 141.84, 137.93, 135.75, 130.20, 125.38, 113.31, 92.39, 86.84, 86.30, 85.89, 72.36, 70.31, 62.51, 55.29 and 41.97.

Reaction of 5'-O-(4,4-*Dimethoxytrityl*)*deoxyadenosine* **7c** *with TrSCl by the Use of Method C.*—In this case, a 1:1 mixture of 5'-*O*-(4,4'-dimethoxytrityl)-6-*N*-(triphenylmethylsulfenyl)deoxyadenosine **8c** and 5'-*O*-(4,4'-dimethoxytrityl)-N^1-(triphenylmethylsulfenyl)deoxyadenosine **8f** was obtained as listed in Table 1. For isomers **8c** and **8f** (Found: C, 70.0; H, 5.5; N, 7.75. $C_{50}H_{45}N_5O_5S\cdot\frac{3}{2}H_2O$ requires C, 70.2; H, 5.7; N, 8.2%); $\delta_H(CDCl_3)$ 2.48 and 2.75 (2 H, m, 2'-H_2), 3.39 (2 H, m, 5'-H_2), 3.76 (3 H, s, OMe), 4.10 (1 H, m, 4'-H), 4.65 (1 H, m, 3'-H), 5.55 (1 H, br, N*H*STr), 6.38 (1 H, m, 1'-H), 6.50 (br, C=NH), 6.78 and 7.14–7.52 (28 H, m, ArH), 7.85 and 7.97 (1 H, s, 8-H) and 8.33 and 8.46 (1 H, s, 2-H).

Method D: 3',5'-O-*Bis*-(tert-*butyldimethylsilyl*)-4-N-(*triphenylmethylsulfenyl*)*deoxycytidine* **10b**.—To a solution of 3',5'-*O*-bis(*tert*-butyldimethylsilyl)deoxycytidine **9b** (205 mg, 0.45 mmol) and pyridine (0.17 cm^3, 2.1 mmol) in CH_2Cl_2 (1 cm^3) was added dropwise a solution of TrSCl (186 mg, 0.6 mmol) in CH_2Cl_2 (2 cm^3). The resulting mixture was stirred vigorously at room temperature for 6 h. After the usual work-up, chromatography gave title compound **10b** (134 mg, 61%), identical with the product reported above.

Method E.—As for method D, but pyridine was replaced with triethylamine.

N-*Triphenylmethylsulfenyl*-D-*phenylalanine* **14**. Amorphous solid (Found: C, 76.2; H, 5.7; N, 3.15; S, 7.1. $C_{28}H_{25}NO_2S$ requires C, 76.50; H, 5.73; N, 3.18; S, 7.29%); $\delta_H(CDCl_3)$ 2.35 (1 H, s, NH), 2.71 (2 H, d, *J* 6.3, CH_2), 3.34 (1 H, t, *J* 6.3, CHN) and 6.89–7.30 (20 H, m, ArH); $\delta_C(CDCl_3)$ 178.92, 143.90, 135.78, 129.86, 129.31, 128.37, 127.82, 126.77, 70.46, 65.00 and 39.23.

N-(*Triphenylmethylsulfenyl*)*phthalimide* **16** (Found: C, 76.8; H, 4.65; N, 2.9. $C_{27}H_{19}NO_2S$ requires C, 76.9; H, 4.5; N, 3.3%), m.p. 198–202 °C (from hexane–EtOAc); $\delta_H(CDCl_3)$ 7.20 (10 H, s, STr), 7.50 (5 H, s, STr) and 7.68 (4 H, m, ArH); $\delta_C(CDCl_3)$ 167.74, 142.07, 134.29, 131.45, 130.28, 127.57, 127.21, 123.43 and 74.88.

1-(*Triphenylmethylsulfenyl*)*imidazole* **18** (Found: C, 96.9; H, 5.3; N, 8.1. $C_{22}H_{18}N_2S$ requires C, 77.16; H, 5.30; N, 8.18%), m.p. 146–148 °C (from hexane–ethyl acetate); $\delta_H(CDCl_3)$ 7.18–7.28 (15 H, m, TrS), 6.65 (1 H, s, ImH), 6.77 (1 H, s, ImH) and 6.92 (1 H, s, ImH); $\delta_C(CDCl_3)$ 144.17, 141.49, 129.61, 129.27, 128.16, 127.67, 125.45 and 73.80.

General Procedure for Removal of the TrS Group.—A sample protected (1 mmol) with the TrS group was dissolved in toluene (10 cm^3) and tributyltin hydride (2.5 mmol) was added. The resulting mixture was refluxed for 5 min. If necessary, after cooling to room temperature, the mixture was subjected to column chromatography on silica gel. Elution was performed with CH_2Cl_2–MeOH to give the deprotected material as listed in Table 3. The products were identified by comparison of their ^1H NMR spectra with those of authentic samples.

General Procedure for Removal of the TrS Group by the Use of TBTH–Et_3B. Typical Procedure.—Compound **2** (152 mg, 0.2 mmol) was dissolved in toluene (2 cm^3) and tributyltin hydride (0.26 cm^3, 1 mmol) was added. The mixture was vigorously stirred. To the solution was added a 0.81 mol dm^{-3} solution of triethylborane in hexane (25 mm^3) every 30 min. Addition of triethylborane was repeated 8 times. After the final addition of reagent, the solution was stirred for an additional 30 min and was then applied to a column of silica gel. Elution was performed with CH_2Cl_2–MeOH (99:1) to give the deprotected material as listed in Table 3. The products were identified by comparison of their ^1H NMR spectra with those of authentic samples.

General Procedure for Removal of the TrS Group by the Use of Ultrasound. Typical Procedure.—Compound **2** (152 mg, 0.2 mmol) was dissolved in toluene (2 cm^3) and tributyltin hydride (0.26 cm^3, 1 mmol) was added. The mixture was kept in an ultrasonic washer (Branson 2200) under sonic irradiation. Every 1 h azoisobutyronitrile (AIBN) (11 mg, 65 μmol) was added. After 8 such additions of AIBN, the solution was sonically irradiated for an additional 1 h in the vessel and then work-up was peformed in a manner similar to that described in the above experiment.

Removal of the TrS Group from N-*Triphenylmethylsulfenyl*-D-*phenylalanine* **14**.—Compound **14** (440 mg, 1 mmol) was treated with Bu_3SnH as described in general procedure for removal of the TrS group. After the reaction was complete, the mixture was diluted with hexane. The hexane solution was extracted with water. The aqueous layer was washed three times with hexane, and the combined organic phases were evaporated under reduced pressure. The residue was dissolved in pyridine–water (6 cm^3–4 cm^3). To the solution were added phenyl isothiocyanate (0.24 cm^3, 2 mmol) and triethylamine (0.14 cm^3, 1 mmol). The resulting solution was stirred at room temperature for 1.5 h. The mixture was diluted with CH_2Cl_2 and washed three times with water. The organic phase was collected, and evaporated under reduced pressure. The residue was chromatographed on a column of silica gel with CH_2Cl_2–MeOH (98:2) to give the *thiourea derivative* **19** (247 mg, 82%) (Found: C, 63.85; H, 5.7; N, 9.1; S, 10.3. $C_{16}H_{16}N_2O_2S$ requires C, 63.97; H, 5.37; N, 9.32; S, 10.70%); $\delta_H(CDCl_3)$ 3.12 and 3.40 (each 1 H, dd, J_{gem} 14.2, J_{vic} 5.9 and 5.3, together CH_2), 5.29 (1 H, br, NCHCS) and 6.98–7.29 (10 H, m, ArH); $\delta_C(CDCl_3)$ 179.44, 174.77, 146.36, 139.21, 135.92, 129.85, 129.34, 128.45, 126.94, 126.81, 124.83, 124.49, 58.38 and 37.06.

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