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# Nucleosides, Nucleotides and Nucleic Acids

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# An Efficient Deprotection of N-Trimethylsilylethoxymethyl (SEM) Groups From Dinucleosides and Dinucleotides

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### AN EFFICIENT DEPROTECTION OF N-TRIMETHYLSILYLETHOXYMETHYL (SEM) GROUPS FROM DINUCLEOSIDES AND DINUCLEOTIDES

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□ A convenient and efficient method for deprotection of N-(trimethyl)silylethoxymethyl (SEM) groups from thymidine dinucleoside and dinucleotide has been achieved. The SEM groups were easily removed in excellent yields from protected nucleosides, dinucleosides, and dinucleotides.

**Keywords** Dinucleosides; spore photoproduct; *S*-adenosylmethionine; spore photoproduct lyase

SAM; *S*-adenosylmethionine; SPL, spore photoproduct lyase; SP, spore photoproduct; TES, triethylsilyl; TBDMS, *tert*-butyldimethylsilyl.

#### INTRODUCTION

The trimethylsilylethoxymethyl (SEM) group is frequently used for the protection of alcohols and amines for the synthesis of carbohydrates and natural products.<sup>[1,2]</sup> The trimethylsilylethoxymethyl group easily survives under bromination, basic hydrolysis, oxidation and other harsh conditions.<sup>[3]</sup> SEM groups can be removed from protected heterocycles or nitrogen containing compounds using hydrochloric acid under refluxing conditions<sup>[4]</sup> or at elevated temperature,<sup>[5]</sup> while SEM protecting groups on nucleosides have been removed using tin tetrachloride at low temperature.<sup>[3]</sup> Magnesium bromide<sup>[6,7]</sup> in ether or nitromethane has proven a useful combination for the deprotection of SEM ethers in the presence of sensitive groups such as tertbutyldimethylsilyl (TBS) and triisopropylsilyl (TIPS). Neat tetrabutylammonium fluoride<sup>[8]</sup> works well for N-SEM deprotection in some cases, with the

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FIGURE 1 5R and 5S-SP with and without a phosphate backbone.

rate of deprotection depending upon the degree of vacuum. In general, however, SEM deprotection from alcohols seems facile<sup>[9–14]</sup> whereas the N-SEM deprotection is frequently problematic.

During the course of our studies on the synthesis of spore photoproduct (SP)<sup>[15,16]</sup> and derivatives (Figure 1) for mechanistic studies of the DNA repair enzyme SPL, we became interested in the efficient deprotection of SEM groups to accomplish optimum yields of the final product. SPL is a radical S-adenosylmethionine (AdoMet) enzyme that utilizes an iron-sulfur cluster and AdoMet to to generate a putative 5'-deoxyadenosyl radical intermediate, which abstracts a hydrogen atom from C-6 of SP to initiate a radical-mediated  $\beta$ -scission.<sup>[17-20]</sup> Our recent work on the synthesis and repair of spore photoproduct using spore photoproduct lyase provides direct evidence for the stereochemical requirements of spore photoproduct repair by spore product lyase (SPL), with only the 5*R*-stereoisomers (dinucleosides/dinucleotide) acting as substrates (Figure 2).<sup>[21,22]</sup> Our need for pure SP substrate for mechanistic studies has led us to develop methods for the synthesis of stereochemically-defined dinucleoside and dinucleotide SP substrates.<sup>[21-23]</sup> The complete multistep synthesis of 5R and 5S-spore photoproducts from thymidine involves the condensation of dihydrothymidine and thymidine, selective deprotection of triethylsilyl groups,<sup>[23]</sup> phosphorylation

















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(5*R*-SP, dinucleoside)



TABLE 1 Yields of 5R and 5S-SP using tin tetrachloride

at the 3' hydroxyl of dihydrothymidine and phosphodiester bond formation between dihydrothymidine and thymidine. Only a few methods are reported for deprotecting the *N*-SEM from nucleosides and nucleotides; these proved unsatisfactory for the deprotection of N-SEM from SP dinucleosides and dinucleotides (Table 1), and led us to develop the alternate method described here.

#### **RESULTS AND DISCUSSION**

The dinucleosides of protected thymidine (5*R* and 5*S*-diastereomers) were prepared by coupling  $N^3$ -trimethylsilylethoxymethyl-3, 5-di-triethylsilyl-5,6-dihydrothymidine and 2-bromomethyl uridine using lithium diisopropyl amide (LDA) as a condensing reagent at  $-78^{\circ}$ C, which afforded 5*R* and 5*S*-diastereomers in excellent yields.<sup>[21,23]</sup> The 5*R* and 5*S*-diastereomers were purified on a silica gel column using a gradient of ethyl acetate and hexanes. The stereochemistry of protected dinucleosides was determined by two-dimensional Nuclear Overhauser Enhancement Spectroscopy (NOESY) and Rotating-frame Overhauser Effect Spectroscopy (ROESY).<sup>[21]</sup> In the next step the *tert*-butyldimethylsilyl (TBDMS) and triethylsilyl (TES) groups were removed using HF:pyridine at room temperature in good yields to produce the di-SEM protected 5*R* (1) and 5*S*-dinucleosides (5).<sup>[23]</sup>

Initial attempts at deprotecting compound **1** were based on literature protocols and involved treating with tin tetrachloride at 0°C; this resulted in only a 40–50% yield of the desired product (Scheme 1, Table 1). A major side



SCHEME 1 Deprotection of N-SEM from 5R-SP using literature protocol.

product was a polar species that did not show any significant nuclear magnetic resonance (NMR) signals; mass analysis demonstrated that the polar species are comprised of tin complexed with the dinucleoside. As such complexation would most likely occur through the sugar hydroxyl groups, we deduced that protection of these hydroxyl groups might improve the yield in SEM deprotection. The sugar hydroxyls were thus protected using acetic anhydride and pyridine at ambient temperature with high purity and yields (Schemes 2 and 3). The structures of these fully protected dinucleosides (**3** and **6**) were easily deduced using one- and two-dimensional NMR techniques. Once the 3',5'- hydroxyls were protected, the SEM groups were easily



SCHEME 2 Deprotection of N-SEM from 5*R*-SP dinucleoside with protected hydroxyls.



SCHEME 3 Deprotection of N-SEM from 5S-SP dinucleoside with protected hydroxyls.

removed from the dinucleosides in excellent yields (Table 1) to produce 4 and 7. Finally, the acetates were removed using ammonium hydroxide at ambient temperature to afford the desired 5R- and 5S-spore photoproducts 2 and 8. NMR and mass spectroscopy (MS) analysis confirmed the structure of the final 5R- and 5S-SP.

To check the validity of the reaction, the acetate protected phosphotriester<sup>[3,21,22]</sup> was also treated with tin tetrachloride under similar reaction conditions as described above and afforded the SEM deprotected product in 95–98% yields (Scheme 4). The SEM from 3' and 5' acetate protected thymidine **14** was also deprotected (Scheme 5) in excellent yields (93%) in a similar fashion as described for the thymine dinucleosides. Finally, the efficacy of this method is illustrated by our ability to use the fully deprotected synthetic dinucleoside spore photoproducts in SPL activity assays,



SCHEME 4 Deprotection of N-SEM from protected phosphotriester.



Reagents and Conditions:

(i) Ac<sub>2</sub>O, pyridine, rt, 95% (ii) SEMCI, MDC, DIEA, rt., 90% (iii) SnCl<sub>4</sub>, 0 °C, 90-93%, (iv) ammonium hydroxide, rt. **SCHEME 5** Deprotection of N-SEM from protected thymidine.

which clearly showed that only the 5R diastereomer was repaired by SPL.<sup>[21]</sup>

#### **EXPERIMENTAL**

All reactions were carried out in oven- or flame-dried glassware under a nitrogen atmosphere. Solvents were distilled prior to use. Dichloromethane and pyridine were distilled from calcium hydride. Purification of reaction products was carried out by flash chromatography using silica gel (230-400 mesh). All reagents were commercially available and used without further purification. All reactions were monitored by thin-layer chromatography (TLC) using silica gel 60, F-254. Column chromatography was conducted using flash silica gel. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a Bruker DPX-300, Bruker DRX-500 or on a Bruker DRX-600 (Brucker, Billerica, MA, USA). NMR spectra were recorded on solutions in deuterated chloroform (CDCl<sub>3</sub>), with residual chloroform ( $\delta$  7.27 ppm for <sup>1</sup>H NMR and  $\delta$  77.0 ppm for <sup>13</sup>C NMR) or deuterated dimethyl sulfoxide (DMSO-*d*6), with residual dimethyl sulfoxide ( $\delta$  2.50 ppm for <sup>1</sup>H NMR and  $\delta$  35.0 ppm for <sup>13</sup>C NMR) taken as the standard, and were reported in parts per million (ppm). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. The multiplicities of the <sup>13</sup>C NMR signals were determined by heteronuclear multiple quantum coherence (HMQC) and distortionless enhancement by polarization transfer (DEPT) techniques. Mass spectra (high resolution FAB [fast-atom bombardment] or ESI [electro spray ionizations]) were recorded on a Q-Tof and 70-VSEs spectrometer at Noyes Laboratory, University of Illinois Urbana-Champaign.

#### General

#### Tetra Acetate Formation of Thymidine Dinucleoside

A solution of **1** or  $5^{21}$  (0.100 g, 0.13 mmol) in pyridine (5.0 mL) and acetic anhydride (1.0 mL) was stirred at room temperature for 5 hours. After

complete acetylation the solvent was removed on a rotary evaporator under reduced pressure. The residue was dissolved in methylene chloride and washed with saturated sodium bicarbonate solution. The methylene chloride layer was dried over anhydrous sodium sulfate, concentrated and finally the residue was purified on a silica gel column (flash chromatography) using a mixture of ethyl acetate:hexanes (50:50), resulting in the desired product as a white fluffy solid with 90–95% yield.

#### Deprotection of N-SEM from Protected Thymidine Dinucleoside

To a cold solution of protected dinucleoside **3** or **6** (100 mg, 0.11 mmol) in methylene chloride (10 mL), tin tetrachloride 1M (1.5 mL) in methylene chloride (5.0 mL) was added dropwise over 25 minutes. The reaction mixture was stirred at 0°C for 1 hour, and then at room temperature for an additional 1 hour. The reaction progress was monitored using TLC. After completion of the reaction, the solution was cooled and the reaction mixture was neutralized with 4% sodium hydroxide (5.0 mL). The mixture was stirred for 10 minutes, and the solid was removed by centrifugation and the organic layer was decanted and the solvent was removed under reduced pressure. The residue was purified on a silica gel column using a mixture of 5% methanol and methylene chloride, which afforded SEM deprotected dinucleosides in 95–98% yield.

(5*R*-Tetra acetate 3): Yield: 95%; viscous oil;  $R_f$ . 0.5; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$ -0.053 (s, 9H, CH<sub>3</sub>), -0.034 (s, 9H, 3CH<sub>3</sub>), 0.80–0.885 (m, 2H, CH<sub>2</sub>), 0.91 (t, J = 8 Hz, 2H, CH<sub>2</sub>, SEM), 1.19 (s, 3H, Me), 1.96–2.34 (m, 4H, CH<sub>2</sub>, 2'), 2.0 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.19 (s, 3H, OAc), 2.2 (s, 3H, OAc), 2.61 (d, J = 14.5 Hz, 1H, CH<sub>2</sub>, bridge), 2.79 (d, J = 14.5 Hz, 1H, CH<sub>2</sub>, bridge), 3.10  $(d, J = 13Hz, 1H, CH_2, base), 3.23 (d, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13 Hz, 1H, CH_2, base), 3.54 (t, J = 13$  $2H, J = 8 Hz, CH_2, SEM$ ,  $3.62 (t, J = 8 Hz, 2H, CH_2, SEM), 4.09 (q, 1H, CH, CH_2, SEM)$ 4'), 4.20 (q, 1H, 4'), 4.25 (bs, 1H, 3'), 4.26 (bs, 1H, 3'), 4.30 (dd, I = 3.5, 8.5Hz, 2H,  $CH_2$ , 5'), 4.35 (dd, J = 3.5, 8.5 Hz, 2H, CH2, 5'), 5.11–5.31 (m, 4H, NCH<sub>2</sub>, SEM), 6.28–6.34 (m, 2H, 1'), 7.58 (s, 1H, base);  ${}^{13}$ C NMR (CDCl<sub>3</sub>):  $\delta$ -1.43 (CH<sub>3</sub>), 18.0 (CH<sub>2</sub>), 18.1 (Cquat), 20.81 (Me, OAc), 20.86 (Me, OAc), 20.87 (Me, OAc), 20.97 (Me, OAc), 22.43 (CH<sub>3</sub>, C-5), 32.3 (CH<sub>2</sub> bridge), 33.7 (CH<sub>2</sub>), 37.1 (CH<sub>2</sub>), 42.2, 43.6 (CH<sub>2</sub>-base), 63.7 (CH<sub>2</sub>), 63.9 (CH<sub>2</sub>), 66.8 (CH<sub>2</sub>), 67.69 (CH<sub>2</sub>), 70.0 (CH<sub>2</sub>, SEM), 70.4 (CH<sub>2</sub>, SEM), 80.7 (C 3'), 82.0 (C 3'), 84.3 (C 4'), 85.0 (C, 1'), 108.9 (Cquat), 139.1 (CH), 150.6 (Cquat), 152.2 (Cquat), 163.4 (Cquat), 170.2 (Cquat); 170.4 (Cquat), 170.7 (Cquat), 170.8 (Cquat), 173.7 (Cquat); MS: (TOF, MS, ESI) m/z 935 (M + Na).

 base); <sup>13</sup>C NMR (CD<sub>3</sub>OD):  $\delta$  21.05 (CH<sub>3</sub>), 22.1 (OAc), 32.31 (CH<sub>2</sub>), 34.34 (CH<sub>2</sub>), 38.0 (CH<sub>2</sub>), 43.92 (Cquat), 46.6 (CH<sub>2</sub>-base), 65.16 (CH<sub>2</sub>), 75.7, 76.18, 82.28, 83.61, 85.41, 86.32, 91.2, 111.0 (Cquat), 141.17 (CH), 152.1 (Cquat), 154.37 (Cquat), 166.2 (Cquat), 172.29 (Cquat), 172.3 (Cquat), 172.6 (Cquat), 172.78 (Cquat), 176.5 (Cquat); MS: (TOF, MS, ESI) *m*/*z* 653, 652, 325, 326.

(5S-Tetra acetate 6): Yield: 90%; viscous oil;  $R_f$ . 0.5; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ -0.058 (s, 9H, CH<sub>3</sub>), -0.041 (s, 9H, 3CH<sub>3</sub>), 0.81-0.92 (m, 4H, CH<sub>2</sub>, SEM), 1.17 (s, 3H, Me), 1.94–2.18 (m, 2H, CH<sub>2</sub>, 2'), 2.0 (s, 3H, OAc), 2.07 (s, 3H, OAc), 2.19 (s, 3H, OAc), 2.2 (s, 3H, OAc), 2.41 (dd, 2H, CH<sub>2</sub>, 2'), 2.64 (d, J = 14.5 Hz, 1H, CH<sub>2</sub>, bridge), 2.70 (d, J = 14.5 Hz, 1H, CH<sub>2</sub>, bridge), 3.10–3.16 (m, 2H, CH<sub>2</sub>, base), 3.48–3.54 (m, 2H, CH<sub>2</sub>), 3.6 (t, 2H, J = 8 Hz, CH<sub>2</sub>, SEM), 4.06 (q, 1H, CH, 4'), 4.1 (q, 1H, 4'), 4.2 (bs, 1H, 3'), 5.11–5.31 (m, 4H, NCH<sub>2</sub>, SEM), 6.26–6.29 (m, 1H, 1'), 6.34–6.37 (m, 1H, 1'), 7.47 (s, 1H, base); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ –1.43 (CH<sub>3</sub>), 18.0 (CH<sub>2</sub>), 18.1 (CH<sub>2</sub>), 20.9 (Me, OAc), 21.6 (CH<sub>3</sub>, C5), 32.31 (CH<sub>2</sub> bridge), 33.9 (CH<sub>2</sub>), 37.4 (CH<sub>2</sub>), 42.6 (Cquat, C-5), 44.4 (CH<sub>2</sub>-base), 64.0 (CH<sub>2</sub>), 66.8 (CH<sub>2</sub>), 67.5 (CH<sub>2</sub>), 70.1 (CH<sub>2</sub>), 70.4 (CH<sub>2</sub> SEM), 74.4 (CH), 74.44 (CH), 80.6 (C 3'), 82.1, 84.5 (C 4'), 85.6 (C, 1'), 109.0 (Cquat), 137.6 (CH), 150.5 (Cquat), 152.7 (Cquat), 163.2 (Cquat), 170.3 (Cquat); 170.4 (Cquat), 170.42 (Cquat), 170.53 (Cquat), 173.2(Cquat); MS: (TOF, MS, ESI) *m/z* 913.

(Compound 7): Yield: 88%; viscous oil;  $R_f$ . 0.4; <sup>1</sup>H NMR (Acetone-*d6*):  $\delta$  1.1 (s, 3H, Me), 2.04 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.1 (s, 3H, OAc), 2.29–2.45 (m, 4H, CH<sub>2</sub>, 2'), 2.5 (d, J = 14 Hz, 1H, CH<sub>2</sub>, bridge), 2.75 (d, J = 14 Hz, 1H, CH<sub>2</sub>, bridge), 3.2 (q, 2H, CH<sub>2</sub>, base), 3.51 (m, 2H, CH<sub>2</sub>, C5'), 4.0 (bt, 1H, 4'), 4.17–4.38 (m, 3H, 4', 5'), 5.0 (bt, 1H, 3'), 5.23 (bt, 1H, 3'), 6.2–6.3 (m, 2H, 1'), 7.5 (s, 1H, base), 9.15 (s, 1H, NH), 10.1 (s, 1H, NH); <sup>13</sup>C NMR (Acetone-*d6*):  $\delta$  21.0 (CH<sub>3</sub>), 21.1 (OAc), 32.2 (CH<sub>2</sub>), 34.2 (CH<sub>2</sub>), 37.6 (CH<sub>2</sub>), 43.2 (Cquat), 46.8 (CH<sub>2</sub>-base), 64.8 (CH<sub>2</sub>), 75.4, 75.6, 81.6, 83.0, 85.0, 85.9, 110.4 (Cquat), 139.7 (CH), 151.0 (Cquat), 153.2 (Cquat), 164.5 (Cquat), 170.8 (Cquat), 171.0 (Cquat), 174.7 (Cquat); MS: (TOF, MS, ESI) *m*/z 653, 652, 325, 326.

(**Compound 8**): A solution of 7 (0.08 g, 0.12 mmol) in ammonium hydroxide (~26%) was kept at room temperature for 24 hours. After complete deprotection of chlorophenyl and acetate, the excess ammonium hydroxide was removed under reduced pressure. The residue was partitioned between methylene chloride and water. The water layer was separated and carefully washed with methylene chloride. The aqueous layer was concentrated on a rotary evaporator under reduced pressure, which afforded the pure 5*S*-SP without any further purification. Yield: 85–95%; white solid; R<sub>f</sub>. 0.2; <sup>1</sup>H NMR (500 MHz, DMSO-*d6*):  $\delta$  1.0 (s, 3H, Me), 1.75–1.79 (m, 2H, CH<sub>2</sub>, 2'), 1.96–2.01 (m, 2H, CH<sub>2</sub>, 2'), 2.25 (d, J = 14 Hz, 1H, CH<sub>2</sub>, bridge), 2.71 (d, J = 14 Hz, 1H, CH<sub>2</sub> bridge), 3.05 (d, J = 13 Hz, 1H, CH<sub>2</sub> bridge), 3.19 (d, J = 13 Hz, 1H, CH<sub>2</sub> bridge), 3.2–3.6 (m, 4H, CH<sub>2</sub>, 5'), 3.61 (m, 1H, 4'), 3.7

(q, 1H, J = 3.5 Hz, CH, 4'), 4.24 (bt, J = 3.5 Hz, 1H, 3'), 4.34–4.36 (bt, J = 3.5 Hz, 1H, 3'), 4.7 (t, 1H), 4.9 (t, 1H), 5.1 (d, 1H), 5.2 (d, 1H), 6.1 (t, J = 7 Hz, 1H, 1'), 6.15 (t, J = 6.5 Hz, 2H, 1'), 7.6 (s, 1H, base, C-6), 10.1 (s, 2H, NH); <sup>13</sup>C NMR (DMSO-*d6*):  $\delta$  20.5 (CH<sub>3</sub>), 32.6 (CH<sub>2</sub>), 37.6 (CH<sub>2</sub>), 41.34 (CH<sub>2</sub>), 43.4 (Cquat), 47.9 (CH<sub>2</sub>-base), 63.1 (CH<sub>2</sub>, 5'), 63.6 (CH<sub>2</sub>, 5'), 72.4 (3'), 72.7 (3'), 85.4 (C 4'), 86.6 (C 1'), 87.6 (C 4'), 89.0 (C 1'), 110.6 (Cquat), 141.4 (CH), 152.2 (Cquat), 154.6 (Cquat), 166.3 (Cquat), 176.4 (Cquat); MS: m/z 507 (M + Na); HRMS: *m/z*: 485.1893 (calcd. for C<sub>20</sub>H<sub>29</sub>N<sub>4</sub>O<sub>10</sub>; 485.1884) (M + H).

(Compound 11): Yield: 80–90%; white solid;  $R_f$ . 0.1; <sup>1</sup>H NMR (CD<sub>3</sub>OD):  $\delta$  1.24 (s, 3H, Me), 2.1 (dd, 1H, CH<sub>2</sub>, 2'), 2.2–2.9 (m, 1H, CH, 2'), 2.3–2.38 (m, 1H, CH, 2'), 2.4–2.49 (m, 1H, CH, 2'), 2.60 (d, J = 14 Hz, 1H, CH<sub>2</sub>, bridge), 2.8 (d, J = 14 Hz, 1H, CH<sub>2</sub>, bridge), 3. 3 (d, J = 14 Hz, 1H, CH<sub>2</sub>, base), 3.4 (d, J = 13.5 Hz, 1H, CH<sub>2</sub>, base), 3.62–3.67 (m, 2H, CH<sub>2</sub>, 5'), 3.7 (dd, J = 3.5, 10 Hz, 2H, CH<sub>2</sub>, 5'), 3.9 (bt, 1H, CH, 4'), 4.0 (bs, 1H, 4'), 4.5–4.53 (m, 1H, 3'), 4.6–4.67 (m, 1H, 3'), 6.1–6.17 (m, 2H, 1'), 7.8 (s, 1H, base); <sup>13</sup>C NMR (CD<sub>3</sub>OD):  $\delta$  24.2 (CH<sub>3</sub>, C5), 36.5 (CH<sub>2</sub> bridge), 37.2 (CH<sub>2</sub>), 39.9 (CH<sub>2</sub>), 41.9, 47.3 (CH<sub>2</sub>-base), 61.5 (CH<sub>2</sub>), 65.2 (CH<sub>2</sub>), 71.2 (C 3'), 73.2 (C 3'), 83.8 (C 4'), 84.3 (C, 1'), 85.2 (C 1'), 86.5 (C 4'), 112.0 (Cquat), 140.1 (CH), 152.5 (Cquat), 155.5 (Cquat), 165.4 (Cquat), 176.9 (Cquat); <sup>31</sup>P NMR (CD<sub>3</sub>OD): 0.064; HRMS: *m/z*: 547.1420 (calcd. for C<sub>20</sub>H<sub>28</sub>N<sub>4</sub>O<sub>12</sub>P; 547.1441) (M + H); MS: (TOF, MS, ESI) *m/z* 547, 449, 362, 314.

(Compound 13): Yield: 95%; white solid;  $R_f$ . 0.5; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  1.8 (s, 3H, Me), 2.0 (s, 3H, OAc), 2.1 (s, 3H, CH<sub>3</sub>), 2.2–2.3 (m, 1H, CH, 2'), 2.4–2.5 (m, 1H, CH, 2'), 4.27 (m, 1H, CH), 4.3 (m, 2H, CH<sub>2</sub>, 5'), 5.2 (m, 1H, 3'), 6.3 (m, 2H, 1'), 7.3 (s, 1H, base), 7.3 (s, 1H, base); <sup>13</sup>C NMR (CD<sub>3</sub>OD):  $\delta$  12.7 (CH<sub>3</sub>, C5), 20.86 (OAc), 20.94 (OAc), 37.5 (CH<sub>2</sub>), 63.9 (CH<sub>2</sub>), 74.1 (C 3'), 82.1 (C 4'), 84.8 (C, 1'), 111.6 (Cquat), 134.5 (CH), 150.5 (Cquat), 163.7 (Cquat), 170.2 (Cquat), 170.49.

(Compound 14): Yield: 90–95%; viscous oil;  $R_f$ . 0.7; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  0.9 (s, 9H, TMS), 0.9 (t, 2H, CH<sub>2</sub>, SEM), 1.9 (s, 3H, Me), 2.0 (s, 3H, OAc), 2.1 (s, 3H, OAc), 2.2–2.3 (m, 1H, CH<sub>2</sub> 2'), 2.3–2.4 (m, 1H, CH<sub>2</sub> 2'), 3.6 (t, 2H, SEM), 4.1 (m, 1H, CH), 4.3 (m, 2H, CH<sub>2</sub>, 5'), 5.2 (m, 1H, 3'), 5.28 (s, 2H, SEM), 6.2 (m, 2H, 1'), 7.23 (s, 1H, base); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  –1.43 (SEM), 13.3 (CH<sub>3</sub>, C5), 18.1 (SEM), 20.8 (OAc), 20.88 (OAc), 37.5 (CH<sub>2</sub>), 63.8 (CH<sub>2</sub>), 67.5, 70.2, 74.0, 82.1, 82.1 (C 4'), 85.4 (C, 1'), 110.7 (Cquat), 133.2 (CH), 150.8 (Cquat), 163.1(Cquat), 170.1 (Cquat), 170.3 (Cquat).

#### CONCLUSION

In summary, we illustrate a simple and convenient methodology for the deprotection of SEM, (trimethylsilyl)ethoxymethyl from thymidine, thymidine dinucleosides and dinucleotides to the subsequent amines in excellent yields. SEM groups from the protected dinucleosides can be removed in 95–98% yields; while the same groups from unprotected dinucleosides produces low yields of the desired product. In addition, the acetate protected 5R and 5S-dinucleosides were easily deprotected into corresponding 5R and 5S-spore photoproduct.

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