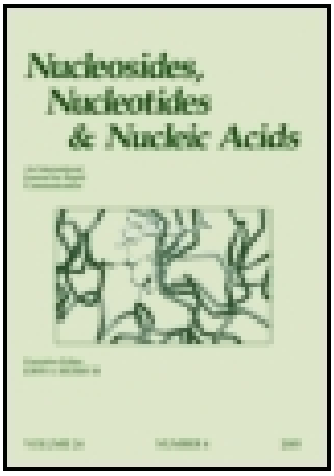

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Syntheses, Crystal Structures, and Hydrogen Bonding Patterns of 3′-C-Methylenecarboxylic-3′-deoxythymidine and 3′-C-Methyleneamidilylic-3′-deoxythymidine

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SYNTHESES, CRYSTAL STRUCTURES, AND HYDROGEN BONDING PATTERNS OF 3'-*C*-METHYLENECARBOXYLIC-3'-DEOXYTHYMIDINE AND 3'-*C*-METHYLENEAMIDILYLIC-3'-DEOXYTHYMIDINE

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ABSTRACT: Thymidine derivatives containing carboxylic acid and amide groups have been synthesized and the hydrogen-bonding patterns of 3'-*C*-methylenecarboxylic-3'-deoxythymidine **6** and 3'-*C*-methyleneamidilylic-3'-deoxythymidine **9** have been characterized by using X-ray crystallography.

INTRODUCTION

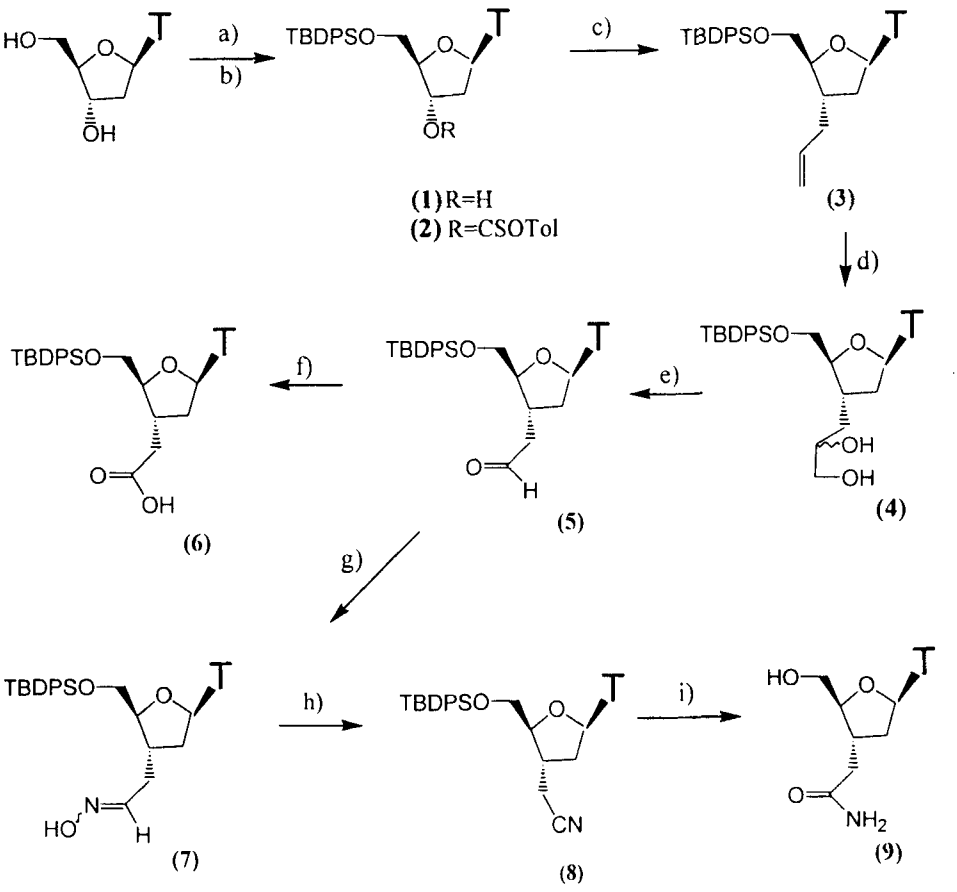
In recent years, considerable interest has been shown in the study of molecular recognition,[1] supramolecular chemistry[2] and crystal engineering[3] by using hydrogen bonding as the principal noncovalent interaction. These hydrogen bonds *in vivo* are known to play an important role in the stabilization of protein , nucleic acid secondary structure and specificity of enzymatic reactions.[4] The specific hydrogen bonding interactions which occur between DNA bases provide the premier example of molecular recognition. Therefore, the pattern of hydrogen bond of nucleoside and nucleotide derivatives as a part of DNA should be paid attention not only to the dimensionability but also to topology of the networks in solid and solution state.[4] Usually it is expected that carboxylic acids and amide groups are crystallized as their dimers. However studies for hydrogen bonding self-assemblies of nucleosides containing carboxylic acid and amide groups are relatively rare. Therefore, in order to investigate the relationship of the

recognition pattern of hydrogen bonding in these nucleosides, we synthesized several thymidine derivatives, studied x-ray crystal structures of **6** and **9**, and investigated their hydrogen bonding patterns in the solid states.

RESULTS AND DISCUSSION

Synthetic details for 3'-*C*-methylenecarboxylic-3'-deoxythymidine (**6**) and 3'-*C*-methyleneamidilylic-3'-deoxythymidine (**9**) are summarized in SCHEME 1. Starting from thymidine we prepared 5'-*O*-silyl protected thymidine **1** with TBDPSCl and imidazole.[5] Treatment of **1** with *p*-tolylchlorothionoformate and Et_3N afforded 3'-*O*-*p*-tolylchlorothionoformyl intermediate **2** in 80% yield. For the radical allylation, compound **2** was reacted with allyltributyltin in the presence of AIBN and 3'-*C*-allylthymidine product **3** was isolated in 84% yield.[6] Oxidative cleavage of **3** with OsO_4 and *N*-methylmorpholine oxide at room temperature gave 3'-*C*-(1,2-dihydroxy)- propyl-3'-deoxythymidine **4** and then following $NaIO_4$ treatment of **4** gave the important intermediate 3'-*C*-methyleneformyl thymidine **5** in 80% yield. Treatment of **5** and $NaClO_2$ afforded the 5'-*O*-(*tert*-butyldiphenylsilyl)-3'-*C*-methylenecarboxylic-3'-deoxy-thymidine (**6**).[7] In order to introduce an amide group in 3'-position of thymidine we have developed a three step sequence from the common intermediate **5**: (1) oximation of **5** with hydroxylamine hydrochloride, (2) nitrile formation by using trifluoroacetic anhydride and pyridine,[8] and (3) oxidative hydrolysis to the amide **9** with KF coated on alumina.[9] Final products **6** and **9** were characterized by spectroscopic methods and X-ray crystallography.

FIG 1, FIG 2, and FIG 3 show the crystal structure, the dimeric form, and the hydrogen-bonding pattern of compound **6**·CH_3OH, respectively.[10] The single crystal of compound **6** was obtained by vapor diffusion technique (solvent: CH_3OH, nonsolvent: hexane) and there was one molecule of **6** along with one CH_3OH solvated molecule per asymmetric unit. Molecule of compound **6** are linked *via* N-H···O hydrogen bonds to produce the centrosymmetrical dimer as shown in FIG 2. The distance between N and O of thymine base is 2.841 Å, which is parallel with the reported values.[11] It is interesting that the solvated CH_3OH plays an important role in the formation of 21-membered quasi-macrocyclic ring as shown in FIG 3. This hydrogen bonding pattern is



Reagents: a) TBDPSCl, Imidazole, DMF, 58%, b) *p*-Tolylchlorothioformate. Et_3N, DMAP, MC, 80%, c) Allyltributyltin, AIBN, Benzene, 84%, d) OsO_4, NMO, aq. Acetone, 58%, e) $NaIO_4$, aq Dioxane, 80%, f) $NaClO_2$, 2-Methyl-2-butene, $NaH_2PO_4.H_2O$, aq. *t*-BuOH, 77%, g) $H_2NOH.HCl$, Na_2CO_3, aq. MeOH, 59%, h) Trifluoroacetic anhydride, Py,THF, 74%, i) KF.alumina, *t*-BuOH, 43%.

T=thymine

SCHEME 1

attributable to the dual abilities of CH_3OH as a hydrogen bond donor and a hydrogen bond acceptor. Thus the solvated CH_3OH connects two molecules of compound **6** by hydrogen bonding with the carbonyl oxygen of thymine [r (O···O) = 2.766 Å] and the carboxylic acid of the other molecule [r (O···O) = 2.599 Å]. We also obtained the

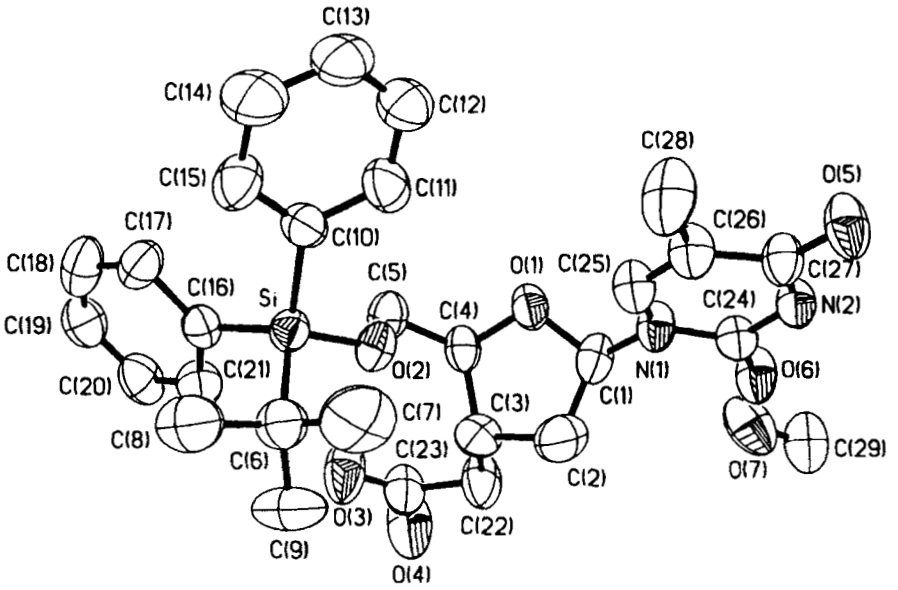


FIG 1. The crystal structure of compound **6**·CH_3OH

single crystal of compound **6**·H_2O and studied the crystal structure and the hydrogen bonding pattern (FIG 4, 5). These results are very similar with the previous ones. FIG 4 shows the centrosymmetric dimers with " head-to-head " hydrogen bonding pattern between two thymine bases. The distance between N and O of thymine bases is 2.855 Å. The solvated H_2O molecules play exactly the same role as CH_3OH molecules in the previous case and interconnect two molecules of **6** through hydrogen bonding to give 21-membered quasi-macrocycle ring (FIG 5). The crystallographic data indicate that hydrophilic solvated molecules such as CH_3OH and H_2O are very important in the stability and hydrogen bonding pattern of certain compounds in the solid state. Due to their dual abilities as a hydrogen bond donor and a hydrogen bond acceptor, these solvated molecules are nicely inserted between a hydrogen bond acceptor group and a hydrogen bond donor group to afford a quasi-macrocyclic ring. As shown in FIG 6 and FIG 7, the crystal pattern of **9** interestingly shows the formation of hydrogen bonding pattern with " head-to-tail " type between thymine base and amide group.[10] This pattern is stabilized by hydrogen bonding interactions in N (1AA) in amide···O (5AA) in

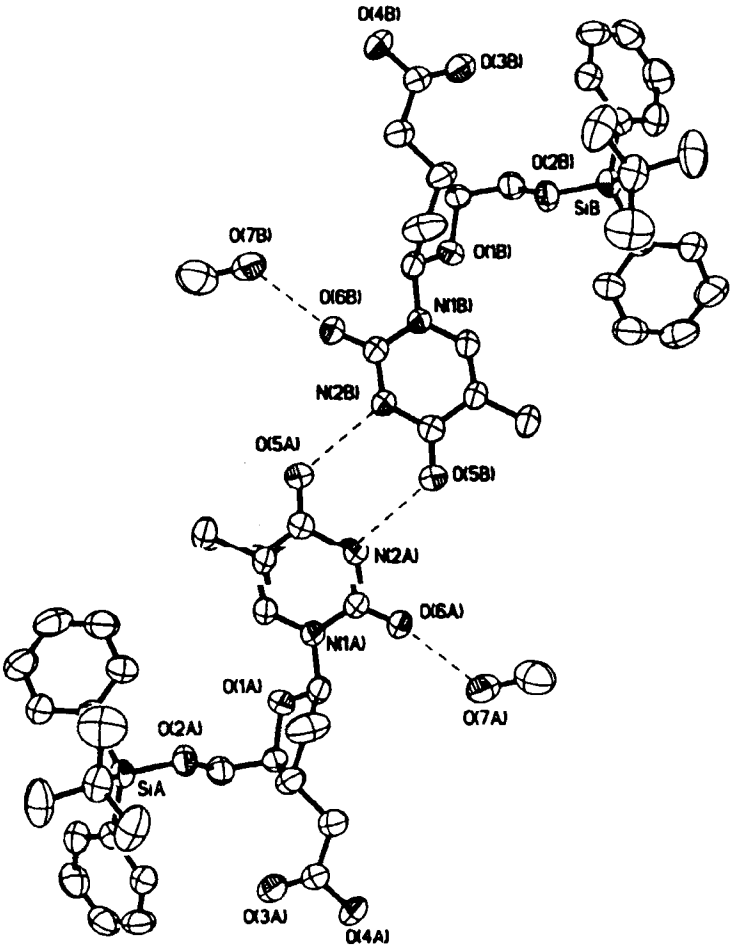


FIG 2. The centrosymmetrical dimeric form of compound **6**·CH_3OH

thymine (r=2.874 Å), O (1AA) in amide···N (3AA) in thymine (r=2.966 Å), O (2AA) in hydroxylic group···O (1AA) in amide (r=2.830 Å), and 3'-CH in carbohydrate···O (2AA) (r=2.571 Å). The hydrogen bonding pattern of " head-to-tail " type may be understood that the amide carbonyl oxygen O (1AA) is a stronger hydrogen bond acceptor than the keto carbonyl oxygen O (5AA) in thymine. The hydrogen bond of 3'-CH in carbohydrate···O (2AA) in this crystal structure of **9** is just the secondary feature. Without any solvated molecules in compound **9**, we could not observe the quasi-macrocycle formation through hydrogen bonding.

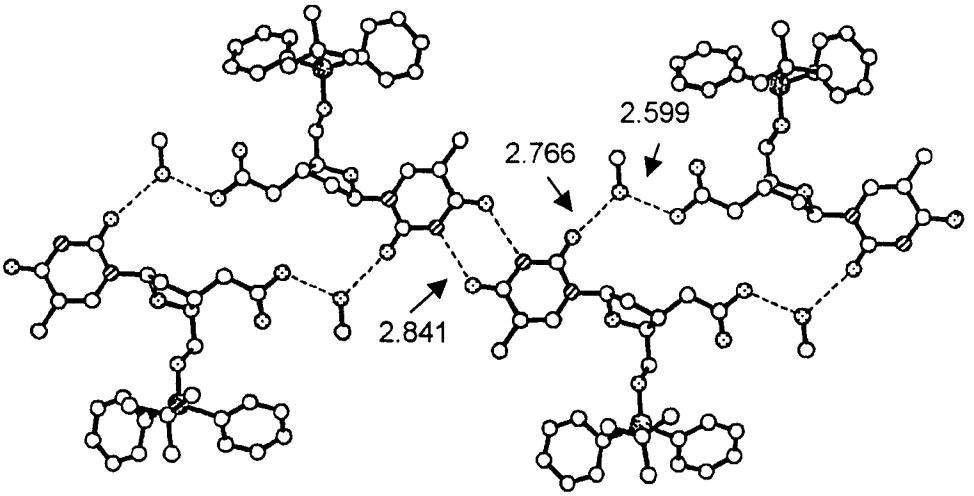


FIG 3. The hydrogen bonding pattern of compound **6**·CH_3OH (r in Å)

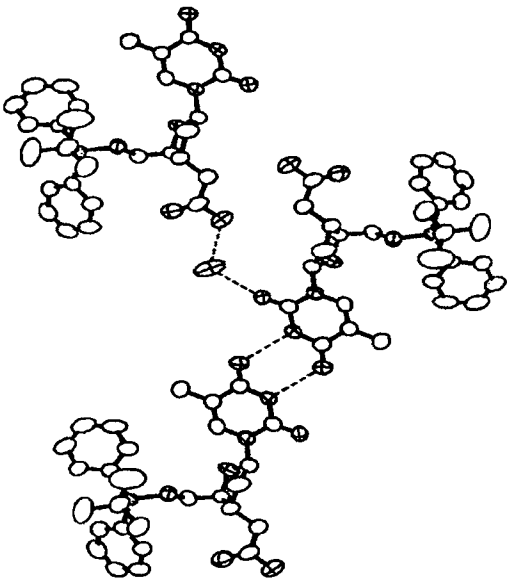


FIG 4. The centrosymmmetrical dimeric form of compound **6**·H_2O

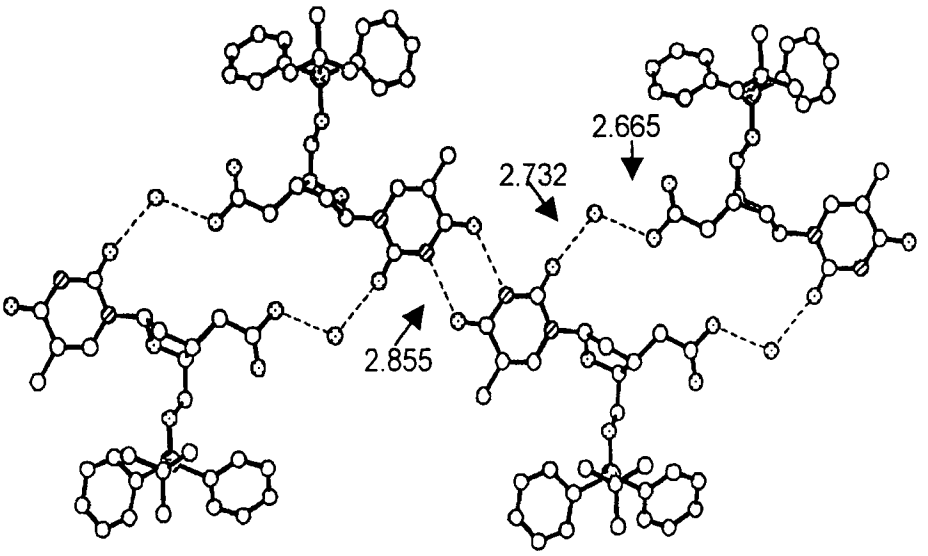


FIG 5. The hydrogen bonding pattern of compound **6**·H_2O (r in Å)

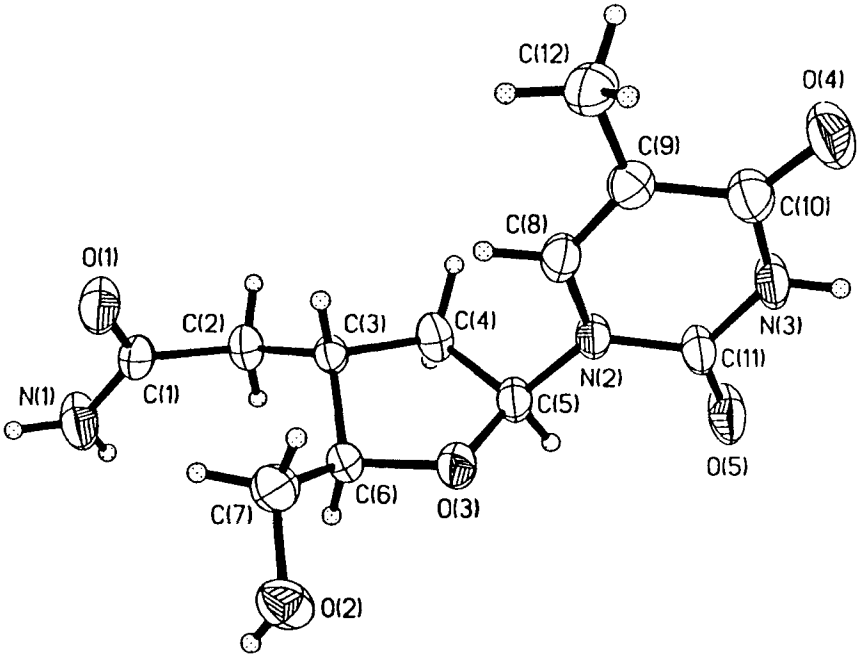


FIG 6. The crystal structure of compound **9**

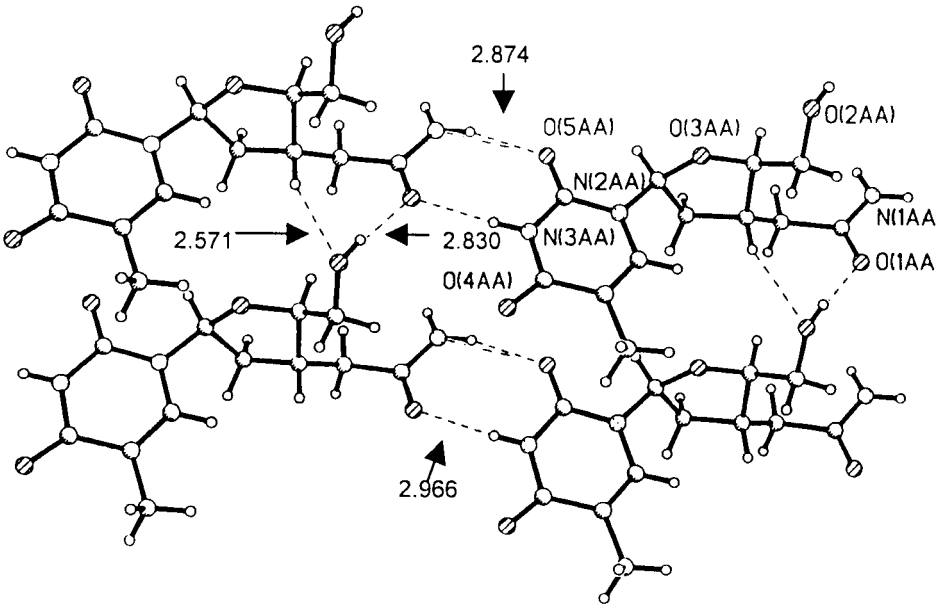


FIG 7. The hydrogen bonding pattern of compound **9** (r in Å)

In summary, we have developed an efficient synthetic route for compound **6** and **9** through the common intermediate **5** in 6 steps (13.9%, overall yield) and 9 steps (3.4%, overall yield) from thymidine, respectively. 3'-*C*-methylenecarboxylic **6** and 3'-*C*-methyleneamidilylic-3'-deoxythymidine **9** have been characterized by using X-ray crystallography. The crystal structure of **6** shows i) the formation of a centrosymmetrical cyclic dimer between thymine and thymine bases, " head-to-head " type, and ii) the stabilization by insertion of hydrophilic molecule (CH_3OH, H_2O) to form 21-membered quasi-macrocyclic ring in solid state. The crystal structure of **9** shows i) the formation of hydrogen bonding pattern of " head-to-tail " type between thymine base and amide group, and ii) the hydrogen bonding between 3'-CH in carbohydrate and O (1AA) of amide carbonyl group.

EXPERIMENTAL

^{1}H NMR and ^{13}C NMR spectra were obtained on FT-300MHz Bruker Apect 3000 spectrometer. The molecular mass was determined by using Jeol JMS-AX505WA

(FAB). The IR spectra was obtained on Bruker FT-IR PS55+ and the mp data were determined by Electrothermal 1A 9000 instrument. Silica gel column chromatography was performed on Merck, Kiesel gel 60 (70-230mesh). X-ray data were obtained on Siemens SMART CCD diffractometer.

5'-*O*-*tert*-Butyldiphenylsilyl thymidine (**1**)

To a mixture of thymidine (10g, 41.3mmol) and imidazole (5.6g, 82.5mmol) in dry dimethylformamide (100mL) was added dropwise *tert*-butyldiphenylsilylchloride (12mL, 45.4mmol) at rt under Ar gas. The reaction mixture was stirred at rt for 15min and then concentrated *in vacuo*. The organic residue was extracted with dichloromethane (3× 200mL), washed with water (2×200mL), dried with $MgSO_4$, filtered and then concentrated. The residue was purified by silica gel column chromatography using dichloromethane/methanol (98:2, v/v) as eluent to give **1** as a white foam (11.4g, 58%): mp=167-168°C (lit[12]: 170-171°C), ^{1}H NMR ($CDCl_3$): δ 9.64 (br, 1H, NH), 7.68, 7.28 (2m, 10H, Ph), 7.42 (s, 1H, C_6-H of thymine), 6.45 (m, 1H, 1'-H), 4.58 (m, 1H, 3'-H), 3.98, 3.87 (dd, 2H, J=9.2Hz, J=9.1Hz, 5'-H), 3.31 (m, 1H, 4'-H), 2.47, 2.21 (2m, 2H, 2'-H), 1.79 (s, 3H, Me), 1.17 (s, 9H, CMe_3), ^{13}C NMR ($CDCl_3$): δ 164.66, 151.25, 135.97, 135.90, 135.71, 133.38, 132.77, 130.55, 130.45, 128.42, 128.37, 111.72, 87.73, 85.24, 72.63, 64.67, 41.43, 27.40, 19.78, 12.49, IR (neat): 3500.3, 3070.6, 2960.5, 2930.7, 2858.9, 1715.3, 1653.0, 1472.9, 1427.6, 1277.4, 1113.5, 1003.7cm^{-1}.

5'-*O*-*tert*-Butyldiphenylsilyl-3'-*O*-(phenoxythiocarbonyl)-3'-deoxythymidine (**2**)

To a solution of anhydrous dichloromethane (100mL) of **1** (5.7g, 11.9mmol) in dry triethylamine (2mL, 14.2mmol) in the presence of dimethylaminopyridine (1.73g, 14.2mmol) was added *p*-tolylchlorothionoformate (2.1mL, 13mmol) at rt, and then the reaction mixture was stirred for 3h. After the reaction solution was washed with water (2×100mL), dried with $MgSO_4$, filtered and then concentrated *in vacuo*. The residue was purified by silica gel column chromatography using dichloromethane / methanol (98:2, v/v) as eluent to give **2** as a yellow foam (5.95g, 80%)[13]: mp=93-94°C, ^{1}H NMR ($CDCl_3$): δ 9.40 (br, 1H, NH), 7.71-6.97 (2m, 15H, Ph, C_6-H of thymine), 6.55 (dd, 1H, J=5.1Hz, 5.1Hz, 1'-H), 5.94 (d, 1H, J=5.7Hz, 3'-H), 4.37 (s, 1H, 4'-H), 4.07 (s, 2H, 5'-H), 2.75 (m, 1H, 2'-H_a), 2.37 (m, 1H, 2'-H_b), 1.64 (s, 3H, Me), 1.11 (s, 9H, CMe_3), ^{13}C

NMR ($CDCl_3$): δ 194.92, 179.05, 164.21, 150.60, 137.01, 136.02, 135.63, 135.23, 133.11, 128.27, 126.30. 121.76, 111.96, 85.19, 84.93, 84.30, 65.10, 38.52, 27.40, 21.35, 19.77, 12.42, IR (neat): 3070.5, 2957.5, 2930.7, 2858.3, 1715.3, 1653.0, 1505.8, 1470.9, 1428.0, 1271.4, 1224.2, 1193.4, 1060.8, 1006.8cm^{-1}.

5'-*O*-(*tert*-Butyldiphenylsilyl)-3'-*C*-allyl-3'-deoxythymidine (**3**)

A mixture of **2** (1.74g, 2.8mmol), allyltributyltin (4.28mL, 13.8mmol), and AIBN (317mg, 1.9mmol) in benzene (28mL) was refluxed. After 15h, the reaction mixture was extracted with dichloromethane (3×200mL), washed with water (2×100mL), dried with $MgSO_4$, filtered and then concentrated *in vacuo*. The residue was purified by silica gel column chromatography using dichloromethane/methanol (98:2, v/v) as eluent to give **3** as a oil (1.17g, 84%)[13]: ^{1}H NMR ($CDCl_3$): δ 8.32 (br, 1H, NH), 7.62-7.30 (2m, 10H, Ph), 7.45 (s, 1H, C_6-H of thymine), 6.05 (t, 1H, J=5.7Hz, 1'-H), 5.56-5.70, 4.94-5.01 (2m, 3H, CH=CH_2), 4.00 (m, 1H, 4'-H), 3.70 (m, 2H, 5'-H), 2.12-1.98 (3m, 5H, 2'-H, 3'-H, CH_2), 1.56 (s, 3H, Me), 1.19 (s, 9H, CMe_3), ^{13}C NMR ($CDCl_3$): δ 164.63, 151.00, 135.97, 135.78, 133.57, 133.14, 130.46, 130.37, 128.29, 117.52, 111.03, 85.98, 64.25, 39.09, 37.51, 36.85, 27.43, 19.83, 12.62, IR (neat): 3052.6, 2999.2, 2958.4, 2858.6, 1687.3, 1472.1, 1266.0, 1113.9cm^{-1}, FAB-Mass: m/z (relative intensity) 379.19 (100), 447.04 (46.2), 505.10 (31.2, M+1).

5'-*O*-(*tert*-Butyldiphenylsilyl)-3'-*C*-(1,2-dihydroxy)propyl-3'-deoxythymidine (**4**)

A mixture of **3** (1.1g, 2.2mmol), *N*-methylmorpholine oxide (280mg, 2.4mmol), and OsO_4 (2.5%, 816 μL, 0.065mmol) was stirred at rt for 3h in acetone (30mL) and water (3mL). After acetone was evaporated, the aqueous residue was extracted with dichloromethane (3×100mL), washed with water (2×100mL), dried with $MgSO_4$, filtered and then concentrated *in vacuo*. The residue was purified by silica gel column chromatography using dichloromethane/methanol (30:1, v/v) as eluent to give **4** as a oil (680mg, 58%): ^{1}H NMR ($CDCl_3$): δ 9.88-9.84 (br, 1H, NH, two isomer), 7.72-7.37 (m, 10H, Ph), 7.51 (d, 1H, C_6-H of thymine, two isomer), 6.08 (m, 1H, 1'-H), 4.25-3.40 (m, 6H, 4'-H, 5'-H, 7'-H, 8'-H), 2.57-2.00 (m, 5H, 2'-H, 3'-H, 6'-H), 1.60-1.58 (d, 3H, Me, two isomer), 1.26 (s, 9H, CMe_3), ^{13}C NMR ($CDCl_3$): δ 164.77, 151.09, 136.25, 136.03, 135.96, 135.85, 135.80, 133.62, 133.54, 133.21, 133.12, 130.46, 130.32, 128.29, 126.28,

110.89, 110.72, 87.11, 86.71, 85.73, 85.66, 71.64, 70.81, 67.41, 67.18, 64.29, 40.03, 39.28, 35.72, 35.60, 34.61, 27.42, 19.78, 19.76, 12.61, IR (neat): 3400.4, 3053.8, 2931.2, 2859.2, 1688.3, 1472.5, 1391.8, 1265.5, 1113.6 cm^{-1}, FAB-Mass: m/z (relative intensity) 213.04 (100), 307.07 (68.1), 335.07 (55.1), 539.03 (33.7, M+1).

5'-*O*-(*tert*-Butyldiphenylsilyl)-3'-*C*-methyleneformyl-3'-deoxythymidine (**5**)

A mixture of **4** (660mg, 1.2mmol) and $NaIO_4$ (446mg, 2.1mmol) was reacted at rt for 0.5h in dioxane (12mL) and water (5mL). After the dioxane was evaporated, the residues was extracted with dichloromethane (3×100mL), washed with water (2×100mL), dried with $MgSO_4$, filtered and then concentrated *in vacuo*. The residue was purified by silica gel column chromatography using dichloromethane/methanol (98:2, v/v) as eluent to give **5** as an oil (492mg, 80%): ^1H NMR ($CDCl_3$): δ 9.72 (s, 1H, CHO), 9.47 (br, 1H, NH), 7.69-7.37 (m, 10H, Ph), 7.42 (s, 1H, C_6-H of thymine), 6.17 (m, 1H, 1'-H), 4.09-3.80 (dd, 2H, 5'-H, J=11.7Hz, J=14.7Hz), 3.76 (m, 1H, 4'-H), 2.86-2.00 (m, 5H, 2'-H, 3'-H, 6'-H), 2.05 (s, 3H, Me), 1.06 (s, 9H, CMe_3), ^{13}C NMR ($CDCl_3$): δ 205.91, 164.41, 150.96, 136.01, 135.81, 135.67, 133.40, 133.00, 130.52, 128.66, 128.38, 128.32, 107.96, 85.60, 84.94, 64.00, 46.86, 39.49, 27.42, 12.68, 6.25, IR (neat): 3053.1, 2930.1, 2858.2, 1748.3, 1692.3, 1472.5, 1391.8, 1265.5cm^{-1}, FAB-Mass: m/z (relative intensity) 307.09 (100), 507.13 (16.8, M+1).

5'-*O*-(*tert*-Butyldiphenylsilyl)-3'-*C*-methylenecarboxylic-3'-deoxythymidine (**6**)

A mixture of **5** (321mg, 0.6mmol), $NaClO_2$ (343mg, 3.8mmol), 2-methyl-2-butene (271 μL, 2.5mmol), and $NaH_2PO_4.H_2O$ (353mg, 2.5mmol) was stirred at rt for 1h in *tert*-butanol (30mL) and water (15mL). After the *tert*-butanol was evaporated, the aqueous solution was acidified with 1N HCl, extracted with dichloromethane (3×100mL), washed with water (2×100mL), dried with $MgSO_4$, filtered and then concentrated *in vacuo*. The residue was purified by silica gel column chromatography using dichloro-methane/methanol (10:1, v/v) as eluent to give **6** as a white solid (250mg, 77%): mp=88.1-89.5°C, ^1H NMR ($CDCl_3$): δ 10.00 (br, 1H, NH), 7.61-7.26 (m, 10H, Ph), 7.44 (s, 1H, C_6-H of thymine), 6.09 (m, 1H, 1'-H), 3.99 (d, 2H, 4'-H, J=9.3Hz,), 3.72 (m, 4H, 2'-H, 6'-H), 2.86-2.00 (m, 5H, 2'-H, 3'-H, 6'-H), 1.56 (s, 3H, Me), 1.01 (s, 9H, CMe_3), ^{13}C NMR ($CDCl_3$): δ 176.41, 165.33, 151.04, 136.32, 135.78, 133.45, 132.94, 130.41, 128.40, 128.34, 111.16, 85.14, 46.86, 39.22, 36.81, 27.42, 19.78, 12.68, IR

(neat): 3250-3200, 2931.6, 1699.3, 1472.9, 1428.0, 1270.7, 1113.5cm^{-1}, FAB-Mass: m/z (relative intensity) 153.9 (100), 198.9 (26.4), 306.9 (27.3), 396.9 (21.3), 464.9 (11.1), 522.9 (19.6, M+1).

5'-*O*-(*tert*-Butyldiphenylsilyl)-3'-*C*-methylene-*N*-oximyl-3'-deoxythymidine (**7**)

A mixture of **5** (207mg, 0.4mmol) and $NH_2OH.HCl$ (34mg, 0.5mmol) was stirred at rt in the presence of Na_2CO_3 (22mg, 0.2mmol) in methanol (8mL) and water (10mL). After the reaction mixture was stirred for 3h at rt, the solvent was evaporated. The aqueous residue was extracted with dichloromethane (3×50mL), washed with water (2×50mL), dried with $MgSO_4$, filtered and then concentrated *in vacuo*. The residue was purified by silica gel column chromatography using dichloromethane/methanol (40:1, v/v) as eluent to give **7** as a white solid, two isomer (119mg, 59%): mp=79.5-80.7°C, ^{1}H NMR ($CDCl_3$): δ 9.72, 9.63 (br, 1H, NH), 7.67-7.35 (2m, 11H, Ph, C_6-H of thymine), 6,74, 6.09 (2m, 2H, oximyl proton, 1'-H), 4.02, 3.76 (2m, 3H, 5'-H, 4'-H), 2.61-2.23 (3m, 5H, 2'-H, 3'-H, 6'-H), 1.65 (s, 3H, Me), 1.06 (s, 9H, CMe_3), ^{13}C NMR ($CDCl_3$): δ 164.89, 164.74(two isomer), 150.92, 150.87(two isomer), 149.14, 136.13, 135.98, 133.47, 133.05, 133.01, 130.50, 130.41, 128.32, 111.05, 110.99 (two isomer), 86.14, 85.81, 85.08, 64.04, 63.88 (two isomer), 39.81, 39.08 (two isomer), 35.77, 35.48 (two isomer), 32.54, 27.42, 19.79, 12.57, IR (neat): 3500-3250, 2931.5, 1689.1, 1469.7, 1427.8, 1269.2cm^{-1}, FAB-Mass: m/z (relative intensity) 396.26 (100), 460.19 (33.1), 522.09 (54.3, M+1).

5'-*O*-(*tert*-Butyldiphenylsilyl)-3'-*C*-methylenenitrilyl-3'-deoxythymidine (**8**)

To a solution of **7** (78mg, 0.15mmol) and pyridine (100 μL, 1.2mmol) in THF (10mL) was added trifluoroacetic acid (92 μL, 0.65mmol) at 0°C. After the reaction mixture was stirred for 24h at rt, the solvent was concentrated *in vacuo*. The organic residue was extracted with dichloromethane (3×50mL), washed with water (2×50mL), dried with $MgSO_4$, filtered and then concentrated *in vacuo*. The residue was purified by silica gel column chromatography using dichloromethane/methanol (50:1, v/v) as eluent to give **8** as a white solid (57mg, 74%): mp=139.5-140.6 °C, ^{1}H NMR ($CDCl_3$): δ 8.28 (br, 1H, NH), 7.69-7.39 (2m, 11H, Ph, C_6-H of thymine), 6.14 (t, 1H, J=5.7Hz,1'-H), 4.07, 3.84 (2m, 3H, 5'-H, 4'-H), 2.79-2.39 (2m, 5H, 2'-H, 3'-H, 6'-H), 1.62 (s, 3H, Me),

1.12 (s, 9H, CMe_3), ^{13}C NMR ($CDCl_3$): δ 164.06, 150.62, 135.93, 135.45, 133.11, 132.74, 130.56, 128.40, 126.29, 117.62, 111.48, 84.89, 84.51, 63.80, 38.30, 35.21, 27.41, 20.06, 19.75, 12.63, IR (neat): 3071.1, 2930.8, 2857.9, 2249.0, 1687.1, 1471.3, 1427.5, 1270.8, 1113.0cm^{-1}, FAB-Mass: m/z (relative intensity) 426.20 (47.5), 446.17 (92.5), 460.19 (47.6), 504.23 (100, M+1).

3'-*C*-methyleneamidilylic-3'-deoxythymidine (**9**)

A mixture of **8** (50mg, 0.1mmol) and KF.alumina (130mg) in *tert*-butanol (10mL) was refluxed. After 5h, the KF.alumina was filtered, washed with MeOH (50mL) and was concentrated *in vacuo*. The organic layer was purified by silica gel column chromatography using dichloromethane/methanol (10:1, v/v) as eluent to give **9** as a white solid (12mg, 43%): ^1H NMR (CD_3OD): δ 8.01 (s, 1H, C_6-H of thymine), 6.09 (m, H, 1'-H), 3.91 (d, 1H, J=10.5Hz, 5'-H), 3.73 (m, 1H, 5'-H), 3.75 (m, 1H, 4'-H), 2.65-2.16 (3m, 5H, 2'-H, 3'-H, 6'-H), 1.89 (s, 3H, Me), 1.06 (s, 9H, CMe_3), ^{13}C NMR (CD_3OD): δ 175.71, 165.53, 151.35, 137, 34, 109.84, 86.50, 85.15, 61.14, 38.84, 37.18, 34.30, 11.42, IR (neat): 3355.7, 2927.3, 1683.9, 1683.7, 1541.0, 1473.5, 1277.3, 1114.7cm^{-1}, FAB-Mass: m/z (relative intensity) 153.90 (100), 284.06 (92.5, M+1).

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10. Crystal data for **6**: $C_{28}H_{34}N_2O_6Si \cdot MeOH$, M=522.21, crystal system: monoclinic, space C2, a=18.814(6)Å, b=7.449(3)Å, c=21.014(8)Å, β=95.58°, Z=4, V(Å)=2931.1(18), Dcalc(Mg/m^3)=1.250, R_1=0.0522, wR_2=0.1218, T=293(2) K. Crystal data for **6**: $C_{28}H_{34}N_2O_6Si \cdot H_2O$, M=522.21, crystal system: monoclinic, space C2, a=18.675(15)Å, b=7.365(6)Å, c=21.675(17)Å, β=97.50°, Z=4, V(Å)=2956.0(4), Dcalc(Mg/m^3)=1.215, R_1=0.0688, wR_2=0.1501, T=293(2) K. Crystal data for **9**: $C_{12}H_{17}N_3O_5$, M=283.29, crystal system: monoclinic, space group: P21, a=5.187(5)Å, b=11.686(8)Å, c=11.187(10)Å, β=99.79°, Z=2, V(Å)= 668.2(10), Dcalc(Mg/m^3)=1.408, R_1=0.0445, wR_2=0.0920, T=188(2) K.

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