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Synthesis of 5',8-Cyclopurine and of 5',6-Cyclodihydropyrimidine Nucleosides using Intramolecular Radical Cyclisation Based on the Aryl Telluride Radical Exchange Process.

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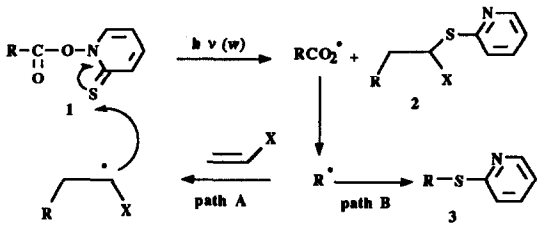
Abstract *- The synthesis of C-cyclopurine and C-cyclodihydropyrimidine nucleosides has been effected using 5'-aryltelluronucleosides. Generation of methyl radicals from the photolysis of the acetyl derivative of N-hydroxy-2-thiopyridone permitted, by radical exchange, the formation of 5'-nucleoside radicals which cyclized in satisfactory yields.*

Nucleosides with a preferred *anti* conformation are substrates of a number of enzymes, for example pancreatic ribonuclease[1]. The best way to be sure of the *anti*-conformation is to make a covalent bond between the sugar and the base as, for example, in the C-cyclonucleosides. The best method for the synthesis of this class of compound, as discussed in detail later, is the generation of a radical at C-5' which then adds to the base and fixes the conformation of the molecule.

Carbon radicals are often generated using a tin hydride[2a]. However, tin reagents do have certain disavantages and the silicon hydrides (silanes) are increasingly being used in their place.

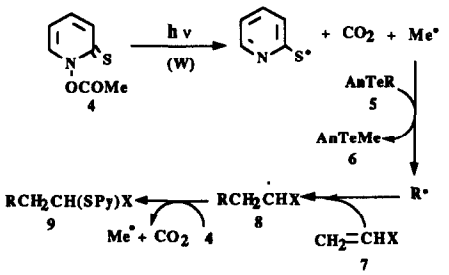
An alternative method to generate 'DISCIPLINED' carbon radicals is provided by the pyrolysis and/or photolysis with tungsten light of the acyl derivatives of thiohydroxamic acids[3]. Scheme 1 shows the derivatives of the readily available *N*-hydroxy-2-thiopyridone **1** which give carbon radicals which afford (path A), in the presence of a suitable trap, the adduct **2**. If the trap is not present, or is not efficient enough, then the rearranged product **3** (path B) is formed.



Scheme 1

The neutral conditions of this type of radical chemistry are well suited to the manipulation or synthesis of complex natural products. Applications have been made in amino-peptides[4] and in sugars and nucleosides[5]. Recently we have reported a simple synthesis of the important nucleoside sinefungin[6] and of its C-6' isomer. These studies have also demonstrated how highly stereoselective[7] radical reactions can be achieved by controlled hindrance of one side of a relatively rigid (five membered ribose) ring.

Another way to prepare carbon radicals is by radical exchange[8]. For example alkyl aryl tellurides will readily furnish an alkyl radical by reaction with another less stabilised alkyl radical. In practise, derivatives of anisyl telluride are easily synthesised by S_N2 displacement on a primary or secondary mesylate or tosylate. The acetyl derivative of *N*-hydroxy-2-thiopyridone **4** is a convenient source of methyl radicals which (Scheme 2) will react with the anisyl telluride derivative **5** to afford anisylmethyl telluride **6** and the desired radical R. Radical R with trap **7** will then afford radical **8** which is disciplined by reaction with thiocarbonyl group of **4** to give **9** with reformation of the methyl radical. This procedure was used recently in a short synthesis of the nucleoside antibiotic showdomycin[8].

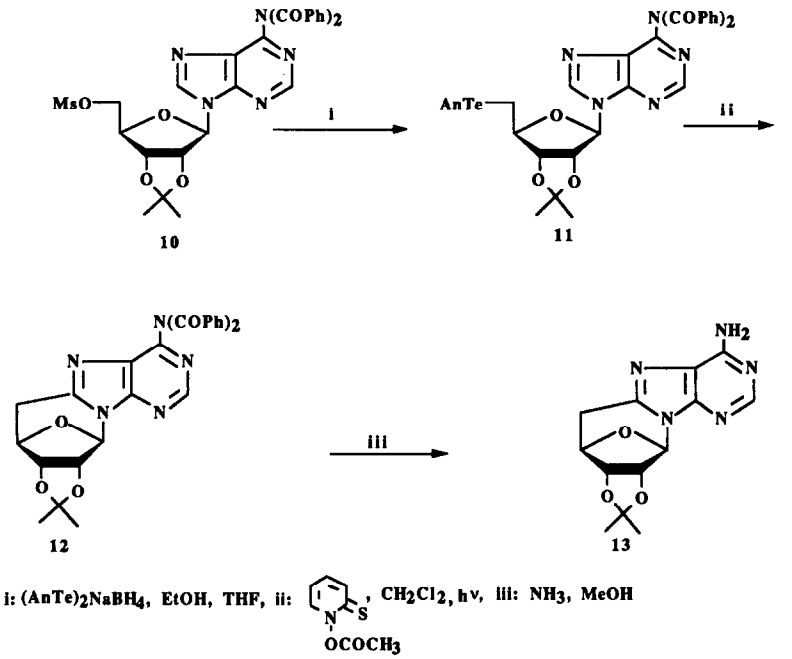


Scheme 2

It seemed to us that this procedure should be applicable to a convenient synthesis of C-cyclonucleosides. In this article we describe the synthesis of cyclonucleosides **12**, **17** and **22** which are obtained by methyl radical exchange on the 5'-anisyl tellurides of 6-*N*,*N*'-dibenzoyl-2',3'-*O*-isopropylidene adenosine **11**, the uridine analogue **16** and the 3'-*O*-tert.butyldiphenylsilylthymidine **21** respectively.

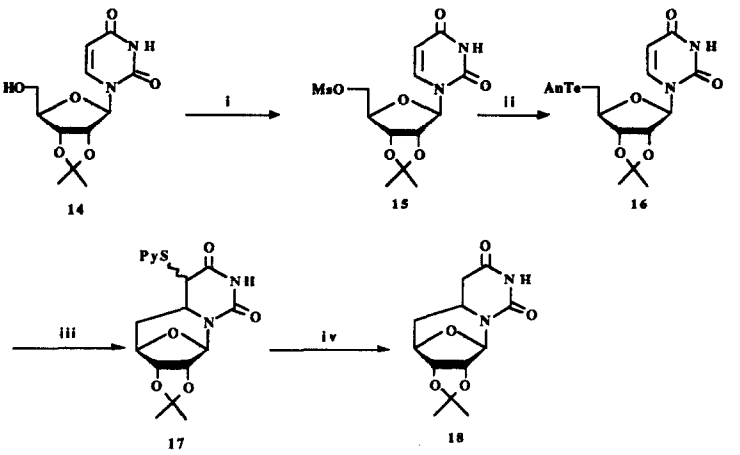
Several syntheses of **12** have already been reported. Thus[9] the reduction of the 5'-iodo-5'-deoxy-6-*N*,*N*-dibenzoyl-2',3'-*O*-isopropylidene adenosine gave a mixture of three compounds from which the 5',8-cyclonucleoside **12** was isolated in low (16%) yield. The second procedure[10], the reduction of the same iodide with zinc gave, as the major product, the 7,8-dihydro derivative of **12**. Dehydrogenation with chloranil afforded the 5',8-cyclonucleoside **12**.

In contrast, we have been able to obtain the desired cyclo-derivative **12** (60%) from the mesylate **10** by transformation into the anisyl telluride **11** and radical exchange (Scheme 3). The derivative **11** (86%) was prepared from the known mesylate[10,11] **10** by reaction with anisyl telluride anion at room temperature. The radical cyclisation was effected in degased methylene dichloride under argon by photolysis with a tungsten lamp in presence of the acetyl derivative **4** (4 equiv.) at a temperature which rose from 20° to 40° to give the crystalline **12** (60%). Treatment of **12** with ammonia afforded the acetonide **13** (90%) with characteristics in agreement with the literature[9,10]. The conversion of **13** to 5',8-cycloadenosine is already known[9,10].



Scheme 3

The cyclo-5,6-dihydrouridine **18** was prepared by a similar procedure (Scheme 4). It had previously been prepared by the photolysis of 2',3'-*O*-isopropylidene-5'-deoxyuridinylcobalamine[12] (40%) and tributyltin hydride reduction of the corresponding 5'-iodide[13] and from 5'-aldehyde[14]. An X-ray determination of the configuration at C-6 showed it to be R.



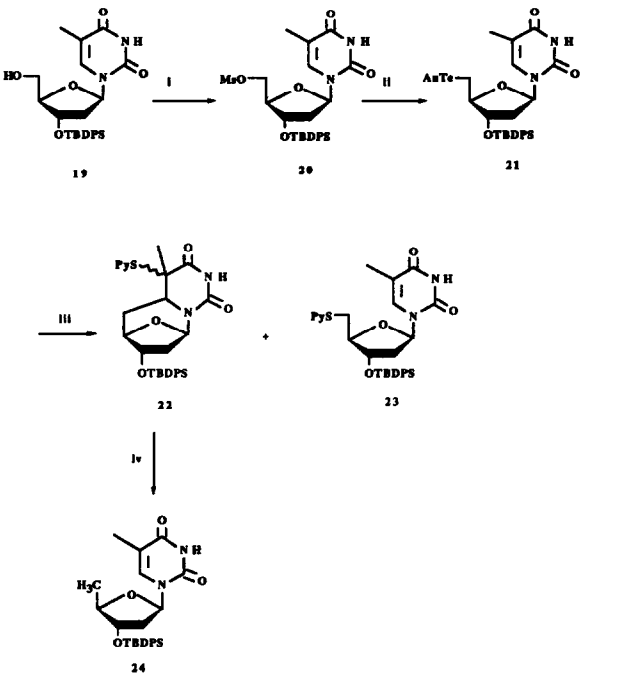
i: MsCl, pyridine, ii: $(AnTe)_2, NaBH_4$, EtOH, THF, iii:  , CH_2Cl_2

iv: Ni Raney, EtOH, reflux

Scheme 4

In our synthesis of **18** the known acetonide[15] of uridine **14** is converted to the mesylate **15** (80%) in the usual way. Treatment with anisyl telluride afforded the telluride **16** (80%) which on photolysis as for **11** gave the cyclonucleoside **17** in good yield (75%). Reduction of the thiopyridyl group with Raney in ethanol under reflux afforded the cyclodihydrouridine derivative **18** (60%) with caracteristics in agreement with the literature.

The radical exchange procedure was also applied (Scheme 5) to the thymidine derivative **19**. The derived mesylate **20** was converted into the anisyl telluride derivative (90%) **21** in the usual way. The radical cyclisation process gave the expected cycloderivative **22** in good (80%) yield as well as the thiopyridyl **23** (15%). Thus the desired radical was produced in nearly quantitative yield. However reduction of **22** with Raney Nickel in ethanol under reflux afforded not the desired product, but a fragmentation product **24**. The same product was formed by tributyltin hydride in toluene under reflux with A.I.B.N. initiation. There was isolated starting material **22** (40%) and fragmentation product **24** (60%). These unexpected results are best explained by a delicate balance between radical cyclisation at lower temperature with decrease in entropy and radical ring opening at higher temperatures with increase in entropy. The radical exchange process using tellurides permits radical generation at any temperature where an acyloxyradical will decarboxylate. Hence it permits radical cyclisation at lower temperature and has definite advantages.



Scheme 5

Experimental section

Column chromatography was carried out on silica gel 60 (0.040 - 0.063 μm). TLC analysis were performed on thin layer analytical plates 60F254 (Merck). Unless stated otherwise ^{1}H and ^{13}C NMR spectra were recorded on Bruker WP200 SY (200 MHz) or at AC 250 (250 MHz). Chemical shifts (δ) are expressed in ppm from Me_4Si as internal standard. Coupling constants *J* are in Hz. Most spectra were taken in $CDCl_3$. In other cases the solvent is specified. Melting points were taken on a Reicher apparatus and are uncorrected. Routine mass spectra were recorded on an AEI MS50, AEI MS9 and Kratos MS80 (for FAB spectra). Elementary analyses were carried out in the Institut de Chimie des Substances Naturelles.

5'-Anisyltelluro-5'-deoxy-2',3'-O-isopropylidene-6-N,N'-dibenzoyl-adenosine ***11***

To a stirred mixture of $NaBH_4$ (0.385 g, 2 eq.) in ethanol (8 ml) and degased tetrahydrofuran (25 ml) in a three necked flask at 0°C under argon was added dropwise a solution of An_2Te_2 (1.3 g, 0.55 eq.) in degased tetrahydrofuran (25 ml). The red solution became colourless. The pH was brought to neutral and a solution of 5'-*O*-mesyl derivative **10** (3 g, 5.07 mmol) in dry and degased tetrahydrofuran (50 ml) was added slowly. The reaction mixture was stirred at room temperature for a period of 3 h and then water was added. The solvent was

evaporated to dryness. After extraction with methylene chloride, the organic layers were dried ($MgSO_4$), filtered and evaporated to dryness. The residue was purified on a silica gel column (ethyl acetate-heptane, 1:1) to yield **11** as a white foam (3.2 g, 86%). Anal.Calcd. for $C_{34}H_{31}N_5O_6Te$, C(55.73); H(4.23); N(9.56); Found: C(56.01); H(4.27); N(9.46). MS (FAB, THIO$^+$): 735 $(MH)^+$, $[\alpha]_D^{20}$ = -38° (c=0.9, CH_2Cl_2). ^1H NMR (200 MHz, $CDCl_3$): δppm: 8.65 (s, 1H, H-2); 8.20 (s, 1H, H-8); 7.8-7.2 (m, 12H, Ph); 6.75 (d, 2H, Ph); 6.10 (d, 1H, H-1', $J_{1',2'}$= 2Hz); 5.45 (dd, 1H, H-2', $J_{2',3'}$= 6.5 Hz, $J_{2',1'}$= 2 Hz); 4.90 (dd, 1H, H-3', $J_{3',4'}$= 3 Hz, $J_{3',2'}$= 6.5 Hz); 4.55 (m, 1H, H-4'); 3.80 (s, 3H, OCH_3); 3.05 (m, 2H, H-5, H-5'); 1.60, 1.35 (2s, 6H, C*Me*$_2$). ^{13}C NMR (200MHz, $CDCl_3$): δppm: 11.4 (C-5'); 25.3, 27.1 (C*Me*$_2$); 55.2 (*CH*$_3$O); 84.2, 84.6 (C-2', C-3'); 87.8 (C-4'); 90.9 (C-1'); 114.7 (*C*Me$_2$); 115.4 (C-5); 128.7, 129.5, 133.0, 134.1 (Ph); 141.4 (C-8); 144.1 (C-4); 152.2 (C-2); 160.1 (C-6); 172 (*CO*Ph).

5',8-Cyclo-5'-deoxy-2',3'-O-isopropylidene-6-N,N'-dibenzoyl-adenosine **12**

To a solution of **11** (0.365 g, 0.5 mmol.) in dry and degased methylene chloride was added under argon *N*-acetoxy-2-thiopyridone (0.17 g, 2 mmol). The reaction mixture was irradiated with a tungsten lamp (150 W) for 3 h and the solution was allowed to warm to 40°C. The reaction was purified on a silica gel column (ether) to yield the 5',8-cyclopurin **12** (60%). Anal. Calcd. for $C_{27}H_{23}N_5O_5$, C(65.18); H(4.66); N(14.08); Found: C(65.10); H(4.82); N(14.15). MS (FAB, THIO$^+$): 498 $(MH)^+$, m.p.135-137°C (from ether-pentane), $[\alpha]_D^{20}$ = 121° (c=0.9, CH_2Cl_2). ^1H NMR (200 MHz, $CDCl_3$): δppm: 8.6 (s, 1H, H-2); 8.0-7.2 (m, 10H, Ph); 6.4 (s, 1H, H-1'); 4.86 (d, 1H, H-4', $J_{4',5'a}$= 6 Hz); 4.7 (s, 2H, H-2', H-3'); 3.5 (dd, 1H, H-5'a, $J_{5'a,5'b}$= 18 Hz, $J_{5'a,4'}$= 6 Hz); 3.1 (d, 1H, H-5b, $J_{5'b,5'a}$= 18 Hz); 1.5 (s, 3H, CH_3); 1.25 (s, 3H, CH_3). ^{13}C NMR (200 MHz, $CDCl_3$): δppm: 25.1, 26.2 (C*Me*$_2$); 29.6 (C-5'); 80.0 (C-4'); 83.3 (C-3'); 85.6 (C-2'); 86.4 (C-1'); 114.1 (*C*Me$_2$); 128.7, 129.6, 134.4, 133.0 (Ph); 149.0 (C-8); 151.8 (C-5); 150.4 (C-2); 172.3 (*CO*Ph).

5',8-Cyclo-5'-deoxy-2',3'-O-isopropylidene-adenosine **13**

The 6-*N*,*N*'-dibenzoyl groups of **12** (0.125 g, 0.25 mmol) were removed with methanol (10 ml) saturated with ammonia gas at room temperature overnight and the solvent was evaporated under reduced pressure to yield **13** as crystals (0.065 g, 90%). m.p. 231-232°C (from ethanol, lit[10] 233-235°C), $[\alpha]_D^{20}$ = -31° (c=1.5, DMSO), MS (CI, m/z): 290 $(MH)^+$.

5'-deoxy-2',3'-O-isopropylidene-5'-O-methanesulfonyl-uridine **15**

To a solution of the alcohol **14** (6.22 g, 22 mmol) in pyridine (100 ml) was added dropwise, at 0°C, mesylchloride (2.55 ml, 33 mmol). The mixture was stirred overnight at room temperature then water was added and the solution was evaporated to dryness. The residue was purified on a silica gel column (ethyl acetate-heptane, 1:1) to yield **15** as crystals (6.34 g, 80%). Anal.Calcd. for $C_{13}H_{18}N_2O_8S$, C(43.09); H(5.0); N(7.73); S(8.85), Found: C(43.41); H(4.83); N(7.92); S(8.92), MS (CI, m/z): 363 $(MH)^+$; 267 (MH-MsOH), m.p. 156-158°C (from methanol-heptane), $[\alpha]_D^{20}$ = + 157° (c=1.16, CH_2Cl_2). ^1H NMR (200 MHz, $CDCl_3$): dppm: 9.27 (s, 1H, NH); 7.28 (d, 1H, H-6, $J_{5,6}$= 8 Hz); 5.67 (d, 1H, H-5, $J_{5,6}$= 8 Hz); 5.62 (d, 1H, H-1', $J_{1',2'}$= 2 Hz); 5.1 (dd, 1H, H-2', $J_{2',3'}$= 6 Hz, $J_{2',1'}$= 2 Hz); 4.9 (dd, 1H, H-3', $J_{3',2'}$= 6 Hz, $J_{3',4'}$= 4 Hz);

4.46 (m, 3H, H-4', H-5', H-5"); 3.05 (s, 3H, CH_3); 1.55, 1.36 (2S, 6H, CMe_2). ^{13}C NMR (200 MHz, $CDCl_3$): δppm: 163 (C-4); 150 (C-2); 143 (C-6); 114 (*C*Me_2); 103 (C-5); 96 (C-1'); 85.7, 84.4 (C-2', C-3'); 81.1 (C-4'); 59 (C-5'); 37.8 (CH_3); 27.1, 25.3 (C*Me*$_2$).

5'-Anisyltelluro-5'-deoxy-2',3'-O-isopropylidene-uridine 16

To a stirred mixture of $NaBH_4$ (0.380 g, 2 eq) in ethanol (8 ml) and degased tetrahydrofuran (25 ml) in a three necked flask at 0°C under argon was added dropwise a solution of An_2Te_2 (1.29 g, 0.55 eq.) in degased tetrahydrofuran (25 ml) The red solution became colourless and the 5'-*O*-mesyl derivative **15** (1.81 g, 5 mmol) in dry and degased THF (50 ml) was added slowly. The reaction mixture was stirred at room temperature for 6 h and then water (40 ml) was added. The solvent was evaporated to dryness. After extraction with ethyl acetate the organic layer was dried ($MgSO_4$), filtered and evaporated to dryness. The residue was purified on a silica gel column (ethyl acetate-heptane, 6:4) to yield **16** as crystals (2 g, 80%). Anal.Calcd. for $C_{19}H_{22}N_2O_6Te$, C(45.24); H(4.36); N(5.55), Found: C(45.26); H(4.43); N(5.53). MS (EI, m/z): 504 $(M)^{+\cdot}$, m.p. 145-147°C (from ethyl acetate-heptane), $[\alpha]_D^{20}$ = + 13.4° (c=1.08, CH_2Cl_2), ^1H NMR (200 MHz, $CDCl_3$): δppm: 9.5 (s, 1H, NH); 7.7 (d, 2H, Ph); 7.2 (d, 1H, H-6, $J_{5,6}$= 8 Hz); 6.7 (d, 2H, Ph); 5.7 (d, 1H, H-5, $J_{5,6}$= 8 Hz); 5.6 (d, 1H, H-1', $J_{1',2'}$= 1 Hz); 5.0 (dd, 1H, H-2', $J_{1',2'}$= 1 Hz, $J_{2',3'}$= 6 Hz); 4.7 (dd, 1H, H-3', $J_{3',2'}$= 6 Hz, $J_{3',4'}$= 4 Hz); 4.35 (m, 1H, H-4', $J_{4',3'}$= 4 Hz, $J_{4',5'a}$= $J_{4',5'b}$= 6 Hz); 3.8 (s, 3H, OCH_3); 3.2 (t, 2H, H-5'a, H-5'b); 1.55-1.3 (2s, 6H, C*Me*$_2$). ^{13}C NMR (200 MHz, $CDCl_3$): δppm: 163 (C-4); 150.1 (C-2); 142.5 (C-6); 141.3 (Ph); 115.3 (*C*Me_2); 102.7 (C-5); 94.3 (C-1'); 87.9 (C-4'); 84.8 (C-2', C-3'); 55.3 (OCH_3); 27.2, 25.4 (C*Me*$_2$); 11.6 (C-5').

5',6-Cyclo-5'-deoxy-5,6-dihydro-5-(2-thiopyridyl)-2',3'-O-isopropylidene-uridine 17

To a solution of **16** (0.252 g, 0.5 mmol.) in dry and degased methylene chloride (5 ml) was added under argon *N*-acetoxy-2-thiopyridone (0.338, 2 mmol). The reaction mixture was irradiated with a tungsten lamp (150 W) for 3 h and the solution was allowed to warm at 40°C. The reaction mixture was purified on a silica gel column (ether-pentane, 8:2) to yield the cyclic compound **17** as a white foam (0.14g, 75%). Anal.Calcd. for $C_{17}H_{19}N_3O_5S$, C(54.11); H(5.07); N(11.14), S(8.48), Found: C(54.32); H(5.18); N(11.02); S(8.40), MS (CI, m/z): 378 $(MH)^+$, 267 $(MH\text{-}Spy)^+$, 112 $(Spy+H)^+$. ^1H NMR (200 MHz, $CDCl_3$) of the major isomer: δppm: 9.5 (s, 1H, NH); 8.45, 7.5, 7.2, 7.0 (d+td+t+t, 5H, Spy); 7.3 (d, 1H, H-5, $J_{5,6}$= 8 Hz); 5.7 (dd, 1H, H-6, $J_{6,5}$= 8 Hz, $J_{6,NH}$= 2 Hz); 5.6 (d, 1H, H-1', $J_{1',2'}$= 2.5 Hz); 5.0 (dd, 1H, H-2', $J_{2',1'}$= 2.5 Hz, $J_{2',3'}$= 7 Hz); 4.83 (dd, 1H, H-3', $J_{3',2'}$= 7 Hz, $J_{3',4'}$= 3 Hz); 4.46 (m, 1H, H-4'); 3.6 (dd, 1H, H-5'a, $J_{5'a,5'b}$= 15 Hz, $J_{5'a,4'}$= 6 Hz); 3.56 (dd, 1H, H-5'b, $J_{5'b,5'a}$= 15 Hz, $J_{5'b,4'}$= 6 Hz); 1,53, 1.33 (2s, 6H, C*Me*$_2$).

5',6-Cyclo-5'-deoxy-2',3'-O-isopropylidene-5,6-dihydrouridine 18

A solution of **17** (02 g, 0.53 mmol) in ethanol was heated under reflux in the presence of Raney Nickel overnight. The solution was filtered on a pad of celite and evaporated to dryness. The residue was purified on a silica gel column (ethyl acetate-heptane, 6:4) to yield **18** (0.085 g, 60%). Anal.Calcd. for $C_{12}H_{16}N_2O_5$, C(53.72); H(6.01); N(10.44), Found: C(53.54); H(6.01); N(10.22). MS (CI, m/z): 269 $(MH)^+$, m.p.: 280-

283°C (from methanol), $[\alpha]_D^{20}$ = -11° (c=1, DMSO). ^{1}H NMR (200 MHz, DMSO-d^6): δppm 7.7 (br s, 1H, NH); 6.1 (s, 1H, H-1'); 4.66 (d, 1H, H-3', $J_{3',2'}$= 6 Hz, $J_{3',4'}$= 0); 4.61 (d, 1H, H-2', $J_{2',3'}$= 6 Hz); 4.50 (t, 1H, H-4', $J_{4',5'a}$= $J_{4',5'b}$= 3 Hz); 3.55 (m, 1H, H-6); 2.70 (dd, 1H, H-5a, $J_{5a,5b}$= 17 Hz, $J_{5a,6}$= 4 Hz); 2.51 (dd, 1H, H-5b, $J_{5b,5b}$= 17 Hz, $J_{5b,6}$= 13 Hz); 1.85 (dd, 2H, H-5'a, H-5'b, $J_{5'a,4'}$= 3 Hz, $J_{5'a,6}$= 8 Hz); 1.5, 1.3 (2s, 6H, CMe_2). ^{13}C NMR (200 MHz,DMSO-d^6): 166.7 (C-4); 150.2 (C-2); 111.3 (*C*Me$_2$); 85.1 (C-1'); 82.6, 80.9, 79.4 (C-2', C-3', C-4'); 44.5 (C-6); 37.1 (C-5); 31.6 (C-5'); 25.6, 24.3 (C*Me$_2$*).

3'-O-tert.-Butyldiphenylsilyl-5'-O-methanesulfonyl-thymidine ***20***

To a solution of the alcohol **19** (6 g, 12.5 mmol) in pyridine (20 ml) was added dropwise, at 0°C, mesylchloride (1.5 ml, 18.75 mmol). The mixture was stirred overnight at room temperature then water was added and the solution was evaporated to dryness. The residue was purified on a silica gel column (methylene chloride-ethanol, 19:1) to yield **20** as a white foam (5 g, 71%). Anal.Calcd. for $C_{27}H_{34}N_2O_7SSi$, C(58.06); H(6.09); N(5.01); S(5.73), Found: C(58.27); H(6.34); N(4.91); S(5.75), MS (CI, m/z): 559 (MH)$^+$; 463 (MH-MsOH)$^+$, $[\alpha]_D^{20}$ = + 34° (c=1, CH_2Cl_2). ^{1}H NMR (200 MHz, $CDCl_3$): δppm: 9.3 (br s, 1H, NH); 7.8-7.4 (m, 10H, Ph); 7.23 (s, 1H, H-6); 6.45 (dd, 1H, H-1', $J_{1',2'a}$= 6 Hz, $J_{1',2'b}$= 7 Hz); 4.45 (m, 1H, H-3'); 4.15 (dd+br s, 2H, H-5'a, H-4'); 3.65 (dd, 1H, H-5'b, $J_{5'b,5'a}$= 14 Hz, $J_{5'b,4'}$= 4 Hz); 2.9 (s, 3H, *C*H_3SO$_2$); 2.4 (ddd, 1H, H-2'a, $J_{2'a,2'b}$= 14 Hz, $J_{2'a,1'}$= 6 Hz, $J_{2'a,3'}$= 3 Hz); 1.96 (m, 1H, H-2'b,); 1.88 (s, 3H, CH_3-5); 1.1 (s, 9H, C*Me$_3$*). ^{13}C NMR (200 MHz, $CDCl_3$): δppm: 12.4 (CH_3-5); 19.0 (*C*Me$_3$); 26.9 (C*Me$_3$*); 37.4 (*C*H_3SO$_2$); 40.4 (C-2'); 68.6 (C-5'); 73.0 (C-3'); 84.5, 85.2 (C-1', C-4'); 111.6 (C-5); 128.2, 130.4, 133.0, 135.8 (Ph); 135.3 (C-6); 150.2 (C-2); 163.8 (C-4).

5'-Anisyltelluro-3'-O-tert.-butyldiphenylsilyl-5'-deoxy-thymidine ***21***

To a stirred mixture of $NaBH_4$ (0.215 g, 2 eq) in ethanol (4 ml) and degased tetrahydrofuran (10 ml) in a three necked flask at 0°C under argon was added dropwise a solution of An_2Te_2 (0.731 g, 0.55 eq.) in degased tetrahydrofuran (15 ml) The red solution became colourless and the 5'-*O*-mesyl derivative **20** (1.585 g, 2.83 mmol) in dry and degased THF (20 ml) was added slowly. The reaction mixture was stirred at room temperature for 2 h and water (40 ml) was added. The solvent was evaporated to dryness. After extraction with ethyl acetate the organic layers were dried ($MgSO_4$), filtered and evaporated to dryness. The residue was purified on a silica gel column (ethyl acetate-heptane, 4:6) to yield **21** as a white foam (1.95 g, 98%). Anal.Calcd. for $C_{33}H_{38}N_2O_5SiTe$, C(56.57); H(5.42); N(4.0), Found: C(56.21); H(5.33); N(3.81), MS (FAB, Thio, NaCl$^+$): 701 (MH)$^+$, $[\alpha]_D^{20}$ = + 41° (c=1, CH_2Cl_2). ^{1}H NMR (200 MHz, $CDCl_3$): δppm: 8.78 (s, 1H, NH); 7.5, 7.26, 6.7 (m+d+d, 15H, Ph, H-6); 6.33 (dd, 1H, H-1', $J_{1',2'a}$= 6 Hz, $J_{1',2'b}$= 7 Hz); 4.16 (m, 2H, H-4', H-3'); 3.78 (s, 3H, OCH_3); 2.8 (dd, 1H, H-5'a, $J_{5'a,5'b}$= 13 Hz, $J_{5'a,4'}$= 4 Hz); 2.6 (dd, 1H, H-5'b, $J_{5'b,5'a}$= 13 Hz, $J_{5'b,4'}$= 5.5 Hz); 2.36 (ddd, 1H, H-2'a, $J_{2'a,2'b}$= 14 Hz, $J_{2'a,1'}$= 6 Hz, $J_{2'a,3'}$= 3 Hz); 1.95 (q, 1H, H-2'b, $J_{2'b,2'a}$= 14 Hz, $J_{2'b,1'}$= 7 Hz); 1.85 (s, 3H, CH_3-5); 1.05 (s, 9H, C*Me$_3$*). ^{13}C NMR (200 MHz, $CDCl_3$): δppm: 12.2 (C-5'); 12.5 (CH_3-5); 18.5 (*C*Me$_3$); 26.8 (C*Me$_3$*); 40.5 (C-2'); 55.1 (Ph*OCH$_3$*); 76.5 (C-3'); 84.3 (C-1'); 86.2 (C-4'); 111.0 (C-5); 115.2, 127.9, 130.1, 135.7 (Ph); 140.4 (C-6); 150.4 (C-2); 164.0 (C-4).

3'-O-tert.-Butyldiphenylsilyl-5',6-Cyclo-5'-deoxy-5-(2-thiopyridyl)-5,6-dihydrothymidine 22 and 3'-O-tert.-Butyldiphenylsilyl-5'-deoxy-5'-(2-thiopyridyl)-thymidine 23

To a solution of **21** (0.74 g, 1.06 mmol.) in dry and degased methylene chloride (10 ml) was added *N*-acetoxy-2-thiopyridone (0.714, 4.2 mmol). The reaction mixture was irradiated with a tungsten lamp (150 W) for 3 h and the solution was allowed to warm at 40°C. The reaction was purified on a silica gel column (ethyl acetate-heptane, 3:7) to yield the cyclic compound **22** as a white foam (0.486 g, 80%) and the rearrangement product **23** (0.09, 15%).

Compound **22**: Anal.Calcd. for $C_{31}H_{35}N_3O_4SSi$, C(64.92); H(6.11); N(7.33), S(5.58), Found: C(65.04); H(6.41); N(7.58); S(5.71), MS (CI, m/z): 574 $(MH)^+$, 463 $(MH\text{-}Spy)^+$, 112 $(Spy+H)^+$, ^1H NMR (250 MHz, $CDCl_3$) of the major isomer: δppm: 9.5 (s, 1H, NH); 8.3,-7.0 (d+m+t, 6H, Spy, H-6); 6.4 (dd, 1H, H-1', $J_{1',2'a}$= 5.5 Hz, $J_{1',2'b}$= 8 Hz); 4.3 (m, 2H, H-3', H-4'); 3.4 (dd, 1H, H-5'a, $J_{5'a,5'b}$= 14 Hz, $J_{5'a,4'}$= 5 Hz); 3.1 (dd, 1H, H-5'b, $J_{5'b,5'a}$= 14 Hz, $J_{5'b,4'}$= 5 Hz); 2.15 (ddd, 1H, H-2'a, $J_{2'a,2'b}$= 13.5 Hz, $J_{2'a,3'}$= 2 Hz, $J_{2'a,1'}$= 5.5 Hz); 1.95-1.8 (m+s, 4H, H-2'b, CH_3-5); 3.3 (s, 9H, C*Me*$_3$). ^{13}C NMR (200 MHz, $CDCl_3$): δppm: 12.6 (CH_3-5); 19.0 (*C*Me_3); 26.9 (CMe_3); 31.7 (C-5'); 40.5 (C-2'); 75.0 (C-3'); 84.9, 85.9 (C-4', C-1'); 115.4 (C-5); 119.7, 122.3, 127.9, 130.0, 132.2, 135.8, 136.1, 149.3 (C-6, Ph, Spy); 150.4 (C-2); 164.3 (C-4).

Compound **23**: Anal.Calcd. for $C_{31}H_{35}N_3O_4SSi$, C(64.92); H(6.11); N(7.33), S(5.58), Found: C(64.71); H(6.41); N(7.04); S(5.58), MS (CI, m/z): 574 $(MH)^+$, 463 $(MH\text{-}Spy)^+$, 387 (463-Ph+H)$^+$, 127 $(Base+H)^+$, 112 $(Spy+H)^+$. $[\alpha]_D^{20}$ = -38° (c= 0.8, CH_2Cl_2), m.p.86-88 °C (from ether-pentane), ^1H NMR (200 MHz, $CDCl_3$): δppm: 8.5, 8.1, 7.8, 7.45-7.25 (d, s, t, m, 15H, Spy, Ph, H-6); 6.2 (d, 1H, H-1', $J_{1',2'}$= 6 Hz); 4.33 (d, 1H, H-4', $J_{4',5'b}$= 4 Hz); 4.25 (dd, 1H, H-3', $J_{3',2'a}$= 3 Hz, $J_{3',2'b}$= 7 Hz); 3.4 (dd, 1H, H-5'a, $J_{5'a,5'b}$= 12 Hz); 2.4 (m, 2H, H-5'b, H-2'a); 2.1 (dd, 1H, H-2'b, $J_{2'b,2'a}$= 14 Hz, $J_{2'b,3'}$= 3 Hz); 1.26 (s, 3H, CH_3-5); 1.05 (s, 9H, C*Me*$_3$). ^{13}C NMR (200 MHz, $CDCl_3$): δppm: 169.0 (C-4); 151.0 (C-2); 137.3, 135.7, 133.5, 133.1, 131.1, 127.9 (Ph, Spy); 133.5 (C-5); 123.8 (C-6); 83.8, 82.6 (C-1', C-4'); 74.1 (C-3'); 54.5 (C-5'); 43.2 (C-2'); 26.8 (C*Me*$_3$); 19.0 (*C*Me_3); 18.4 (CH_3-5).

1-(3'-O-tert.-Butyldiphenylsilyl-2',5'-dideoxy-β-D-erythro-pentofuranosyl)-thymine 24

A solution of **22** (0.1 g, 0.174 mmol) in ethanol (15 ml) was refluxed in presence of Raney Nickel overnight. The solution was filtered over celite and evaporated to dryness. The residue was purified on a silica gel column (ethyl acetate-heptane, 6:4) to yield **24** as a white foam (0.057 g, 70%). Anal.Calcd. for $C_{26}H_{32}N_2O_4Si$, C(67.22); H(6.94); N(6.03), Found: C(67.03); H(7.05); N(5.73). MS (CI, m/z): 465 $(MH)^+$, 127 $(Base+H)^+$, $[\alpha]_D^{20}$ = +51° (c=0.8, CH_2Cl_2). ^1H NMR (200 MHz, $CDCl_3$): 9.4 (s, 1H, NH); 7.9-7.2 (m, 10H, Ph); 7.0 (s, 1H, H-6); 6.3 (t, 1H, H-1', $J_{1',2'a}$= $J_{1',2'b}$= 6.5 Hz); 4.0 (m, 2H, H-3', H-4'); 2.35 (ddd, 1H, H-2'a, $J_{2'a,2'b}$= 13Hz, $J_{2'a,1'}$= 6.5 Hz, $J_{2'a,3'}$= 3 Hz); 1.9 (s, 3H, CH_3-5); 1.8-1.65 (m, 1H, H-2'b); 1.25 (s, 3H, CH_3-5'); 1.1 (s, 9H, C*Me*$_3$). δppm: ^{13}C NMR (200 MHz, $CDCl_3$): δppm: 12.7 (CH_3-5); 18.8 (CH_3-5'); 19.0 (*C*Me_3); 26.9 (C*Me*$_3$); 40.2 (C-2'); 77.1 (C-3'); 82.8 (C-4'); 84.7 (C-1'); 110.9 (C-5); 127.9, 130.0, 133.2, 135.7 (Ph); 134.8 (C-6); 150.3 (C-2); 164.0 (C-4).

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