A versatile approach to novel homo-C-nucleosides based on aldehydes and acetylenic ketones derived from ribo- and 2-deoxy-ribofuranose C-glycosides

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Dedicated to Prof. Dr. Rainer Beckert on the Occasion of his 60th Birthday

Abstract

A series of ribofuranosyl- and 2-deoxyribofuranosyl homo- and spacered-C-nucleosides have been synthesized by reaction of fully protected 3-(1-deoxy-β-D-ribofuranosyl-1-yl)propanal (**1**), 3-(1,2-dideoxy-β-D-ribofuranos-1-yl)propanal (**14**), 1-(1-desoxy-β-D-ribofuranos-1-yl)pent-4-yn-3-on (**19**), 1-(1-desoxy-β-D-ribofuranos-1-yl)-5-phenyl-pent-4-yn-3-on (**20**), 1-(1,2-didesoxy-β-D-ribofuranos-1-yl)pent-4-yn-3-on (**29**), and 1-(1,2-didesoxy-β-D-ribofuranos-1-yl)-5-phenyl-pent-4-yn-3-on (**30**) with different nucleophiles. The preparation of **1** and **14** proceeds by Knoevenagel reaction with malononitrile, cyanoacetamide and 2-cyano-*N*-(4-methoxy-phenyl)acetamide and subsequent cyclization with sulphur to thiophenes **5**, **7**, **8**, **16** and then by cyclization with triethyl orthoformate to give thienopyrimidine **6** and thienopyrimidinone **9**, **10**, and **17**. Treatment of acetylenic ketones **19**, **20**, **29**, and **30** with acetamidinium chloride, benzamidinium chloride, and *S*-methylisothiouronium sulphate provided the corresponding pyrimidines **21**–**26**, **31**, **32**. Finally, the use of 4*H*-1,2,4-triazol-3-amine and 2-aminobenz-imidazole as 1,3-*N*,*N'*-dinucleophiles afforded the triazolopyrimidines **35**, **39** and the pyrimidobenzimidazoles **36**, **37**, and **40**, respectively. Deprotection of a selected number of C-nucleosides was achieved by one or two steps procedure without serious problems. That makes these C-nucleosides promising candidates for the synthesis of monomers suitable for solid phase nucleic acid oligomerization.

Keywords: Ribose, 2-deoxy-ribose, C-nucleosides, thiophenes, pyrimidines, thienopyrimidines

Introduction

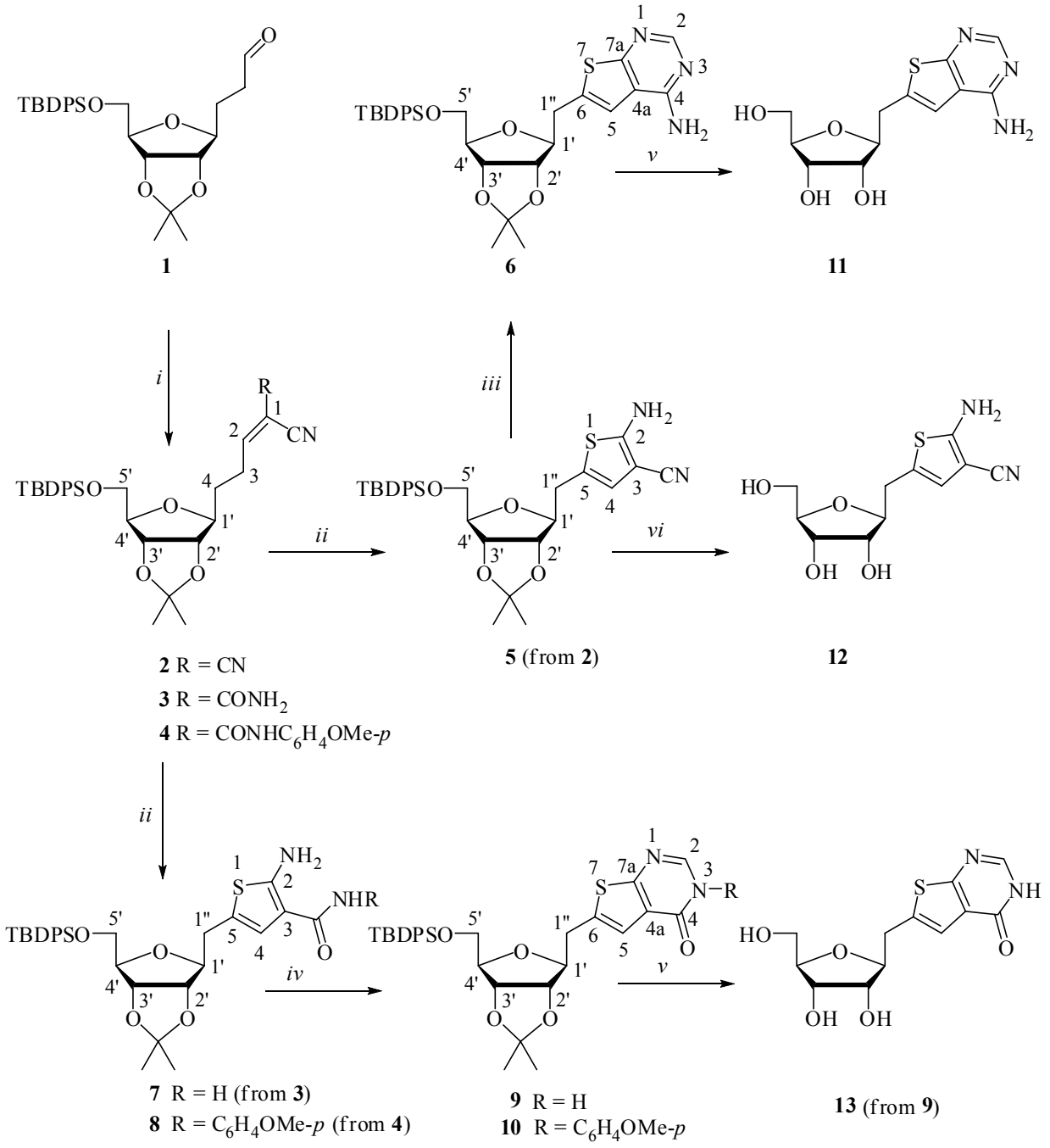
The interest in nucleoside analogues is unbroken and their design and synthesis have been done with quite different intentions e.g. synthesis of homo-C-nucleosides with potential biological activity,[1-3] tools for elucidating the structural and functional properties of damaged DNA,[4] illustration of hybridizations and conformational changes of DNA and RNAs,[5] and to give an answer to the question why DNA evolved on Earth to have the structure that it does.[6-10]

Pursuing a program directed at the synthesis of homo-C-nucleosides, we have described previously an efficient route for the preparation of β-allyl C-glycosides of D-ribofuranose and 2-deoxy-D-ribofuranose.[11] Recently we have reported the synthesis of consecutive compounds e.g. alcohols, amines, aldehydes, and acetylenic ketones.[12] In this contribution we present our results on transformation of the furnished aldehydes (**1**,**14**) and acetylenic ketones (**19**, **20**, **29**, **30**) as versatile intermediates into a selected number of different heterocycles to make the synthetic potential of these precursors visible.

Results and Discussion

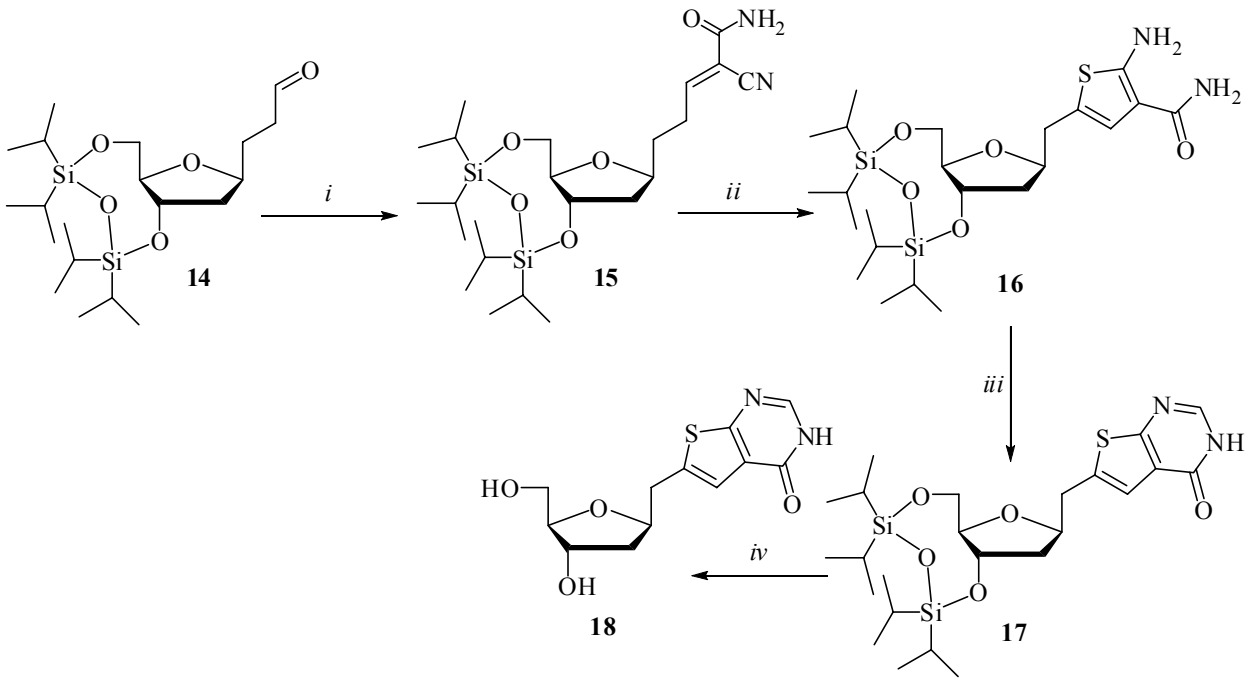
Synthesis of thienopyrimidine homo-C-nucleosides

The synthesis started from the aldehyde **1** which was readily obtainable from β-allyl C-glycoside of D-ribose[11] via hydroboration/ oxidation and selective oxidation of the corresponding alcohol.[12] Treatment of **1** with malononitrile, cyanoacetamide and 2-cyano-*N*-(4-methoxy-phenyl)acetamide provided the corresponding Knoevenagel products **2**-**4** in 60%, 51%, and 77%, respectively (Scheme 1). The reaction was carried out by using an excess of the CH-acidic compounds and basic aluminium oxide in boiling toluene.[13] The reaction time varied between 2 and 16 h as monitored by TLC. All analytical data were in accordance with the proposed structures. Additionally, the values for the coupling constants $J_{H2\text{-}CN}$ and $J_{H2\text{-}C=O}$ (13-14 Hz and 5-6 Hz, respectively) determined from coupled ^{13}C NMR spectra confirmed the *E*-configuration of structures **3** and **4**. When the compounds **2**-**4** were treated with elemental sulphur and triethylamine in *N*,*N*-dimethylformamide (DMF)[13,14] for 2 h at r.t. the light yellow aminothiophenes **5**, **7**, and **8** were obtained in about 80% yield. The ^1H NMR spectra showed signals at δ 2.81–3.02 and the ^{13}C NMR spectra provided signals at δ 33.7–33.9 characteristic of the methylene unit of homo-C-nucleosides. For the synthesis of 4-aminothienopyrimidine **6** compound **5** was reacted with triethyl orthoformate under reflux for 2 h. Without purification the resulting formimidate was treated with a saturated ethanolic ammonia solution to afford the desired compound **6** in 74% overall yield.[15] Cyclization to the thienopyrimidinones **9** and **10** were achieved when a mixture of compounds **7** or **8** and triethyl orthoformate were heated at reflux in DMF for 7–10 h. In spite of the drastic reaction conditions the desired derivatives **9** and **10** were obtained in about 70% yield. In the ^1H NMR spectra singlets were observed at δ 8.05 and 8.02 characteristic of H-2 of **9** and **10**, respectively.



Scheme 1. Syntheses of thiophenes **5**, **7**, **8**, pyrimidine **6**, and pyrimidinone **17** *via* Knoevenagel products **2**–**4**. *Reagents and conditions*: (*i*) CH-acid compounds, Al_2O_3, dry toluene, reflux, 2–16 h; (*ii*) sulfur, NEt_3, DMF, r.t. 2 h; (*iii*) $HC(OEt)_3$, reflux 2h, then ethanol-ammonia, reflux 2 h; (*iv*) $HC(OEt)_3$, dry DMF, reflux, 7–10 h; (*v*) 90% aq CF_3CO_2H, CH_2Cl_2, r.t.; (*vi*) Bu_4NF, 1,4-dioxane, r.t. 5 h, then 90% aq CF_3CO_2H, CH_2Cl_2, r.t.

Finally, treatment of **9** and **6** with 90% trifluoroacetic acid in CH_2Cl_2 removed both the silyl and isopropylidene protecting groups, providing the unprotected derivatives **11** and **13** in 90 % yield. In contrast, deprotection of thiophene **5** required a two step procedure. Firstly, the *tert*-butyldiphenylsilyl group (TBDPS) was cleaved off by treatment of **5** with a solution of tetrabutylammonium fluoride (TBAF) in 1,4-dioxane. After 5 h, the isopropylidene group was then removed with 90% trifluoroacetic acid in CH_2Cl_2 to give **12** in 87% overall yield.



Scheme 2. Synthesis of thiophenecarboxamide **16** and pyrimidinon **17**. *Reagents and conditions*: (*i*) 2-cyanoacetamide, Al_2O_3, dry toluene, reflux, 24 h; (*ii*) sulfur, NEt_3, DMF, r.t. 2 h; (*iii*) $HC(OEt)_3$, dry DMF, reflux, 10 h; (i*v*) Bu_4NF, 1,4-dioxane, r.t. 2 h.

In a previous paper,[11] we described an efficient route to transfer β-allyl C-glycoside of D-ribose into the corresponding 2-deoxy ribofuranose. Employment of exactly the same conditions of hydroboration-oxidation and consecutive selective oxidation of the corresponding alcohol furnished aldehyde **14**.[12] The versatility of **14** was demonstrated by the preparation of thieonopyrimidinone **18** by the same sequence of reaction steps as described for compound **13** (Scheme 2). Even the reaction conditions were identical only slightly differences of reaction time and yield occur. Thus, Knoevenagel product **15** was obtained in 52% yield. Transformation of **15** into thiophene **16** (73%) was followed by ring closure reaction to provide **17** in 69% yield. Deprotection was simply achieved by treatment of **17** with TBAF in a solution of 1,4-dioxane. After 2 h at r.t. derivative **18** was obtained in 78% yield.

As described previously,[12] aldehydes **1** and **14** can be converted to acetylenic ketones **19**, **20** and **29**, **30** by reaction with ethynylmagnesium bromide or phenylethynyllithium, respectively,

and followed by oxidation of the diastereomeric alcohols. Analytical sample of **20** was obtained by crystallization from ethyl acetate–*n*-hexane. Its constitution was confirmed by X-ray diffraction studies (Figure 1).

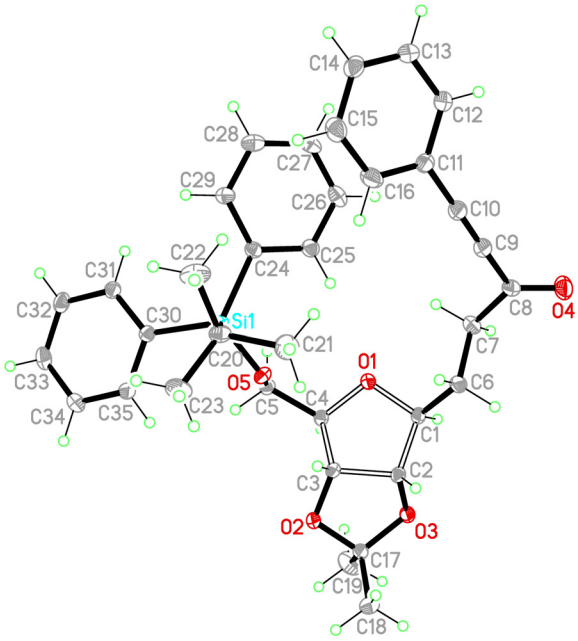


Figure 1

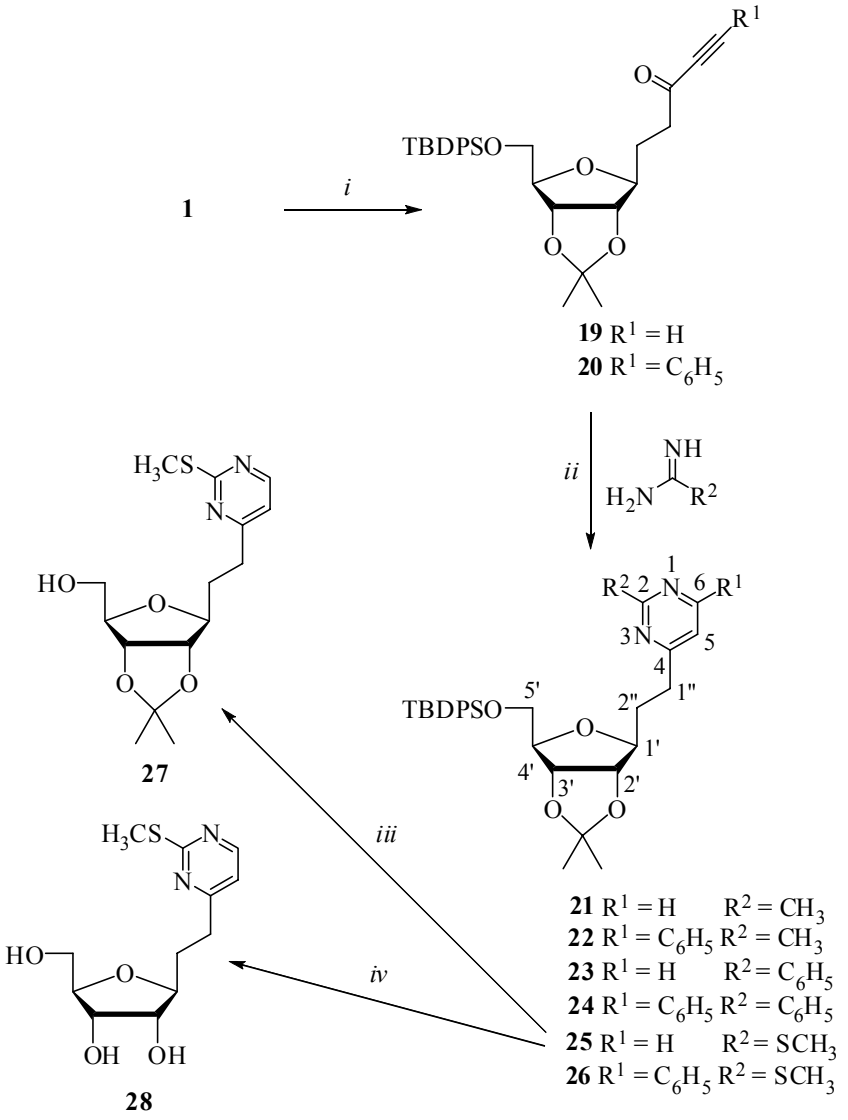
Molecular structure of alkynyl ketone **20** with atom labeling scheme. Thermal ellipsoids are drawn at the 30% probability level. Puckering parameters are q2 = 0.3233(1) and Φ2 = –35.96(1) for the tetrahydrofuran ring.

Synthesis of pyrimidine-spacered C-nucleosides

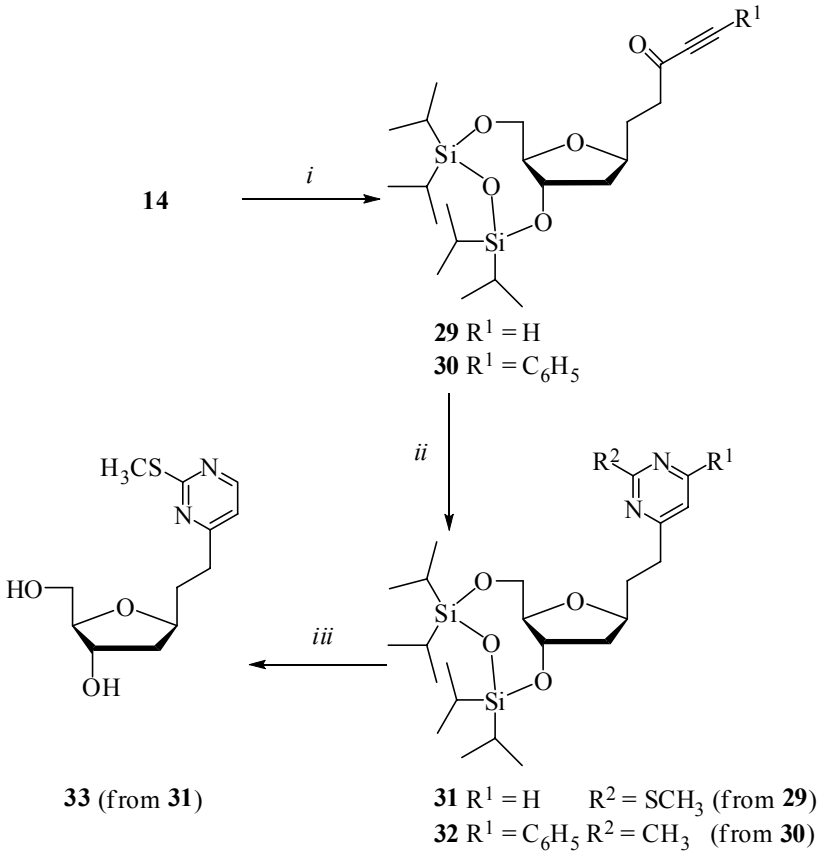
Acetylenic ketones are a versatile class of compounds which can be used as starting materials for the synthesis of a broad variety of heterocycles.[16-20] Herein we report efficient short synthesis of substituted pyrimidines and triazolopyrimidines. Following the strategy of Addlington et al,[17] who reported the reaction of acetylenic ketones with amidinium salts using ethyl acetate/water as solvent and sodium carbonate as base, **19** and **20** were treated with acetamidinium chloride, benzamidinium chloride, and *S*-methylisothiouronium sulphate to give the corresponding pyrimidines **21**–**26** separated from the tetrahydrofuran ring by an ethylene group (Scheme 3).

All reactions proceeded in good (60%) to excellent yield (quantitative). As expected, all analytical data were in agreement with the proposed structures. We examined the stepwise and complete deprotection of the obtained pyrimidines using the example of compound **25**. Treatment of **25** with aq HCl in EtOH resulted in simultaneous removal of both silyl and isopropylidene protecting groups to give **28** in 74% yield. On the other hand, in the presence of

TBAF in 1,4-dioxane only the TBDPS group was removed and the partial protected derivative **27** was obtained in 85% yield. Again, the 2-deoxy acetylenic ketones **29** and **30** were allowed to react with selected amidinium salts e.g. *S*-methylisothiouronium sulphate and acetamidinium chloride to provide the pyrimidines **31** and **32**, respectively (Scheme 4). Deprotection of **31** with TBAF in 1,4-dioxane afforded **33** in 78% yield.



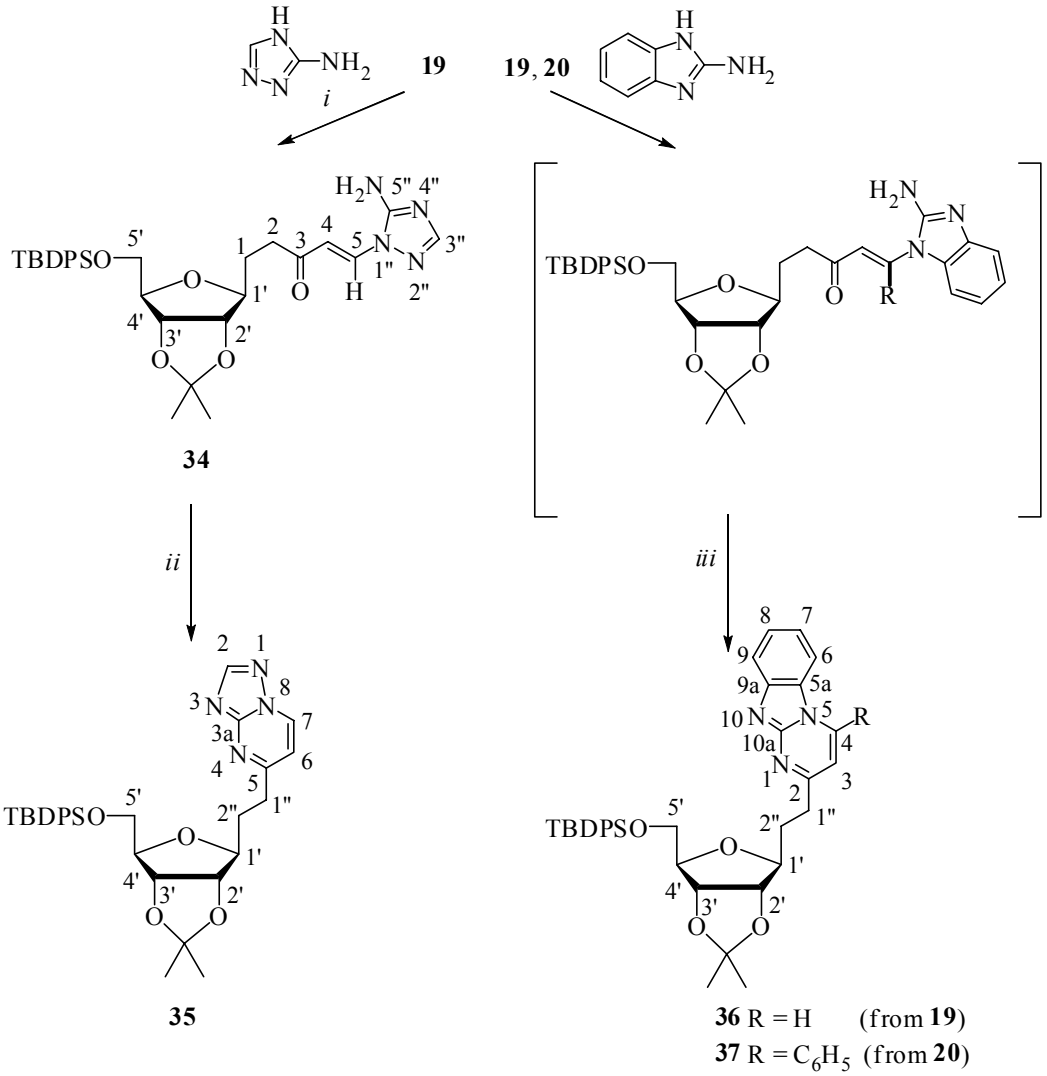
Scheme 3. Synthesis of pyrimidines **21**–**26** *via* acetylenic ketones **19** and **20**. *Reagents and conditions*: (*i*) ethynylmagnesium bromide or phenylethynyllithium, dry THF, r.t. 4 h, then Dess-Martin oxidation; (*ii*) acetamidinium, benzamidinium or *S*-methylisothiouronium salts, cat. H_2O, Na_2CO_3, AcOEt, reflux, 2–24 h; (*iii*) Bu_4NF, 1,4-dioxane, r.t. 4 h; (*iv*) aq HCl (1M), EtOH, r.t. 12 h.



Scheme 4. Synthesis of pyrimidines **31** and **32** *via* acetylenic ketones **29** and **30**. *Reagents and conditions*: (*i*) ethynylmagnesium bromide or phenylethynyllithium, dry THF, r.t. 4 h, then Dess-Martin oxidation; (*ii*) *S*-methylisothiouronium sulphate (for **31**) and acetamidinium chloride (for **32**), cat. H_2O, Na_2CO_3, AcOEt, reflux, 3–24 h; (*iii*) Bu_4NF, 1,4-dioxane, r.t. 24 h.

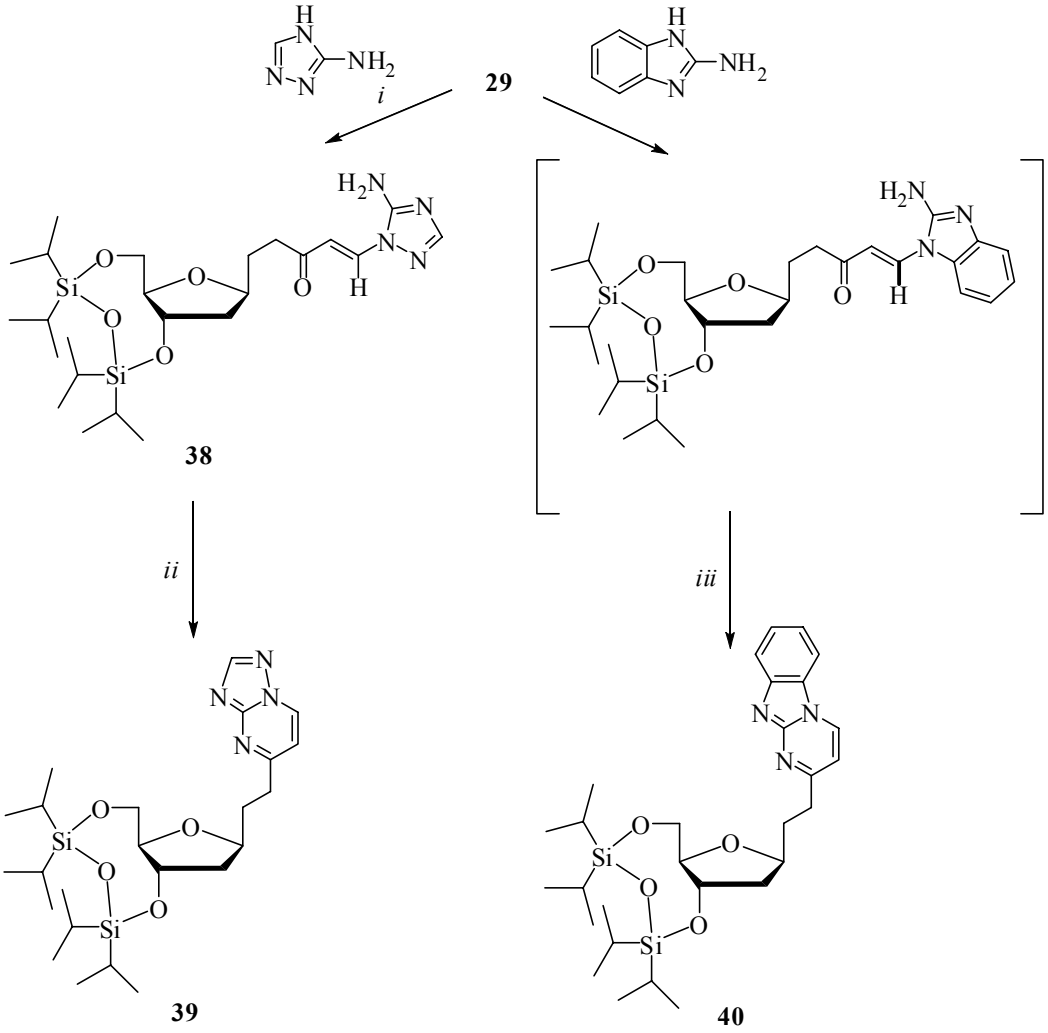
Synthesis of triazolo- and pyrimidinobenzimidazole-spacered C-nucleosides

Nucleophilic attack of 4*H*-1,2,4-triazol-3-amine on the triple bond of ynone **19** in boiling EtOH resulted in compound **34** in 89% yield (Scheme 5).[21] The ^{1}H and ^{13}C NMR spectra of **34** were fully consistent with the assigned structure. As expected, no signals of acetylenic carbon atoms were observed in the ^{13}C-NMR spectra, but a resonance was visible at δ 151.7 for C-3'' of the triazole ring. The *E*-configuration of the addition product was evident from the large coupling constant $^3J_{4,5}$ 13.3 Hz in the ^{1}H NMR spectra. In order to prepare a fused heterocycle enone **34** was treated with sodium ethanolate at r.t. for 1 h to afford triazolopyrimidine **35** in 62% yield. Analogous to that addition reaction 2-aminobenzimidazole was used as 1,3-*N,N'*-dinucleophile and allowed to react with ynone **19** and **20**. Suprisingly, the TLC of the reaction solution showed in each case the formation of a mixture two products after reflux (EtOH) for 2 h. The stepwise formation of compound **35** strongly suggested that here a mixture of an addition products (in parenthesis Scheme 5) and the fused heterocycles **36** and **37** were observed.



Scheme 5. Synthesis of triazolopyrimidine **35** and pyrimidobenzimidazoles **36** and **37**. *Reagents and conditions*: (*i*) 4*H*-1,2,4-triazol-3-amine, dry EtOH, reflux, 4 h; (*ii*) ethanolic NaOMe (1M), r.t., 1 h; (*iii*) 1*H*-benzo[*d*]imidazole-2-amine, dry EtOH, reflux, 2 h, then ethanolic NaOMe 1 M), r.t. 1 h.

Indeed, treatment of the unseparated reaction mixture with sodium ethanolate at r.t. for 1 h caused disappearance of the side-products and provided **36** and **37** in 76% and 80% yield, respectively. The protocol of the formation of triazolopyrimidine and pyrimidobenzimidazole by reaction of 4*H*-1,2,4-triazole-3-amine and 2-aminobenzimidazole, respectively, was now transferred to the ynone **29** (Scheme 6). Fortunately, the course of all reactions was comparable to ynone **19.** Consequently, triazolopyrimidine **39** and pyrimidobenzimidazole **40** were obtained in 69% and 63%, respectively. The regioselectivity of the ring closure reactions was evident from NOESY and HMBC experiments.



Scheme 6. Synthesis of triazolopyrimidine **39** and pyrimidobenzimidazole **40**. *Reagents and conditions*: (*i*) 4*H*-1,2,4-triazol-3-amine, dry EtOH, reflux, 4 h; (*ii*) ethanolic NaOMe (1M), r.t., 1 h; (*iii*) 1*H*-benzo[*d*]imidazole-2-amine, dry EtOH, reflux, 2 h, then ethanolic NaOMe 1 M), r.t. 1 h.

In summary, we have shown that fully protected ribofuranosylpropanal (**1**), 2-deoxy-ribofuranosylpropanal (**14**) and the corresponding alkynyl ketones **19**, **20**, **29**, and **30** are suitable intermediates for the preparation of homo- and spacered C-nucleosides. The tetrahydrofuran ring and the protecting group pattern is stable enough even under drastic reaction conditions to allow the synthesis of a broad variety of heterocyclic systems. In one of our next papers, we will describe the conversion of some of our C-nucleosides into building blocks suitable for solid phase synthesis of nucleic acid oligomers.

Experimental Section

General. Melting points were determined with a Boetius micro-heating plate BHMK 05 (Rapido, Dresden) and were not corrected. Optical rotation was measured for solutions in a 2-cm cell with an automatic polarimeter GYROMAT (Dr. Kernchen Co.). ^{1}H NMR spectra (250.13 and 300.13 MHz) and ^{13}C NMR spectra (62.9 and 75.5 MHz) were recorded on Bruker spectrometers AVANCE 250 and AVANCE 300, respectively, at 298 K. The chemical shifts are referenced to solvent signals ($CDCl_3$: δ ^{1}H = 7.26, δ ^{13}C = 77.0; DMSO-d_6: δ ^{1}H = 2.49, δ ^{13}C = 39.7; CD_3OD: δ ^{1}H = 3.30, δ ^{13}C = 49.3). Signal assignment was performed by recording the DEPT spectra, in some cases also by recording of two-dimensional ^{1}H,^{1}H COSY, ^{13}C,^{1}H HETCOR and ^{1}H,^{13}C HMBC spectra. For NMR numbering of atoms see Scheme 1, 3 and 5. Mass spectra were recorded on an AMD 402/3 spectrometer (AMD Intectra GmbH). Elemental analysis was performed on a CHNS-Flash-EA-1112 instrument (Thermoquest)**.** For the X-ray structure determination of compound **20** an X8Apex system with CCD area detector was used (λ = 0.71073 Å, graphite monochromator). The structures were solved by direct methods (Bruker-SHELXTL). The refinement calculations were done by the full-matrix least-squares method of Bruker SHELXTL, Vers.5.10, Copyright 1997, Bruker Analytical X-ray Systems. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were put into idealised positions and refined using the riding models. Crystallographic data for the structure analysis has been deposited with the Cambridge Crystallographic Data Centre, CCDC No 827042 for compound **20**. Copies of this information may be obtained free of charge from: The Director, CCDC, 12 Union Road Cambridge, CB2 1EZ UK, Fax. (int code) +44(1223)336-033 or via Email: deposit @ccdc. cam.ac.uk or www:http://www. ccdc. cam.ac.uk. All washing solutions were cooled to ~5 °C. The $NaHCO_3$ solution was saturated. Reactions were monitored by thin-layer chromatography (TLC, Silica Gel 60, F_{254}, Merck KGaA). The followings solvent systems (v/v) were used: (A) ethyl acetate, (B_1) 2:1, (B_2) 1:1, (B_3) 2:3, (B_4) 1:2, (B_5) 1:3, (B_6) 1:4, (B_7) 1:5 ethyl acetate – *n*-hexane; (C_1) 1:1, (C_2) 4:1, (C_3) 5:1, (C_4) 6:1 ethyl acetate – methanol; (D) 12:1:0.1 ethyl acetate – methanol – acetic acid. The spots were made visible by dipping the TLC plates into a methanolic 10% H_2SO_4 solution and charring with a heat gun for 3–5 min. Preparative flash chromatography was performed by elution from columns of slurry-packed Silica Gel 60 (Merck, 63–200 μm). All solvents and reagents were purified and dried according to standard procedures.[22] After classical work up of the reactions mixtures, the organic layer were dried over $MgSO_4$, and then concentrated under reduced pressure (rotary evaporator).

KNOEVENAGEL reaction with aldehyde (1). General procedure

Malononitrile (377 mg, 5.7 mmol), 2-cyanoacetamide (479 mg, 5.7 mmol) or 2-cyano-*N*-(4-methoxyphenyl)acetamide (1.08 g. 5.7 mmol) was added to a stirred solution of 3-(5-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranosyl-1-yl)propanal (**1**, 1.17 g, 2.5 mmol) and aluminium oxide (653 mg, 6.4 mmol, basic activated 90, 101076 MERCK) in dry toluene (75 mL). After heating under reflux for 2–16 h (monitored by TLC), the reaction mixture

was cooled to r.t., the insoluble solids were filtered off, and the filtrate was concentrated. The residue was purified by flash chromatography.

2-[3-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)propylidene]malononitrile (2). Reaction time 2.5 h; flash chromatography solvent B_6; (775 mg, 60%) colorless syrup; $[\alpha]_D^{21}$ −12.5 (*c* 1.0, CH_2Cl_2); R_f = 0.16 (solvent B_7). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.07 [s, 9H, $C(CH_3)_3$]; 1.35, 1.54 [2 x s, 6H, $C(CH_3)_2$]; 1.71–1.94 (m, 2H, H-4); 2.66–2.75 (m, 2H, H-3); 3.80 (m, 2H, H-5'); 3.82–3.86 (m, 1H, H-1'); 4.07 (q, 1H, $^3J_{3',4'}$ 3.5, $^3J_{4',5'}$ 3.5 Hz, H-4'); 4.28 (dd, 1H, $^3J_{1',2'}$ 5.4 Hz, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.74 (dd, 1H, H-3'); 7.28 (t, 1H, $^3J_{2,3}$ 7.8 Hz, H-2); 7.35–7.69 (m, 10H, 2 x Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.3 [*C*$(CH_3)_3$]; 25.5, 27.5 [C(*C*$H_3)_2$]; 26.9 [C(*C*$H_3)_3$]; 29.7, 31.4 (C-3, C-4); 64.0 (C-5'); 81.9 (C-3'); 83.5 (C-1'); 84.4 (C-4'); 84.5 (C-2'); 110.4, 112.0 (2 CN); 114.4 [*C*$(CH_3)_2$]; 127.8, 127.8, 129.8, 129.9, 135.6 (2) (2 *o*-, *m*-, *p*-Ph); 133.1, 133.2 (2 *i*-Ph); 169.0 (C-2). CI-MS**:** *m*/*z* (%) = 517 (3, $[M+H]^+$).
Anal. Calcd for $C_{30}H_{36}N_2O_4Si$ (516.70): C, 69.73; H, 7.02; N, 5.42. Found: C, 69.41; H, 7.03; N, 5.41.

(*E*)-2-Cyano-5-(5-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)pent-2-enamide (3). Reaction time 16 h; flash chromatography solvent B_3; (682 mg, 51%) colorless syrup; $[\alpha]_D^{21}$ −12.7 (*c* 1.0, $CHCl_3$); R_f = 0.17 (solvent B_4). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.06 [s, 9H, $C(CH_3)_3$]; 1.34, 1.53 [2 s, 6H, $C(CH_3)_2$]; 1.78–1.88 (m, 2H, H-4); 2.63–2.72 (m, 2H, H-3); 3.78 (m, 2H, H-5'); 3.82–3.89 (m, 1H, H-1'); 4.05 (q, 1H, $^3J_{3',4'}$ 3.6, $^3J_{4',5'}$ 3.6 Hz, H-4'); 4.30 (dd, 1H, $^3J_{1',2'}$ 5.2 Hz, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.72 (dd, 1H, H-3'); 5.71, 6.09 (2 br s, 2H, NH_2); 7.34–7.47, 7.61–7.73 (2m, 11H, 2 Ph, H-2). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.3 [*C*$(CH_3)_3$]; 25.5, 27.5 [C(*C*$H_3)_2$]; 26.8 [C(*C*$H_3)_3$]; 28.5 (C-3); 31.8 (C-4); 64.0 (C-5'); 81.9 (C-3'); 83.4 (C-1'); 84.2 (C-4'); 84.7 (C-2'); 110.1 (C-1); 114.3 [*C*$(CH_3)_2$]; 114.9 (CN); 127.7, 129.8, 135.6 (2 *o*-, *m*-, *p*-Ph); 133.1, 133.2 (2 *i*-Ph); 160.8 ($CONH_2$); 161.3 (C-2). CI-MS**:** *m*/*z* (%) = 535 (3, $[M+H]^+$). Anal. Calcd for $C_{30}H_{38}N_2O_5Si$ (534.72): C, 67.39; H, 7.16; N, 5.24. Found: C, 67.64; H, 7.22; N, 5.27.

(*E*)-2-Cyano-5-(5-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)-*N*-(4-methoxyphenyl)pent-2-enamide (4). Reaction time 12 h; flash chromatography solvent B_5; (1.23 g, 77%) colorless syrup; $[\alpha]_D^{21}$ −16.1 (*c* 1.0, $CHCl_3$); R_f = 0.45 (solvent B_4).
^{1}H NMR (250 MHz, $CDCl_3$) δ 1.06 [s, 9H, $C(CH_3)_3$]; 1.35, 1.54 [2 s, 6H, $C(CH_3)_2$]; 1.81–1.91 (m, 2H, H-4); 2.67–2.76 (m, 2H, H-3); 3.79 (m, 2H, H-5'); 3.81 (s, 3H, OCH_3); 3.84–3.91 (m, 1H, H-1'); 4.06 (q, 1H, $^3J_{3',4'}$ 3.5 Hz, $^3J_{4',5'}$ 3.5 Hz, H-4'); 4.32 (dd, 1H, $^3J_{1',2'}$ 5.3 Hz, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.74 (dd, 1H, H-3'); 6.87–6.93 (m, 2H, *m*-NHC_6H_4); 7.35–7.70 (m, 10H, 2 Ph); 7.44–7.49 (m, 2H, *o*-NHC_6H_4); 7.77 (t, 1H, $^3J_{2,3}$ 7.9 Hz, H-2). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.3 [*C*$(CH_3)_3$]; 25.5, 27.5 [C(*C*$H_3)_2$]; 26.8 [C(*C*$H_3)_3$]; 28.6 (C-3); 31.9 (C-4); 55.5 (OCH_3); 64.1 (C-5'); 81.9 (C-3'); 83.4 (C-1'); 84.3 (C-4'); 84.7 (C-2'); 111.1 (C-1); 114.3 (*m*-NHC_6H_4); 114.3

[*C*(CH_3)$_2$]; 114.9 (CN); 122.4 (*o*-NHC_6H_4); 129.7 (*i*-NHC_6H_4); 127.7, 129.8, 135.5 (2 *o*-, *m*-, *p*-Ph); 133.2, 133.3 (2 *i*-Ph); 157.2 (CONH); 160.7 (C-2). CI-MS**:** *m*/*z* (%) = 641 (8, $[M+H]^+$).
Anal. Calcd for $C_{37}H_{44}N_2O_6Si$ (640.84): C, 69.35; H, 6.92; N, 4.37. Found: C, 69.14; H, 6.97; N, 4.24.

(*E*)-2-Cyano-5-[3,5-*O*-(tetraisopropyldisiloxan-1,3-diyl)-1,2-dideoxy-β-D-ribofuranos-1-yl] pent-2-enamide (15). Starting from aldehyde **14** (1.04 g, 2.5 mmol) and 2-cyanoacetamide (479 mg, 5.7 mmol) Knoevenagel product **15** (628 mg, 52%) was obtained as colorless syrup according to the procedure described for compound **3**; reaction time 24 h; flash chromatography solvent B_2; $[\alpha]_D^{22}$ –25.9 (*c* 1.0, CH_2Cl_2); R_f = 0.35 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.00–1.06 [m, 28H, 4 CH(CH_3)$_2$]; 1.65–1.77 (m, 2H, H-4); 1.80 (dt, 1H, $^3J_{1',2'a}$ 7.8 Hz, $^3J_{2'a,3'}$ 7.8 Hz, $^2J_{2'a,2'b}$ 12.5 Hz, H-2'a); 2.05 (ddd, 1H, $^3J_{2'b,3'}$ 4.5 Hz, $^3J_{1',2'b}$ 6.6 Hz, H-2'b); 2.63 (m, 2H, H-3); 3.70 (m, 2H, H-5'a, H-4'); 4.00 (m, 1H, H-5'b); 4.07 (m, 1H, H-1'); 4.37 (dt, 1H, $^3J_{3',4'}$ 7.8 Hz, H-3'); 5.80, 6.18 (2 x br s, 2H, NH_2); 7.69 (t, 1H, $^3J_{2,3}$ 7.9 Hz, H-2). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 12.5, 12.9, 13.3, 13.5 [4 *C*H(CH_3)$_2$]; 16.9, 17.0, 17.1, 17.3 (2), 17.4, 17.5 (2) [4 CH(*C*H_3)$_2$]; 28.6 (C-3); 33.5 (C-4); 40.2 (C-2'); 63.7 (C-5'); 73.4 (C-3'); 77.2 (C-1'); 86.0 (C-4'); 109.9 (C-1); 114.9 (CN); 161.0 ($CONH_2$); 161.8 (C-2). ESI-MS **(–):***m*/*z* = 481 (100, $[M-H]^-$).
Anal. Calcd. For $C_{23}H_{42}N_2O_5Si_2$ (482.76): C, 57.22; H, 8.77; N, 5.80. Found: C, 57.23; H, 8.74; N, 5.72.

Preparation of thiophenes 5, 7, 8, and 16 – General procedure
Sulfur (50 mg, 1,6 mmol) and triethylamine (0.22 mL, 1.6 μmol) were added to a stirred solution of compounds **2**, **3**, **4** or **15** (1.0 mmol) in dry *N*,*N*-dimethylformamide (5.0 mL). After stirring for 2 h at r.t. aq sat NaCl (75 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic phases were washed with water (2 x 75 mL), dried and concentrated. The residue was purified by flash chromatography.

2-Amino-5-[(5-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)methyl]thiophene-3-carbonitrile (5). Flash chromatography solvent B_4; (439 mg, 80%) yellow syrup; $[\alpha]_D^{21}$ –20.1 (*c* 1.0, CH_2Cl_2); R_f = 0.42 (solvent B_4). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.07 [s, 9H, C(CH_3)$_3$]; 1.34, 1.53 [2 s, 6H, C(CH_3)$_2$]; 2.85 (dd, 1H, $^3J_{1''a,1'}$ 7.3 Hz, $^2J_{1''a,\ 1''b}$ 15.3 Hz, H-1''a); 2.97 (dd, 1H, $^3J_{1''b,1'}$ 4.6 Hz, H-1''b); 3.81 (m, 2H, H-5'); 4.02 (dt, 1H, H-1'); 4.08 ('q', 1H, $^3J_{3',4'}$ 3.6 Hz, $^3J_{4',5'}$ 3.6 Hz, H-4'); 4.36 (dd, 1H, $^3J_{2',3'}$ 6.7 Hz, $^3J_{1',2'}$ 5.0 Hz, H-2'); 4.70 (dd, 1H, H-3'); 6.45 (s, 1H, H-4); 7.34–7.71 (m, 10H, 2 Ph). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.3 [*C*(CH_3)$_3$]; 25.5, 27.5 [C(*C*H_3)$_2$]; 26.8 [C(*C*H_3)$_3$]; 33.7 (C-1''); 64.1 (C-5'); 81.8 (C-3'); 83.7 (C-1'); 84.1 (C-4'); 84.6 (C-2'); 87.3 (C-3); 114.3 [*C*(CH_3)$_2$]; 115.6 (CN); 123.3 (C-4); 124.9 (C-5); 127.8, 129.8, 135.6 (2 *o*-, *m*-, *p*-Ph); 133.1, 133.2 (2 *i*-Ph); 161.7 (C-2). EI-MS: *m*/*z* (%) = 548 (3, $[M]^+$). Anal. Calcd for $C_{30}H_{36}N_2O_4SSi$ (548.77): C, 65.66; H, 6.61; N, 5.10; S, 5.84. Found: C, 65.45; H, 6.92; N, 4.94; S, 5.68.

2-Amino-5-[(5-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)methyl]thiophene-3-carboxamide (7). Flash chromatography solvent B_1; (453 mg, 80%)

yellow crystals; m.p. 88–90 °C (ethyl acetate – *n*-heptane); $[\alpha]_D^{21}$ –13.6 (*c* 1.0, $CHCl_3$); R_f = 0.14 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.06 [s, 9H, $C(CH_3)_3$]; 1.34, 1.53 [2 s, 6H, $C(CH_3)_2$]; 2.81–3.02 (m, 2H, H-1''); 3.81 (m, 2H, H-5'); 4.04–4.10 (m, 2H, H-1', H-4'); 4.38 (dd, 1H, $^3J_{1',2'}$ 5.0 Hz, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.68 (dd, 1H, $^3J_{3',4'}$ 3.7 Hz, H-3'); 5.55 (br, NH_2); 6.41 (s, 1H, H-4); 7.33–7.72 (m, 10H, 2 Ph); one NH_2 signal not detected. ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.3 [*C*$(CH_3)_3$]; 25.6, 27.4 [C(*C*$H_3)_2$]; 26.9 [C(*C*$H_3)_3$]; 33.8 (C-1''); 64.2 (C-5'); 81.8 (C-3'); 83.7 (C-1'); 84.3 (C-4'); 84.6 (C-2'); 106.6 (C-3); 114.2 [*C*$(CH_3)_2$]; 121.3 (C-4); 121.7 (C-5); 127.8, 129.7, 129.7, 135.7 (2 *o*-, *m*-, *p*-Ph); 133.1, 133.3 (2 *i*-Ph); 161.7, 167.7 (C-2, C=O). $C_{30}H_{38}N_2O_5SSi$ (566.78); HRMS (EI): m/z calculated for $[M^+]$ = 566.22679, found 566.22652.

2-Amino-5-[(5-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)methyl]-*N*-(4-methoxyphenyl)thiophene-3-carboxamide (8). Flash chromatography solvent B_2; (511 mg, 76%) yellow foam; $[\alpha]_D^{23}$ –8.9 (*c* 1.0, CH_2Cl_2); R_f = 0.38 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.08 [s, 9H, $C(CH_3)_3$]; 1.36, 1.55 [2 s, 6H, $C(CH_3)_2$]; 2.89 (dd, 1H, $^3J_{1''a,1'}$ 7.2 Hz, $^2J_{1''a,\ 1''b}$ 15.5 Hz, H-1''a); 2.99 (dd, 1H, $^3J_{1''b,1'}$ 5.0 Hz, H-1''b); 3.80 (s, 3H, OCH_3); 3.83 (m, 2H, H-5'); 4.07–4.16 (m, 2H, H-1', H-4'); 4.42 (dd, 1H, $^3J_{1',2'}$ 4.8 Hz, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.72 (dd, 1H, $^3J_{3',4'}$ 3.7, H-3'); 6.53 (s, 1H, H-4); 6.86 (m, 2H, *m*-NHC_6H_4); 7.18 (br s, NH_2); 7.35 (m, 2H, *o*-NHC_6H_4); 7.35–7.70 (m, 10H, 2 Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.3 [*C*$(CH_3)_3$]; 25.6, 27.5 [C(*C*$H_3)_2$]; 26.9 [C(*C*$H_3)_3$]; 33.9 (C-1''); 55.5 (OCH_3); 64.2 (C-5'); 81.8 (C-3'); 83.8 (C-1'); 84.3 (C-4'); 84.6 (C-2'); 108.1 (C-3); 114.1 (*m*-NHC_6H_4); 114.2 [*C*$(CH_3)_2$]; 122.4 (*o*-NHC_6H_4); 127.7, 127.8, 129.7, 129.8, 135.6 (2) (2 *o*-, *m*-, *p*-Ph); 130.8 (*i*-NHC_6H_4); 133.2, 133.3 (2 *i*-Ph); 156.3 (C=O); 160.9, 163.9 (C-2, *p*-NHC_6H_4). $C_{37}H_{44}N_2O_6SSi$ (672.91); HRMS (EI): m/z calculated for $[M^+]$ = 672.26814, found 672.26830.

2-Amino-5-[[3,5-*O*-(tetraisopropyldisiloxan-1,3-diyl)-1,2-dideoxy-β-D-ribofuranos-1-yl]methyl]thiophene-3-carboxamide (16). Flash chromatography solvent B_2; (398 mg, 73%) yellow syrup; $[\alpha]_D^{24}$ –25.8 (*c* 1.0, CH_2Cl_2); R_f = 0.20 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.00–1.08 [m, 28H, 4 $CH(CH_3)_2$]; 1.87 (dt, 1H, $^3J_{1',2'a}$ 7.9 Hz, $^3J_{2'a,3'}$ 7.9 Hz, $^2J_{2'a,2'b}$ 12.9 Hz, H-2'a); 2.02 (ddd, 1H, $^3J_{2'b,3'}$ 4.4 Hz, $^3J_{1',2'b}$ 6.6 Hz, H-2'b); 2.80 (m, 2H, H-1''); 3.70–3.79 (m, 2H, H-5'a, H-4'); 4.04 (m, 1H, H-5'b); 4.23 (m, 1H, H-1'); 4.33 (dt, 1H, $^3J_{3',4'}$ 7.9 Hz, H-3'); 5.37 (br s, 2H, NH_2); 6.06 (br s, 2H, NH_2); 6.42 (s, 1H, H-4). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 12.5, 13.0, 13.3, 13.4 [4 *C*$H(CH_3)_2$]; 16.9, 17.0, 17.1, 17.2, 17.3, 17.4, 17.5, 17.6 [4 $CH(CH_3)_2$]; 35.4 (C-1''); 39.5 (C-2'); 64.0 (C-5'); 73.8 (C-3'); 77.3 (C-1'); 86.2 (C-4'); 107.1 (C-3); 121.4 (C-4); 121.5 (C-5); 161.4, 167.6 (C-2, C=O). ESI-MS **(–):***m*/*z* = 513 (100, $[M–H]^-$). Anal. Calcd for $C_{23}H_{42}N_2O_5SSi_2$ (514.83): C, 53.66; H, 8.22; N, 5.44; S, 6.23. Found: C, 53.38; H, 8.41; N 5.21; S; 5.94.

4-Amino-6-[(5-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)methyl]thieno[2,3-*d*]pyrimidine (6)

A mixture of compound **5** (165 mg, 0.3 mmol) and triethylorthoformiate (3.0 mL, 18 mmol) was heated under reflux for 2 h. The reaction mixture was concentrated and the obtained syrup was dissolved in a solution of ethanol–ammonia (1:1, 6.0 mL). After heating under reflux for 2 h the

mixture was allowed to attain r.t. and then concentrated. Purification by flash chromatography solvent B_2 afforded compound **6** (128 mg, 74%) as a colorless foam, $[\alpha]_D^{21}$ −15.5 (*c* 1.0, $CHCl_3$); R_f = 0.18 (solvent B_2).

^{1}H NMR (250 MHz, $CDCl_3$) δ 1.07 [s, 9H, $C(CH_3)_3$]; 1.35, 1.54 [2 s, 6H, $C(CH_3)_2$]; 3.12 (dd, 1H, $^3J_{1',1''a}$ 7.9 Hz, $^2J_{1''a,1''b}$ 15.3 Hz, H-1''a); 3.23 (dd, 1H, $^3J_{1',1''b}$ 4.8 Hz, H-1''b); 3.82 (m, 2H, H-5'); 4.13 (q, 1H, $^3J_{3',4'}$ 3.6 Hz, $^3J_{4',5'}$ 3.6 Hz, H-4'); 4.22 (dt, 1H, $^3J_{1',2'}$ 4.8 Hz, H-1'); 4.44 (dd, 1H, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.74 (dd, 1H, H-3'); 5.50 (br s, NH_2); 6.88 (s, 1H, H-5); 7.33–7.72 (m, 10H, 2 Ph); 8.40 (br s, 1H, H-2). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.2 [*C*$(CH_3)_3$]; 25.5, 27.5 [C(*C*$H_3)_2$]; 26.8 [C(*C*$H_3)_3$]; 34.9 (C-1''); 64.2 (C-5'); 81.9 (C-3') ; 84.1 (C-1') ; 84.2 (C-4') ; 84.7 (C-2'); 114.3 [*C*$(CH_3)_2$]; 115.7 (C-5); 115.7 (C-4a); 127.7, 127.8, 129.8, 129.9, 135.6 (2) (2 *o*-, *m*-, *p*-Ph); 133.1, 133.2 (2 *i*-Ph); 138.8 (C-6); 152.7 (C-2); 156.7 (C-7a); 167.4 (C-4).

EI-MS**:** *m*/*z* (%) = 576 (3, $[M+H]^+$). Anal. Calcd for $C_{31}H_{37}N_3O_4SSi$ (575.79): C, 64.66; H, 6.48; N, 7.30; S, 5.57. Found: C, 64.66; H, 6.91; N, 7.12; S, 5.71.

Preparation of thienopyrimidinones (9, 10, and 17). General procedure

Triethylorthoformiate (0.25 mL, 1.5 mmol) was added to a solution of compound **7** (283 mg, 0.5 mmol), **8** (337 mg, 0.5 mmol), or **16** (257 mg, 0.5 mmol) in dry DMF (5.25 mL) and the reaction mixture was heated under reflux for 7–10 h (monitored by TLC). After cooling to r.t. the mixture was concentrated and the residue was purified by flash chromatography.

6-[(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)methyl] thieno[2,3-*d*]pyrimidin-4(3*H*)-one (9). Reaction time 7 h; flash chromatography solvent B_1; (205 mg, 72%) light yellow solid; m.p. 71–73 °C; $[\alpha]_D^{22}$ −22.5 (*c* 0.9, $CHCl_3$); R_f = 0.13 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.07 [s, 9H, $C(CH_3)_3$]; 1.34, 1.53 [2 s, 6H, $C(CH_3)_2$]; 3.09–3.29 (m, 2H, H-1''); 3.82 (m, 2H, H-5'); 4.11–4.21 (m, 2H, H-4', H-1'); 4.44 (dd, 1H, $^3J_{1',2'}$ 5.0 Hz, $^3J_{2',3'}$ 6.6 Hz, H-2'); 4.74 (dd, 1H, $^3J_{3',4'}$ 3.5 Hz, H-3'); 7.29 (s, 1H, H-5); 7.33–7.72 (m, 10H, 2 Ph); 8.05 (br s, 1H, H-2); 12.49 (br s, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.2 [*C*$(CH_3)_3$]; 25.6, 27.5 [C(*C*$H_3)_2$]; 26.9 [C(*C*$H_3)_3$]; 34.8 (C-1''); 64.1 (C-5'); 82.0 (C-3') ; 84.0 (C-1') ; 84.2 (C-4') ; 84.7 (C-2'); 114.3 [*C*$(CH_3)_2$]; 119.6 (C-5); 124.7 (C-4a); 127.7, 127.8, 129.7, 129.8, 135.6 (2) (2 *o*-, *m*-, *p*-Ph); 133.0, 133.1 (2 *i*-Ph); 139.4 (C-6); 143.1 (C-2); 159.5 (C-7a); 165.0 (C-4).

CI-MS**:** *m*/*z* (%) = 577 (6, $[M+H]^+$). Anal Calcd for $C_{31}H_{36}N_2O_5SSi$ (576.21): C, 64.55; H, 6.29; N, 4.86; S, 5.56. Found: C, 64.28; H, 6.49; N, 4.64; S, 5.35.

6-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)methyl)-3-(4-methoxyphenyl)thieno[2,3-*d*]pyrimidin-4(3*H*)-one (10). Reaction time 7 h; flash chromatography solvent B_4; (236 mg, 69%) yellow syrup; $[\alpha]_D^{24}$ −14.4 (*c* 1.0, CH_2Cl_2); R_f = 0.42 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.08 [s, 9H, $C(CH_3)_3$]; 1.34, 1.54 [2 s, 6H, $C(CH_3)_2$]; 3.12 (dd, 1H, $^3J_{1',1''a}$ 7.5 Hz, $^2J_{1''a,1''b}$ 15.3 Hz, H-1''a); 3.22 (dd, 1H, $^3J_{1',1''b}$ 5.0 Hz, H-1''b); 3.82 (m, 2H, H-5'); 3.87 (s, 3H, OCH_3); 4.12 (q, 1H, $^3J_{3',4'}$ 3.5 Hz, $^3J_{4',5'}$ 3.5 Hz, H-4'); 4.17 (dt, 1H, $^3J_{1',2'}$ 5.0 Hz, H-1'); 4.44 (dd, 1H, $^3J_{2',3'}$ 6.6 Hz, H-2'); 4.74 (dd, 1H, H-3'); 7.03 (m, 2H, *m*-NHC_6H_4); 7.30 (m, 2H, *o*-NHC_6H_4); 7.31 (s, 1H, H-5); 7.37–7.72 (m, 10H, 2 Ph); 8.02 (s, 1H, H-2).

^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.3 [*C*$(CH_3)_3$]; 25.6, 27.5 [C(*C*$H_3)_2$]; 26.9 [C(*C*$H_3)_3$]; 34.9 (C-1''); 55.6 (OCH_3); 64.2 (C-5'); 82.0 (C-3'); 84.0 (C-1'); 84.4 (C-4'); 84.7 (C-2'); 114.2 [*C*$(CH_3)_2$]; 114.8 (*m*-NHC_6H_4); 120.7 (C-5); 124.8 (C-4a); 127.8, 128.2, 135.6 (2 *o*-, *m*-, *p*-Ph); 129.8 (*o*-NHC_6H_4); 129.9 (*i*-NHC_6H_4); 133.0, 133.1 (2 *i*-Ph); 139.3 (C-6); 145.9 (C-2); 157.2 (C-7a); 160.0 (*p*-NHC_6H_4); 162.9 (C-4). CI-MS: *m*/*z* (%) = 683 (100, $[M+H]^+$). $C_{38}H_{42}N_2O_6SSi$ (682.90); HRMS (EI): m/z calculated for $[M^+]$ = 682.25328, found 682.25341.

6-[[3,5-*O*-(tetraisopropyldisiloxan-1,3-diyl)-1,2-dideoxy-β-D-ribofuranos-1-yl]methyl] thieno[2,3-*d*]pyrimidin-4(3*H*)-one (17). Reaction time 10 h; flash chromatography solvent B_2; (181 mg, 69%) colorless crystals; m.p. 150–152 °C (ethyl acetate – *n*-heptane); $[\alpha]_D^{24}$ −17.0 (*c* 1.0, CH_2Cl_2); R_f = 0.20 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.98–1.05 [m, 28H, 4 $CH(CH_3)_2$]; 1.88 (dt, 1H, $^3J_{1',2'a}$ 7.9 Hz, $^3J_{2'a,3'}$ 7.9 Hz, $^2J_{2'a,2'b}$ 13.0 Hz, H-2'a); 2.05 (ddd, 1H, $^3J_{2'b,3'}$ 4.5 Hz, $^3J_{1',2'b}$ 6.6 Hz, H-2'b); 3.07 (m, 2H, H-1''); 3.69–3.81 (m, 2H, H-5'a, H-4'); 4.05 (m, 1H, H-5'b); 4.34 (m, 2H, H-1', H-3'); 7.22 (s, 1H, H-5); 8.03 (s, 1H, H-2); 12.77 (br s, 1H, NH).
^{13}C NMR (62.9 MHz, $CDCl_3$) δ 12.5, 12.9, 13.3, 13.4 [4 *C*$H(CH_3)_2$]; 16.9, 17.0, 17.1, 17.2, 17.3, 17.4, 17.5, 17.6 [4 CH(*C*$H_3)_2$]; 36.3 (C-1''); 39.6 (C-2'); 63.9 (C-5'); 73.7 (C-3'); 76.8 (C-1'); 86.4 (C-4'); 119.6 (C-5); 124.6 (C-4a); 139.3 (C-6); 143.1 (C-2); 159.9 (C-7a); 165.3 (C-4).
Anal. Calcd for $C_{24}H_{40}N_2O_5SSi_2$ (524.82): C, 54.92; H, 7.68; N, 5.44; S, 6.11. Found: C, 54.97, H, 7.82; N, 5.26, S; 5.83.

Deprotection of compounds (6) and (9)

90% Trifluoroacetic acid (25 mL) was added to a solution of compound **6** (576 mg, 1.0 mmol) or compound **9** (576 mg, 1.0 mmol) in CH_2Cl_2 (10 mL). After stirring at r.t. (monitored by TLC), the reaction mixture was concentrated. Traces of acid were removed by evaporation with repeated addition of toluene. The residue was then subjected to flash chromatography.

4-Amino-6-[(1-deoxy-β-D-ribofuranos-1-yl)methyl]thieno[2,3-*d*]pyrimidine (11)

Flash chromatography solvent C_2; (268 mg, 90%) colorless foam; $[\alpha]_D^{21}$ –7.8 (*c* 1.0, MeOH); R_f = 0.14 (solvent C_2). ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.92 (dd, 1H, $^3J_{1''a,1'}$ 7.8 Hz, $^2J_{1''a,\ 1''b}$ 15.2 Hz, H-1''a); 3.13 (dd, 1H, $^3J_{1''b,1'}$ 3.5 Hz, H-1''b); 3.39 (m, 2H, H-5'); 3.60 (q, 1H, $^3J_{1',2'}$ 6.2 Hz, $^3J_{2',3'}$ 6.2 Hz, $^3J_{2',OH}$ 6.2 Hz, H-2'); 3.66 (q, 1H, $^3J_{3',4'}$ 4.5 Hz, $^3J_{4',5'}$ 4.5 Hz, H-4'); 3.73 (m, 1H, H-3'); 3.83 (m, 1H, H-1'); 4.65 (t, 1H, $^3J_{5',OH}$ 5.6 Hz, OH-5'); 4.81 (d, 1H, $^3J_{3',OH}$ 5.1 Hz, OH-3'); 4.88 (d, 1H, OH-2'); 7.29 (s, 1H, H-5); 7.34 (br s, NH_2); 8.18 (s, 1H, H-2). ^{13}C NMR (75.5 MHz, DMSO-D_6) δ 34.3 (C-1''); 62.0 (C-5'); 71.1 (C-3'); 73.8 (C-2'); 81.6 (C-1'); 85.0 (C-4'); 115.7 (C-4a); 117.6 (C-5); 136.9 (C-6); 153.3 (C-2); 157.7 (C-7a); 165.9 (C-4). EI-MS: *m*/*z* (%) = 297 (15, $[M]^+$). Anal. Calcd for $C_{12}H_{15}N_3O_4S$ (297.33): C, 48.47; H, 5.08; N, 14.13; S, 10.78. Found: C, 48.30; H, 4.94; N, 14.23; S, 10.49.

6-[(1-Deoxy-β-D-ribofuranos-1-yl)methyl]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (13). Flash chromatography solvent C_2; (268 mg, 90%) colorless foam; $[\alpha]_D^{21}$ –7.5 (*c* 1.1, MeOH); R_f = 0.20 (solvent C_2). ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.94 (dd, 1H, $^3J_{1''a,1'}$ 7.6 Hz, $^2J_{1''a,1''b}$ 15.3 Hz, H-

1"a); 3.12 (dd, 1H, $^3J_{1"b,1'}$ 3.8 Hz, H-1"b); 3.38–3.42 (m, 2H, H-5'); 3.59 (q, 1H, $^3J_{1',2'}$ 6.1 Hz, $^3J_{2',3'}$ 6.1 Hz, $^3J_{2',OH}$ 6.1 Hz, H-2'); 3.66 (q, 1H, $^3J_{4',3'}$ 4.4 Hz, $^3J_{4',5'}$ 4.4 Hz, H-4'); 3.71 (m, 1H, H-3'); 3.81 (ddd, 1H, H-1'); 4.66 (t, 1H, $^3J_{5',OH}$ 5.6 Hz, OH-5'); 4.79 (d, 1H, $^3J_{3',OH}$ 5.1 Hz, OH-3'); 4.87 (d, 1H, OH-2'); 7.15 (s, 1H, H-5); 8.04 (s, 1H, H-2); 12.40 (br s, NH). ^{13}C NMR (75.5 MHz, DMSO-D_6) δ 33.8 (C-1"); 62.1 (C-5'); 71.2 (C-3'); 73.7 (C-2'); 81.6 (C-1'); 84.9 (C-4'); 119.7 (C-5); 124.5 (C-4a); 138.5 (C-6); 145.0 (C-2); 157.1 (C-7a); 163.5 (C-4). CI-MS**:** *m*/*z* (%) = 299 (6, $[M+H]^+$). Anal. Calcd for $C_{12}H_{14}N_2O_5S$ (298.31): C, 48.31; H, 4.73; N, 9.39; S, 10.75. Found: C, 48.52; H, 4.64; N, 9.12; S, 10.71.

2-Amino-5-[(1-desoxy-β-D-ribofuranos-1-yl)methyl]thiophene-3-carbonitrile (12)

A solution of tetrabutylammonium fluoride (TBAF) in 1,4-dioxane (1.0 M, 0.8 mL) was added dropwise to a solution of compound **5** (283 mg, 0.5 mmol) in 1,4-dioxane (7 mL). The reaction mixture was stirred at r.t. for 5 h, and then concentrated. The residue was dissolved in CH_2Cl_2 (4 mL) and a solution 90% trifluoroacetic acid (6 mL) was added. After stirring at r.t. (monitored by TLC), the reaction mixture was concentrated. Traces of acid were removed by evaporation with repeated addition of toluene. Purification by flash chromatography (solvent C_4) afforded compound **12** (118 mg; 87%) as yellow foam; $[\alpha]_D^{25}$ –32.9 (*c* 0.5, MeOH); R_f = 0.31 (solvent D). ^{1}H NMR (300 MHz, CD_3OD) δ 2.91–3.16 (m, 2H, H-1"); 3.35–3.68 (m, 2H, H-5'); 3.72–3.75, 3.81–3.87, 3.92–3.97 (3 m, 4H) (H-1',2',3',4'); 7.19 (s, 1H, H-4). ^{13}C NMR (75.5 MHz, CD_3OD) δ 34.2 (C-1"); 63.7 (C-5'); 72.8 (C-3'); 75.3 (C-2'); 83.8 (C-1'); 86.2 (C-4'); 106.2 (C-3); 118.0 (CN); 122.6 (C-4); 122.7 (C-5); 169.3 (C-2). $C_{11}H_{14}N_2O_4S$ (270.30); HRMS (CI): m/z calculated for $[M+H]^+$ = 271.07470, found 271.07486.

6-[(1,2-Dideoxy-β-D-ribofuranos-1-yl)methyl]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (18). A solution of TBAF in 1,4-dioxane (1.0 M, 1.5 mL) was added dropwise to a solution of compound **17** (525 mg, 1.0 mmol) in 1,4-dioxane (15 mL). The reaction mixture was stirred at r.t. for 2 h, and then concentrated. Flash chromatography (solvent C_1) of the residue provided compound **18** (220 mg, 78%) as colorless solid; m.p. 204 °C; $[\alpha]_D^{23}$ +5.6 (*c* 1.0, DMSO); R_f = 0.22 (solvent C_3). ^{1}H NMR (250 MHz, DMSO-d_6) δ 1.62 (ddd, 1H, $^3J_{1',2'a}$ 9.7 Hz, $^3J_{2'a,3'}$ 5.9 Hz, $^2J_{2'a,2'b}$ 12.7 Hz, H-2'a); 1.77 (ddd, 1H, $^3J_{2'b,3'}$ 2.1 Hz, $^3J_{1',2'b}$ 5.6 Hz, H-2'b); 3.02 (m, 2H, H-1"); 3.26 (dd, 1H, $^3J_{4',5'a}$ 6.0 Hz, $^2J_{5'a,5'b}$ 11.4 Hz, H-5'a); 3.36 (dd, 1H, $^3J_{4',5'b}$ 4.6 Hz, H-5'b); 3.64 (ddd, 1H, $^3J_{3',4'}$ 2.6 Hz, H-4'); 4.02 (m, 1H, H-3'); 4.22 (m, 1H, H-1'); 4.63 (br s, 1H, OH-5'); 4.90 (br s, 1H, OH-3'); 7.15 (s, 1H, H-5); 8.04 (s, 1H, H-2); 12.38 (br s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 35.7 (C-1"); 39.6 (C-2'); 62.4 (C-5'); 72.0 (C-3'); 77.4 (C-1'); 87.6 (C-4'); 119.7 (C-5); 124.5 (C-4a); 138.5 (C-6); 145.1 (C-2); 157.1 (C-7a); 163.4 (C-4). ESI-MS(+)**:** *m*/*z* = 283 $[M+H]^+$. Anal. Calcd for $C_{12}H_{13}N_2O_4S$ (282.32): C, 51.05; H 5.00; N, 9.92; S, 11.36. Found: C, 50.94; H, 4.95; N, 9.65; S, 11.16.

Preparation of pyrimidines (21–26, 31 and 32). General procedure

H_2O (75 μL) was added to a solution of compound **19** (493 mg, 1.0 mmol); **20** (569 mg, 1.0 mmol), **29** (455 mg, 1.0 mmol), or **30** (517 mg, 1.0 mmol) in ethyl acetate (7.5 mL). Sodium

carbonate (254 mg, 2.4 mmol) and acetamidinium hydrochloride (132 mg, 1.4 mmol), benzamidinium hydrochloride (219 mg, 1.4 mmol) or *S*-methylisothiouronium sulphate (264 mg, 1.4 mmol) was added to the solution above and the reaction mixture was heated under reflux (monitored by TLC). The reaction mixture was cooled, diluted with ethyl acetate (50 mL) and washed with water (2 x 50 mL), dried, and concentrated. The residue was then purified by flash chromatography.

4-[2-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)ethyl]-2-methylpyrimidine (21). Reaction time 4 h; flash chromatography solvent B_2; (426 mg, 80%) colorless solid; m.p. 90–92 °C (ethyl acetate – *n*-heptane); $[\alpha]_D^{23}$ −10.7 (*c* 1.0, $CHCl_3$); R_f = 0.21 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.04 [s, 9H, $C(CH_3)_3$]; 1.34, 1.51 [2 s, 6H, $C(CH_3)_2$]; 1.90–2.13 (m, 2H, H-2"); 2.69 (s, 3H, 2-CH_3); 2.81–2.92 (m, 2H, H-1"); 3.78 (m, 2H, H-5'); 3.88 (dt, 1H, $^3J_{1',2'}$ 5.4 Hz, $^3J_{1',2''}$ 7.8 Hz, H-1'); 4.04 (q, 1H, $^3J_{3',4'}$ 3.7 Hz, $^3J_{4',5'}$ 3.7 Hz, H-4'); 4.36 (dd, 1H, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.73 (dd, 1H, H-3'); 6.94 (d, 1H, $^3J_{5,6}$ 5.0 Hz, H-5); 7.35–7.47, 7.63–7.71 (2 m, 10H, 2 Ph); 8.46 (d, 1H, H-6). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.3 [*C*$(CH_3)_3$]; 25.5, 27.5 [C(*C*$H_3)_2$]; 25.8 (2-CH_3); 26.8 [C(*C*$H_3)_3$]; 32.7, 33.9 (C-1", C-2"); 64.2 (C-5'); 81.9 (C-3'), 83.5 (C-1'); 84.3 (C-4'); 84.4 (C-2'); 114.1 [*C*$(CH_3)_2$]; 117.4 (C-5); 127.6, 127.7, 129.7, 129.8, 135.6, 135.7 (2 *o*-, *m*-, *p*-Ph); 133.2, 133.3 (2 *i*-Ph); 156.3 (C-6); 167.7 (C-2); 170.2 (C-4). $C_{31}H_{40}N_2O_4Si$ (532.74); HRMS (EI): m/z calculated for $[M]^+$ = 532.27519; found 532.27465.

4-[2-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)ethyl]-2-methyl-6-phenylpyrimidine (22). Reaction time 24 h; flash chromatography solvent B_5; (365 mg, 60%) colorless solid; m.p. 96–98 °C (ethyl acetate – *n*-heptane); $[\alpha]_D^{23}$ −5.4 (*c* 1.0, $CHCl_3$); R_f = 0.39 (solvent B_4). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.05 [s, 9H, $C(CH_3)_3$]; 1.34, 1.50 [2 s, 6H, $C(CH_3)_2$]; 1.99–2.13 (m, 2H, H-2"); 2.76 (s, 3H, 2-CH_3); 2.88–2.96 (m, 2H, H-1"); 3.80 (m, 2H, H-5'); 3.93 (dt, 1H, $^3J_{1',2'}$ 5.4 Hz, $^3J_{1',2''}$ 7.5 Hz, H-1'); 4.05 (q, 1H, $^3J_{3',4'}$ 3.7 Hz, $^3J_{4',5'}$ 3.7 Hz, H-4'); 4.39 (dd, 1H, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.74 (dd, 1H H-3'); 7.33 (s, 1H, H-5); 7.36–7.48, 7.67–7.72, 7.96–8.01 (3 m, 15H, 3 Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.3 [*C*$(CH_3)_3$]; 25.5, 27.5 [C(*C*$H_3)_2$]; 26.2 (2-CH_3); 26.8 [C(*C*$H_3)_3$]; 33.0, 34.2 (C-1", C-2"); 64.2 (C-5'); 81.9 (C-3'); 83.6 (C-1'); 84.3 (C-4'); 84.9 (C-2'); 113.0 (C-5); 114.0 [*C*$(CH_3)_2$]; 127.3, 127.7, 127.8, 128.8, 129.7, 129.8, 130.5, 135.6 (3 *o*-, *m*-, *p*-Ph); 133.2, 133.3,137.3 (3 *i*-Ph); 164.0 (C-6); 168.1 (C-2); 170.2 (C-4). CI-MS: *m*/*z* (%) =609 (100, $[M+H]^+$). Anal. Calcd for $C_{37}H_{44}N_2O_4Si$ (608.84): C, 72.99; H, 7.28; N, 4.60. Found: C, 72.63; H, 7.26; N, 4.33.

4-[2-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)ethyl]-2-phenylpyrimidine (23). Reaction time 2.5 h; flash chromatography solvent B_5; (559 mg, 94%) colorless foam; $[\alpha]_D^{25}$ −12.5 (*c* 1.0, $CHCl_3$); R_f = 0.30 (solvent B_5). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.06 [s, 9H, $C(CH_3)_3$]; 1.36, 1.53 [2 s, 6H, $C(CH_3)_2$]; 2.08–2.28 (m, 2H, H-2"); 2.96 (m, 2H, H-1"); 3.81 (m, 2H, H-5'); 3.97 (dt, 1H, $^3J_{1',2'}$ 5.3 Hz, $^3J_{1',2''}$ 8.0 Hz, H-1'); 4.08 (q, 1H, $^3J_{3',4'}$ 3.6 Hz, $^3J_{4',5'}$ 3.6 Hz, H-4'); 4.40 (dd, 1H, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.76 (dd, 1H, H-3'); 7.01 (d, 1H, $^3J_{5,6}$ 5.2 Hz, H-5); 7.34–7.41, 7.44–7.48, 7.67–7.72, 8.43–8.47 (4 m, 15H, 3 Ph); 8.64 (d, 1H, H-6).
^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.3 [*C*$(CH_3)_3$]; 25.6, 27.5 [C(*C*$H_3)_2$]; 26.8 [C(*C*$H_3)_3$]; 32.3, 34.0 (C-1", C-2"); 64.2 (C-5'); 81.9 (C-3'); 83.7 (C-1'); 84.3 (C-4'); 84.9 (C-2'); 114.1 [*C*$(CH_3)_2$];

118.2 (C-5); 127.6, 127.7, 128.2, 128.5, 129.7, 129.8, 130.6, 135.6, 135.7 (3 *o*-, *m*-, *p*-Ph); 133.2, 133.3, 137.7 (3 *i*-Ph); 156.8 (C-6); 164.2 (C-2); 170.0 (C-4). CI-MS: *m*/*z* (%) = 595 (100, $[M]^+$). Anal. Calcd for $C_{36}H_{42}N_2O_4Si$ (594.82): C, 72.69; H, 7.12; N, 4.71. Found: C, 72.39; H, 7.31; N, 4.45.

4-[2-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)ethyl]-2,6-diphenylpyrimidine (24). Reaction time 10 h; flash chromatography solvent B_6; (537 mg, 80%) colorless foam; $[\alpha]_D^{25}$ −13.7 (*c* 0.5, $CHCl_3$); R_f = 0.44 (solvent B_5). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.07 [s, 9H, $C(CH_3)_3$]; 1.37, 1.53 [2 s, 6H, $C(CH_3)_2$]; 2.11–2.32 (m, 2H, H-2''); 3.03 (m, 2H, H-1''); 3.83 (m, 2H, H-5'); 4.02 (dt, 1H, $^3J_{1',2'}$ 5.4 Hz, $^3J_{1',2''}$ 7.8 Hz, H-1'); 4.09 (q, 1H, $^3J_{3',4'}$ 3.7 Hz, $^3J_{4',5'}$ 3.7 Hz, H-4'); 4.44 (dd, 1H, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.78 (dd, 1H, H-3'); 7.36–7.41, 7.47–7.52, 7.69–7.75, 8.15–8.19, 8.59–8.63 (5 m, 20H, 4 Ph); 7.44 (s, 1H, H-5). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.3 [$C(CH_3)_3$]; 25.6, 27.5 [$C(CH_3)_2$]; 26.8 [$C(CH_3)_3$]; 32.7, 34.2 (C-1'',C-2''); 64.2 (C-5'); 81.9 (C-3'); 83.8 (C-1'); 84.3 (C-4'); 85.0 (C-2'); 113.6 (C-5); 114.1 [$C(CH_3)_2$]; 127.2, 127.7, 127.8, 128.3, 128.4, 128.9, 129.7, 129.8, 130.5, 130.6 135.6, 135.7 (4 *o*-, *m*-, *p*-Ph); 133.2, 133.3, 137.3, 138.1 (4 *i*-Ph); 163.8, 164.2 (C-2, C-6); 170.4 (C-4). CI-MS: *m*/*z* (%) = 671 (100, $[M]^+$). Anal. Calcd for $C_{42}H_{46}N_2O_4Si$ (670.91): C, 75.19; H, 6.91; N, 4.18. Found: C, 75.25; H, 7.11; N, 3.97.

4-[2-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)ethyl]-2-methylthiopyrimidine (25). Reaction time 3 h; flash chromatography solvent B_6; (554 mg, 98%) colorless syrup; $[\alpha]_D^{22}$ −10.5 (*c* 1.0, CH_2Cl_2), R_f = 0.45 (B_4). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.05 [s, 9H, $C(CH_3)_3$]; 1.34, 1.51 [2 s, 6H, $C(CH_3)_2$]; 1.93–2.14 (m, 2H, H-1''); 2.53 (s, 3H, SCH_3); 2.78–2.86 (m, 2H, H-2''); 3.78 (m, 2H, H-5'); 3.88 (d't', 1H, $^3J_{1',2'}$ 5.4 Hz, $^3J_{1',2''}$ 8.0 Hz, H-1'); 4.04 (q, 1H, $^3J_{3',4'}$ 3.7 Hz, $^3J_{4',5'}$ 3.7 Hz, H-4'); 4.36 (dd, 1H, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.72 (dd, 1H, H-3'); 6.76 (d, 1H, $^3J_{5,6}$ 5.0 Hz, H-5); 7.33–7.42, 7.66–7.71 (2 m, 10H, 2 Ph); 8.34 (d, 1H, H-6). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.0 (SCH_3); 19.3 [$C(CH_3)_3$]; 25.4, 27.5 [$C(CH_3)_2$]; 26.8 [$C(CH_3)_3$]; 32.2, 33.7 (C-1'', C-2''); 64.2 (C-5'); 81.9 (C-3'); 83.5 (C-1'); 84.2 (C-4'); 84.9 (C-2'); 114.1 [$C(CH_3)_2$]; 115.4 (C-5); 127.6, 127.7, 129.7, 129.8, 135.6, 135.7 (2 *o*-, *m*-, *p*-Ph); 133.2, 133.3 (2 *i*-Ph); 156.6 (C-6); 170.2 (C-4); 172.3 (C-2). $C_{31}H_{40}N_2O_4SSi$ (564.81); HRMS (CI-MS): m/z calculated for $[M+H]^+$ = 565.25344; found 565.25508.

4-[2-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)ethyl]-2-methylthio-6-phenylpyrimidine (26). Reaction time 24 h; flash chromatography solvent B_7; (513 mg, 80%) colorless syrup; $[\alpha]_D^{22}$ −8.1 (*c* 1.0, CH_2Cl_2); R_f = 0.51 (solvent B_4). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.05 [s, 9H, $C(CH_3)_3$]; 1.34, 1.51 [2 s, 6H, $C(CH_3)_2$]; 1.98–2.18 (m, 2H, H-2''); 2.62 (s, 3H, SCH_3); 2.82–2.97 (m, 2H, H-1''); 3.80 (m, 2H, H-5'); 3.94 (dt, 1H, $^3J_{1',2'}$ 5.2 Hz, $^3J_{1',2''}$ 7.6 Hz, H-1'); 4.05 (q, 1H, $^3J_{3',4'}$ 3.8 Hz, $^3J_{4',5'}$ 3.8 Hz, H-4'); 4.38 (dd, 1H, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.74 (dd, 1H, H-3'); 7.20 (s, 1H, H-5); 7.33–7.49, 7.67–7.72, 7.99–8.04 (3 m, 15H, 3 Ph). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.1 (SCH_3); 19.3 [$C(CH_3)_3$]; 25.5, 27.5 [$C(CH_3)_2$]; 26.8 [$C(CH_3)_3$]; 32.6, 33.7 (C-1'', C-2''); 64.2 (C-5'); 81.8 (C-3'); 83.6 (C-1'); 84.3 (C-4'); 84.9 (C-2'); 111.1 (C-5); 114.1 [$C(CH_3)_2$]; 127.2, 127.6, 127.7, 128.8, 129.7, 129.8, 131.0, 135.6 (3 *o*-, *m*-, *p*-Ph); 133.2, 133.3, 136.5 (3 *i*-Ph); 164.0 (C-6); 170.3 (C-4); 172.0 (C-2). CI-MS: m/z (%) = 641 (100,$[M]^+$).

Anal. Calcd for $C_{37}H_{44}N_2O_4SSi$ (640.91): C, 69.34; H, 6.92; N, 4.37; S, 5.00. Found: C, 69.63; H, 7.16; N, 4.12 ; S, 4.89.

4-[2-[3,5-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-1,2-dideoxy-β-D-ribofuranos-1-yl]ethyl]-2-methylthiopyrimidine (31). Reaction time 3 h; flash chromatography solvent B_5; (503 mg, 98%) colorless syrup; $[\alpha]_D^{22}$ –25.7 (*c* 1.0, CH_2Cl_2); R_f = 0.50 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.99–1.05 [m, 28H, 4 $CH(CH_3)_2$]; 1.75–2.14 (m, 4H, H-2", H-2'); 2.53 (s, 3H, SCH_3); 2.75 (m, 2H, H-1"); 3.66–3.76 (m, 2H, H-5'a, H-4'); 3.92–4.02 (m, 1H, H-5'b); 4.03–4.12 (m, 1H, H-1'); 4.36 (dt, 1H, $^3J_{2'b,3'}$ 4.5 Hz, $^3J_{2'a,3'}$ 7.9 Hz, $^3J_{3',4'}$ 7.9 Hz, H-3'); 6.80 (d, 1H, $^3J_{5,6}$ 5.1 Hz, H-5); 8.35 (d, 1H, H-6). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 12.5, 12.9, 13.3, 13.4 [4 *C*H$(CH_3)_2$]; 14.0 (SCH_3); 16.9, 17.0, 17.1, 17.2, 17.3, 17.4, 17.5 (2) [4 CH(*C*$H_3)_2$]; 33.8, 33.9 (C-1",C-2"); 40.3 (C-2'); 63.8 (C-5'); 73.6 (C-3'); 76.8 (C-1'); 85.9 (C-4'); 115.4 (C-5); 156.8 (C-6); 170.4 (C-4); 172.3 (C-2). Anal. Calcd for $C_{24}H_{44}N_2O_4SSi_2$ (512.85): C, 56.21; H, 8.65; N, 5.46; S, 6.25. Found: C, 56.31; H, 8.82; N, 5.22; S, 6.01.

4-[2-[3,5-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-1,2-dideoxy-β-D-ribofuranos-1-yl]ethyl]-2-methyl-6-phenylpyrimidine (32). Reaction time 24 h; flash chromatography solvent B_7; (496 mg, 89%) colorless syrup; $[\alpha]_D^{25}$ **:** –25.1 (*c* 1.0, CH_2Cl_2); R_f = 0.31 (solvent B_7). ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.99–1.10 [m, 28H, 4 $CH(CH_3)_2$]; 1.86 (dt, 1H $^3J_{1',2'a}$ 8.0 Hz, $^3J_{2'a,3'}$ 8.0 Hz, $^2J_{2'a,2'b}$ 12.9 Hz, H-2'a); 1.92–2.03 (m, 2H, H-2"); 2.06 (ddd, 1H, $^3J_{2'b,3'}$ 4.6 Hz, $^3J_{1',2'b}$ 6.7 Hz, H-2'b); 2.75 (s, 3H, 2-CH_3); 2.86 (m, 2H, H-1"); 3.74 (m, 2H, H-5'a, H-4'); 4.03 (m, 1H, H-5'b); 4.11 (m, 1H, H-1'); 4.39 (dt, 1H, $^3J_{3',4'}$ 8.0 Hz, H-3'); 7.37 (s, 1H, H-5); 7.46–7.50, 8.02–8.06 (2 m, 5H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 12.5, 12.9, 13.4, 13.5 [4 *C*H$(CH_3)_2$]; 16.9, 17.0, 17.1, 17.2, 17.3, 17.4, 17.6 (2) [4 CH(*C*$H_3)_2$]; 26.3 (2-CH_3); 34.3, 34.8 (C-1",2"); 40.3 (C-2'); 63.8 (C-5'); 73.6 (C-3'); 76.9 (C-1'); 85.9 (C-4'); 113.0 (C-5); 127.2, 128.9, 130.5 (*o*-, *m*-, *p*-Ph); 137.3 (*i*-Ph); 164.1 (C-6); 168.0 (C-2); 170.5 (C-4).

ESI-MS (+): *m*/*z* = 557 $[M+H]^+$. Anal. Calcd for $C_{30}H_{48}N_2O_4Si_2$ (556.88): C, 64.70; H, 8.69; N, 5.03. Found: C, 64.51; H, 8.76; N, 4.88.

4-[2-(2,3-*O*-Isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)ethyl]-2-methylthiopyrimidine (27). A solution of TBAF in 1,4-dioxane (1.0 M, 1.5 mL) was added dropwise to a solution of compound **25** (565 mg, 1.0 mmol) in 1,4-dioxane (15 mL). The reaction mixture was stirred at r.t. for 4 h (monitored by TLC), and then concentrated. Flash chromatography (B_1) of the residue provided compound **27** (277 mg, 85%) as a colorless syrup; $[\alpha]_D^{23}$ –14.6 (*c* 1.0, CH_2Cl_2); R_f = 0.28 (solvent B_1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33, 1.51 [2 s, 6H, $C(CH_3)_2$]; 1.98–2.12 (m, 2H, H-2"); 2.54 (s, 3H, SCH_3); 2.72–2.89 (m, 2H, H-1"); 3.66 (ddd, 1H, $^3J_{4',5'a}$ 4.0 Hz, $^3J_{5'a,OH}$ 7.8 Hz, $^2J_{5'a,5'b}$ 11.9 Hz, H-5'a); 3.78 (ddd, 1H, $^3J_{5'b,OH}$ 3.2 Hz, $^3J_{4',5'b}$ 4.0 Hz, H-5'b); 3.90 (dt, 1H, $^3J_{1',2'}$ 5.8 Hz, $^3J_{1',2"}$ 7.0 Hz, H-1'); 3.98 (q, 1H, $^3J_{3',4'}$ 4.0 Hz, H-4'); 4.34 (dd, 1H, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.64 (dd, 1H, H-3'); 6.82 (d, 1H, $^3J_{5,6}$ 5.0 Hz, H-5); 8.37 (d, 1H, H-6); OH signal not detected. ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.1 (SCH_3); 25.4, 27.5 [$C(CH_3)_2$]; 31.8, 33.5 (C-1",C-2"); 62.7 (C-5'); 81.5 (C-3'); 83.8 (C-1'); 84.3 (C-4'); 84.8 (C-2'); 114.6 [*C*$(CH_3)_2$]; 115.5 (C-5); 156.9 (C-6); 170.1 (C-4); 172.4 (C-2). CI-MS: *m*/*z* (%) = 327 (100, $[M+H]^+$). $C_{15}H_{22}N_2O_4S$ (326.41): C, 55.19; H, 6.79; N, 8.58; S, 9.82. Found: C, 55.09, H, 7.07; N, 8.36; S, 9.58.

4-[2-(2,3-*O*-Isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)ethyl]-2-methylthiopyrimidine (28). Aq HCl (0.1 M, 2.5 mL) was added to a solution of compound **25** (565 mg, 1.0 mmol) in EtOH (8 mL), and the mixture was stirred overnight at r.t (monitored by TLC). The mixture was then neutralized by addition of solid $NaHCO_3$, and concentrated after addition of a small amount of silica gel. The residue was purified by flash chromatography (solvent C_4) to afford compound **28** (74%) as a colorless syrup; $[\alpha]_D^{23}$ –24.3 (*c* 0.5, MeOH); Rf = 0.32 (solvent C_4). ^{1}H NMR (250 MHz, DMSO-d_6) δ 1.68–2.01 (m, 2H, H-2''); 2.49 (s, 3H, SCH_3); 2.65–2.85 (m, 2H, H-1''); 3.36–3.46 (m, 2H, H-5'); 3.56 (m, 2H, H-1', H-2'); 3.62 (m, 1H, H-4'); 3.76 (m, 1H, H-3'); 4.63 (t, 1H, $^3J_{5',OH}$ 5.6 Hz, OH-5'); 4.72 (m, 2H, OH-2', OH-3'); 7.08 (d, 1H, $^3J_{5,6}$ 5.1 Hz, H-5); 8.48 (d, 1H, H-6). ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 13.4 (SCH_3); 31.7 (C-2''); 33.2 (C-1''); 62.0 (C-5'); 71.3 (C-3'); 74.4 (C-2'); 80.9 (C-1'); 84.6 (C-4'); 116.0 (C-5); 157.2 (C-6); 170.6, 170.9 (C-2,4). $C_{12}H_{19}N_2O_4S$ (286.35); HRMS (CI-MS): m/z calculated for $[M+H]^+$ = 287.10600; found 287.10513

4-[2-(1,2-Dideoxy-β-D-ribofuranos-1-yl)ethyl]-2-methylthiopyrimidine (33). Starting from compound **31** (513 mg, 1.0 mmol), compound **33** (211 mg, 78%) was obtained after a reaction time of 24 h and purification by flash chromatography (solvent C_4) as colorless a solid according to the procedure described for compound **18**; m.p. 112–114 °C; $[\alpha]_D^{23}$ –2.0 (*c* 1.0, MeOH); R_f = 0.36 (solvent C_3). ^{1}H NMR (250 MHz, DMSO-d_6) δ 1.56 (ddd, 1H, $^3J_{2'a,3'}$ 6.0 Hz, $^3J_{1',2'a}$ 9.8 Hz, $^2J_{2'a,2'b}$ 12.7 Hz, H-2'a); 1.84 (m, 2H, H-2''); 2.02 (ddd, 1H, $^3J_{2'b,3'}$ 1.6 Hz, $^3J_{1',2'b}$ 5.4 Hz, H-2'b); 2.48 (s, 3H, SCH_3); 2.72 (m, 2H, H-1''); 3.27–3.35 (m, 2H, H-5'a, H-4'); 3.59 (ddd, 1H, $^3J_{4',5'b}$ 2.6 Hz, $^3J_{5'b,OH}$ 5.3 Hz, $^2J_{5'a,5'b}$ 7.8 Hz, H-5'b); 3.97 (m, 1H, H-1'); 4.03 (m, 1H, H-3'); 7.09 (d, 1H, $^3J_{5,6}$ 5.1 Hz, H-5); 8.49 (d, 1H, H-6). ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 13.4 (SCH_3); 33.4, 33.6 (C-1'',2''); 40.2 (C-2'); 62.5 (C-5'); 72.1 (C-3'); 76.8 (C-1'); 87.3 (C-4'); 115.9 (C-5); 157.2 (C-6); 170.6, 170.9 (C-2,4). ESI-MS (+): *m*/*z*: 271 $[M+H]^+$. Anal. Calcd for $C_{12}H_{18}N_2O_3S$ (270.35): C, 53.31; H, 6.71; N, 10.36; S, 11.86. Found: C, 53.08; H, 6.50; N, 10.32; S, 11.69.

Preparation of aminotriazoles (34 and 38). General procedure

A mixture of compound **19** (246 mg, 0.5 mmol) or **29** (227 mg, 0.5 mmol) and 4*H*-1,2,4-triazol-3-amine (50 mg, 0.6 mmol) in dry EtOH (5 mL) was heated under reflux for 4 h (monitored by TLC), and concentrated. The residue was purified by flash chromatography.

(*E*)-1-(5-Amino-1*H*-1,2,4-triazol-1-yl)-5-(5-*O*-*tert*-butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)pent-1-en-3-one (34). Flash chromatography solvent A; (257 mg, 89%); yellow solid; m.p. 118–119 °C; $[\alpha]_D^{23}$ –2.6 (*c* 1.0, CH_2Cl_2); R_f = 0.25 (solvent A). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.04 [s, 9H, $C(CH_3)_3$]; 1.35, 1.52 [2 s, 6H, $C(CH_3)_2$]; 1.74–1.97 (m, 2H, H-1); 2.76 (m, 2H, H-2); 3.76 (m, 2H, H-5'); 3.82 (m, 1H, H-1'); 4.01 (q, 1H, $^3J_{3',4'}$ 3.6 Hz, $^3J_{4',5'}$ 3.6 Hz, H-4'); 4.29 (dd, 1H, $^3J_{1',2'}$ 5.5 Hz, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.70 (dd, 1H, H-3'); 5.81 (br s, 2H, NH_2); 6.74 (d, 1H, $^3J_{4,5}$ 13.3 Hz, H-4); 7.32–7.42, 7.64–7.69 (2 m, 10H, 2 Ph); 7.57 (s, 1H, H-3''); 8.06 (d, 1H, H-5). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.3 [*C*$(CH_3)_3$]; 25.5, 27.4 [C(*C*$H_3)_2$]; 26.8 [C(*C*$H_3)_3$]; 27.4 (C-1); 39.1 (C-2); 64.1 (C-5'); 82.0 (C-3'); 83.2 (C-1'); 84.2 (C-4'); 84.7 (C-2'); 113.2 (C-4); 114.5 [*C*$(CH_3)_2$]; 127.6, 127.7, 129.7, 129.8, 135.6, 135.7 (2

o-, m-, p- Ph); 132.1 (C-5); 133.2, 133.3 (2 *i*-Ph); 151.7 (C-3"); 199.6 (C-3); C-5" signal not detected. $C_{31}H_{40}N_4O_5Si$ (576.76); HRMS (CI-MS): m/z calculated for $[M+H]^+$ = 577.28462; found 577.28429.

(*E*)-1-(5-Amino-1*H*-1,2,4-triazol-1-yl)-5-[(3,5-*O*-(tetraisopropyldisiloxan-1,3-diyl)-1,2-dideoxy -β-D-ribofuranos-1-yl]pent-1-en-3-one (38). Flash chromatography solvent B_1; (152 mg, 58%) yellow solid; m.p. 170 °C; $[\alpha]_D^{25}$ –34.2 (*c* 0.8, CH_2Cl_2); R_f = 0.19 (solvent B_1).

^{1}H NMR (250 MHz, $CDCl_3$) δ 0.99–1.05 [m, 28H, 4 $CH(CH_3)_2$]; 1.72–1.87 (m, 3H, H-1, H-2'a); 2.02 (ddd, 1H, $^3J_{2'b,3'}$ 4.8 Hz, $^3J_{1',2'b}$ 6.8 Hz, $^2J_{2'a,2'b}$ 12.5 Hz, H-2'b); 2.68 (m, 2H, H-2); 3.66–3.76 (m, 2H, H-5'a, H-4'); 3.99 (m, 1H, H-5'b); 4.04 (m, 1H, H-1'); 4.35 (dt, 1H, $^3J_{2'a,3'}$ 8.0 Hz, $^3J_{3',4'}$ 8.0 Hz, H-3'); 6.11 (br s, 2H, NH_2); 6.72 (d, 1H, $^3J_{4,5}$ 13.3 Hz, H-4); 7.56 (s, 1H, H-3"); 8.05 (d, 1H, H-5). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 12.5, 12.9, 13.3, 13.4 [4 *C*H$(CH_3)_2$]; 16.9, 17.0, 17.1, 17.2, 17.3, 17.4, 17.5 (2) [4 CH(*C*$H_3)_2$]; 29.8 (C-1); 39.3 (C-2); 40.0 (C-2'); 63.5 (C-5'); 73.2 (C-3'); 76.5 (C-1'); 85.8 (C-4'); 113.0 (C-4); 132.4 (C-5); 151.6 (C-3"); 200.1 (C-3); C-5" signal not detected. ESI-MS (–): *m/z* = 523 $[M–H]^-$. Anal. Calcd for $C_{24}H_{44}N_4O_5Si_2$ (524.80): C, 54.93; H, 8.45; N, 10.68. Found: C, 54.79; H, 8.15; N, 10.72.

Preparation of triazolopyrimidines (35 and 39). General procedure

Ethanolic NaOMe (1 M, 1.4 mL) was added to a solution of compound **34** (288 mg, 0.5 mmol) or **38** (262 mg, 0.5 mmol) in dry EtOH (10 mL). After stirring at r.t. for 1 h, the reaction mixture was neutralized with IR 120 (H^+) Amberlite resin, filtered, dried, and concentrated. The residue was purified by flash chromatography (solvent B_2).

5-[2-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)ethyl]-[1,2,4]triazolo[1,5-*a*]pyrimidine (35). Yield (173 mg, 62%); colorless syrup; $[\alpha]_D^{22}$ –15.4 (*c* 1.0, CH_2Cl_2); R_f = 0.18 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.04 [s, 9H, $C(CH_3)_3$]; 1.33, 1.50 [2 s, 6H, $C(CH_3)_2$]; 2.04–2.29 (m, 2H, H-2"); 3.07 (m, 2H, H-1"); 3.79 (m, 2H, H-5'); 3.93 (dt, 1H, $^3J_{1',2'}$ 5.1 Hz, $^3J_{1',2''}$ 8.3 Hz, H-1'); 4.04 (q, 1H, $^3J_{3',4'}$ 3.8 Hz, $^3J_{4',5'}$ 3.8 Hz, H-4'); 4.38 (dd, 1H, $^3J_{2',3'}$ 6.6 Hz, H-2'); 4.72 (dd, 1H, H-3'); 6.89 (d, 1H, $^3J_{6,7}$ 7.0 Hz, H-6); 7.32–7.42, 7.65–7.70 (2 m, 10H, 2 Ph); 8.43 (s, 1H, H-2); 8.63 (d, 1H, H-7). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.3 [*C*$(CH_3)_3$]; 25.5, 27.4 [C(*C*$H_3)_2$]; 26.8 [C(*C*$H_3)_3$]; 32.1, 34.6 (C-1", C-2"); 64.1 (C-5'); 81.8 (C-3'); 83.4 (C-1'); 84.3 (C-4'); 84.8 (C-2'); 110.9 (C-6); 114.1 [*C*$(CH_3)_2$]; 127.6, 127.7, 129.7, 129.8, 135.5, 135.6 (2 *o*-, *m*-, *p*-Ph); 133.2, 133.3 (2 *i*-Ph); 134.9 (C-7); 155.1 (C-3a); 156.1 (C-2); 168.4 (C-5). Anal. Calcd for $C_{31}H_{38}N_4O_4Si$ (558.74): C, 66.64; H, 6.85; N, 10.03. Found: C, 66.56; H, 6.72; N, 10.26.

5-[2-[3,5-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-1,2-dideoxy-β-D-ribofuranos-1-yl]ethyl]-[1,2,4]triazolo[1,5-*a*]pyrimidine (39). Yield (175 mg, 69%); colorless solid; m.p. 80–82 °C; $[\alpha]_D^{25}$ –31.6 (*c* 1.0, CH_2Cl_2); R_f = 0.13 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.00–1.06 [m, 28H, 4 $CH(CH_3)_2$]; 1.86 (dt, 1H, $^3J_{2'a,1'}$ 7.7 Hz, $^3J_{2'a,3'}$ 7.7 Hz, $^2J_{2'a,2'b}$ 12.5 Hz, H-2'a); 2.07 (ddd, 1H, $^3J_{2'b,3'}$ 4.6 Hz, $^3J_{1',2'b}$ 6.7 Hz, $^2J_{2'a,2'b}$ 12.5 Hz, H-2'b); 1.94–2.21 (m, 2H, H-1"); 3.05 (m, 2H, H-2"); 3.66–3.77 (m, 2H, H-5'a, H-4'); 4.00 (m, 1H, H-5'b); 4.07–4.18 (m, 1H, H-1'); 4.38 (d't', 1H, $^3J_{2'a,3'}$ 8.0 Hz, $^3J_{3',4'}$ 8.0 Hz, H-3'); 6.99 (d, 1H, $^3J_{6,7}$ 7.0 Hz, H-6); 8.43 (s, 1H, H-2); 8.68 (d,

1H, H-7). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 12.5, 12.9, 13.3, 13.5 [4 *C*H(CH_3)$_2$]; 16.9, 17.0, 17.1, 17.3, 17.4, 17.4, 17.4, 17.5 [4 CH(*C*H$_3$)$_2$]; 34.0, 34.7 (C-1", C-2"); 40.3 (C-2'); 63.7 (C-5'); 73.4 (C-3'); 76.5 (C-1'); 86.0 (C-4'); 111.0 (C-6); 134.9 (C-7); 156.1 (C-2); 156.1 (C-3a); 168.8 (C-5). ESI-MS (–): *m*/*z* = 505 [M-H]$^-$. Anal. Calcd for $C_{24}H_{42}N_4O_4Si_2$ (506.79): C, 56.88; H, 8.35; N, 11.06. Found: C, 56.77; H, 8.15; N, 10.82.

Preparation of pyrimidobenzimidazoles (36, 37 and 40). General procedure

A mixture of compound **19** (493 mg, 1.0 mmol), **20** (569 mg, 1.0 mmol) or **29** (455 mg, 1.0 mmol) and 1*H*-benzo[*d*]imidazole-2-amine (266 mg, 2.0 mmol) in dry EtOH (10 mL) was heated under reflux for 2 h (monitored by TLC). The reaction mixture was cooled to r.t. and ethanolic NaOMe (1.0 M, 3.0 mL) was added. After stirring at r.t. for 1 h, the reaction mixture was neutralized with IR 120 (H^+) Amberlite resin, filtered, dried, and concentrated. The residue was purified by flash chromatography.

2-[2-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)ethyl]-pyrimido[1,2-*a*]benzimidazole (36). Flash chromatography solvent B_2; (462 mg, 76%) yellow foam; $[\alpha]_D^{24}$ –21.3 (*c* 1.0, CH_2Cl_2); R_f = 0.14 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.05 [s, 9H, C(CH_3)$_3$]; 1.34, 1.51 [2 s, 6H, C(CH_3)$_2$]; 2.07–2.30 (m, 2H, H-2"); 3.06 (m, 2H, H-1"); 3.80 (m, 2H, H-5'); 3.96 (dt, 1H, $^3J_{1',2'}$ 5.0 Hz, $^3J_{1',2''}$ 8.0 Hz, H-1'); 4.04 (q, 1H, $^3J_{3',4'}$ 3.8 Hz, $^3J_{4',5'}$ 3.8 Hz, H-4'); 4.41 (dd, 1H, $^3J_{2',3'}$ 6.6 Hz, H-2'); 4.74 (dd, 1H, H-3'); 6.77 (d, 1H, $^3J_{3,4}$ 7.0, H-3); 7.33–7.42, 7.66–7.71 (2 m, 11H, 2 Ph, H-7); 7.54 (m, 1H, H-8); 7.83 (d, 1H, $^3J_{6,7}$ 8.0 Hz, H-6); 8.01 (d, 1H, $^3J_{8,9}$ 8.2 Hz, H-9); 8.59 (d, 1H, H-4). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.3 [*C*(CH_3)$_3$]; 25.5, 27.5 [2 C(*C*H$_3$)$_2$]; 26.8 [C(*C*H$_3$)$_3$]; 31.8 (C-1"); 35.1 (C-2"); 64.2 (C-5'); 81.8 (C-3'), 83.5 (C-1'); 84.3 (C-4'); 84.9 (C-2'); 107.8 (C-3); 110.4 (C-6); 114.1 [*C*(CH_3)$_2$]; 120.1 (C-9); 121.9 (C-7); 126.4 (C-8); 126.6 (C-5a); 127.6, 127.7, 129.7, 129.8, 135.5, 135.6 (2 *o*-, *m*-, *p*-Ph); 132.5 (C-4); 133.3, 133.4 (2 *i*-Ph); 143.3 (C-9a); 150.4 (C-10a); 169.3 (C-2). $C_{36}H_{41}N_3O_4Si$ (607.81); HRMS (EI-MS): m/z calculated for $[M]^+$ = 607.28663; found 607.28608.

2-[2-(5-*O*-*tert*-Butyldiphenylsilyl-2,3-*O*-isopropylidene-1-deoxy-β-D-ribofuranos-1-yl)ethyl]-4-phenyl- pyrimido[1,2-*a*]benzimidazole (37). Flash chromatography solvent B_2; (547 mg, 80%) yellow foam; $[\alpha]_D^{24}$ –20.2 (*c* 1.0, CH_2Cl_2); R_f = 0.21 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.03 [s, 9H, C(CH_3)$_3$]; 1.34, 1.51 [2 s, 6H, C(CH_3)$_2$]; 2.10–2.36 (m, 2H, H-2"); 3.07 (m, 2H, H-1"); 3.80 (m, 2H, H-5'); 4.01 (dt, 1H, $^3J_{1',2'}$ 5.0 Hz, $^3J_{1',2''}$ 8.1 Hz, H-1'); 4.05 (q, 1H, $^3J_{3',4'}$ 3.8 Hz, $^3J_{4',5'}$ 3.8 Hz, H-4'); 4.42 (dd, 1H, $^3J_{2',3'}$ 6.7 Hz, H-2'); 4.74 (dd, 1H, H-3'); 6.58 (s, 1H, H-3); 6.64 (d, 1H, $^3J_{6,7}$ 8.4 Hz, H-6); 6.99 (m, 1H, H-7); 7.30–7.38, 7.49–7.70 (2 m, 15H, 3 Ph); 7.44 (m, 1H, H-8); 7.94 (d, 1H, $^3J_{8,9}$ 8.2 Hz, H-9). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 19.2 [*C*(CH_3)$_3$]; 25.5, 27.5 [C(*C*H$_3$)$_2$]; 26.8 [C(*C*H$_3$)$_3$]; 31.9 (C-1"); 34.8 (C-2"); 64.2 (C-5'); 81.8 (C-3'); 83.6 (C-1'); 84.3 (C-4'); 84.9 (C-2'); 108.7 (C-3); 114.1 [*C*(CH_3)$_2$]; 114.4 (C-6); 120.1 (C-9); 120.9 (C-7); 125.7 (C-8); 127.3 (C-5a); 127.6, 127.7, 128.2, 129.6, 129.7, 130.9, 135.6 (3 *o*-, *m*-, *p*-Ph); 132.2, 133.2, 133.3 (3 *i*-Ph); 144.6 (C-9a); 148.5 (C-4); 151.9 (C-10a); 168.1 (C-2). $C_{42}H_{45}N_3O_4Si$ (683.91); HRMS (EI-MS): m/z calculated for $[M]^+$ = 683.31793; found 683.31738.

2-[2-[3,5-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-1,2-didesoxy-β-D-ribofuranos-1-yl]ethyl]-pyrimido[1,2-*a*]benzimidazole (40). Flash chromatography solvent B_1; (350 mg, 63%) colorless syrup; $[\alpha]_D^{22}$ –25.7 (*c* 1.0, CH_2Cl_2); R_f = 0.14 (solvent B_2). ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.00–1.07 [m, 28H, 4 $CH(CH_3)_2$]; 1.83–2.24 (m, 4H, H-1'', H-2'); 3.01 (m, 2H, H-2''); 3.72 (m, 2H, H-5'a, H-4'); 4.01 (m, 1H, H-5'b); 4.16 (m, 1H, H-1'); 4.39 (dt, 1H, $^3J_{3',2'b}$ 5.0 Hz, $^3J_{3',2'a}$ 8.0 Hz, $^3J_{3',4'}$ 8.0 Hz, H-3'); 6.81 (d, 1H, $^3J_{3,4}$ 7.0 Hz, H-3); 7.38 (m, 1H, H-7); 7.53 (m, 1H, H-8); 7.83 (d, 1H, $^3J_{6,7}$ 8.2 Hz, H-6); 7.97 (d, 1H, $^3J_{8,9}$ 8.2 Hz, H-9); 8.60 (d, 1H, H-4). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 12.5, 12.9, 13.3, 13.5 [4 *C*H$(CH_3)_2$]; 16.9, 17.0, 17.1, 17.2, 17.3, 17.4, 17.5 (2) [4 CH(*C*$H_3)_2$]; 33.5 (C-1''); 35.1 (C-2''); 40.3 (C-2'); 63.8 (C-5'); 73.5 (C-3'); 76.8 (C-1'); 85.9 (C-4'); 107.6 (C-3); 110.3 (C-6); 120.3 (C-9); 121.7 (C-7); 126.2 (C-8); 126.9 (C-5a); 132.3 (C-4); 144.0 (C-9a); 150.7 (C-10a); 169.1 (C-2). ESI-MS (–): *m*/*z* = 554 $[M–H]^-$. Anal. Calcd for $C_{29}H_{45}N_3O_4Si_2$ (555.86): C, 62.66; H, 8.16; N, 7.56. Found: C, 62.89; H, 8.29; N, 7.37.

Acknowledgements

This work has been supported by the DFG Research Training Group 1213 “New Methods for Sustainability in Catalysis and Technique”.

References

1. Bobek, M. ; Farkas, J. *Collect. Czech. Chem. Commun.* **1969**, *34*, 1684.
2. Sato, T.; Noyori, R. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2700.
3. Bisht, S. S.; Jaiswal, N.; Sharma, A.; Fatima, S.; Sharma, R.; Rahuja, N.; Srivastava, A. K.; Bajpai, V.; Kumar, B.; Tripathi, R. P. *Carbohydr. Res.* **2011**, *346*, 1191.
4. Haraguchi, K.; Delaney, M. O.; Wiederholt, C. J.; Sambandam, A.; Hantosi, Z.; Greenberg, M. M. *J. Am. Chem. Soc.* **2002**, *124*, 3263.
5. Ciba, J. Takeshima, S.; Mishima, K.; Maeda, H.; Nanai, Y.; Mizuno, K.; Inouye, M. *Chem. Eur. J.* **2007**, *13*, 8124.
6. Liu, H.; Gao, J. Kool, E. T. *J. Am. Chem. Soc.* **2005**, *127*, 1396.
7. Lee, A. H. F.; Kool, E. T. *J. Am. Chem. Soc.* **2005**, *127*, 3332.
8. Lee, A. H. F.; Kool, E. T. *J. Org. Chem.* **2005**, *70*, 132.
9. Liu, H.; Gao, J. Kool, E. T. *J. Org. Chem.* **2005**, *70*, 639.
10. Krueger, A. T.; Kool, E. T. *J. Am. Chem. Soc.* **2008**, *130*, 3989.
11. Otero Martinez, H. Reinke, H. Michalik, D.; Vogel, C. *Synthesis* **2009**, 1834.
12. Waechtler, H.; Pena Fuentes, D.; Michalik, D.; Koeckerling, M.; Villinger, A.; Kragl, U. Cedeno, Q. A.; Vogel, C. *Synthesis* **2011**, 3099.
13. Otero, I.; Feist, H.; Herrera, L.; Michalik, M.; Quincoces, J.; Peseke, K. *Carbohydr. Res.* **2005**, *340*, 547.

14. Gewald, K.; Schinke, E.; Boettcher, H. *Chem.Ber.* **1966**, *99*, 94.
15. Taylor, E. C.; Berger, J. G. *J. Org. Chem.* **1967**, *32*, 2376.
16. Brennan, C. M.; Johnson, C. D ; McDonnell, P. D. *J. Chem. Soc., Perkin Trans. 2* **1989**, 957.
17. Adlington, R. M.; Baldwin, J. E.; Catterick, D.; Pritchard, G. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 855.
18. Adlington, R. M.; Baldwin, J. E.; Catterick, D.; Pritchard, G. J.; Tang, L. T. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2311.
19. Logue, M. W.; Sarangan, S. *Nucleos Nucleot* **1982**, 1, 89.
20. Otero, I.; Feist, H.; Herrera, L.; Michalik, M.; Quincoces, J. Peseke, K. *Aust. J. Chem.* **2005**, *58*, 104.
21. Otero, I.; Feist, H.; Herrera, L.; Michalik, D.; Michalik, M.; Quincoces, J. Peseke, K. *Z. Naturforsch.* **2005**, *60b*, 1175.
22. Perrin, D. D.; Armarego, W. L. F., *Purification of Laboratory Chemicals*, 3rd Ed.; Pergamon Press: Oxford, 1988.

