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Construction of C-nucleosides diversified by [3+2] cycloaddition from a sugar-based mesoionic ring

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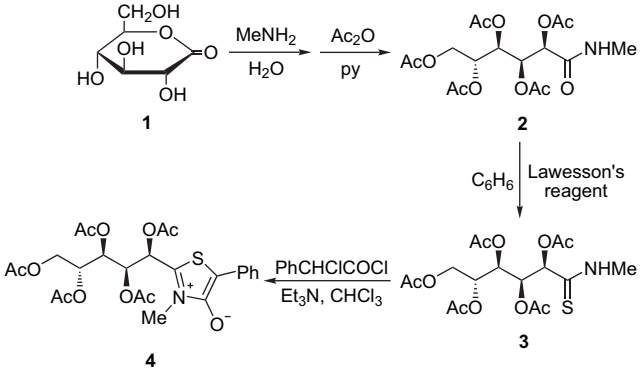
Abstract—A mesoionic acyclic C-nucleoside (**4**), serves as the starting chiron to construct highly functionalized 2-aza-7-thiabicyclo[2.2.1]-heptanes and heptenes by means of a [3+2] cycloaddition with acetylenic and olefinic dipolarophiles. Further elimination of either sulfur or hydrogen sulfide leads to acyclic C-nucleosides bearing a heterocyclic moiety of 2-pyridone.

1. Introduction

The synthesis of modified nucleosides and glycoconjugates has come of age.[1,2] Construction of a heterocyclic aglycon or spacer by means of cycloaddition reactions represents a convenient atom-economy strategy. Of particular relevance are stereocontrolled [3+2] cycloadditions, which can be employed to access numerous natural products and pharmaceuticals.[3] Renewed interest in [3+2] cycloadditions emerges from a few reactions of orthogonal functionalization, well suited for biological applications, such as in click chemistry repertories.[4] Our research group has been largely involved in asymmetric [3+2] cycloadditions of 1,3-thiazolium-4-olates (thioisomünchnones) using carbohydrates as stereodifferentiating elements.[5] In a recent study we were able to synthesize a mesoionic nucleus with an acyclic carbohydrate chain as substituent and we explored the reactivity of the heterocyclic moiety.[6] The present work extends such results to other unsaturated dipolarophiles to produce new C-nucleosides containing highly functionalized and polycyclic fragments derived from pyrid-2-ones. It has been recently demonstrated that C-nucleosides bearing the pyrid-2-one core serve as a non-disruptive pyrimidine analog in DNA duplex.[7] Moreover, the pyridone chromophore absorbs in the near UV range (λ>300 nm) where common nucleic acid bases are transparent, and exhibit room temperature fluorescence. These properties enabling selective excitation in an oligonucleotide chain make these compounds interesting as potential fluorescent and/or photochemical probes in nucleic acids.[8]

2. Results and discussion

As reported in a previous communication,[6] the 1,3-thiazolium-4-olate system **4** (Scheme 1), can easily be prepared from *N*-methyl-δ-thiogluconamide[9] (**3**) in a few step sequence using δ-gluconolactone (**1**) as raw material.



Scheme 1.

Despite **4** turned out to be air sensitive and slowly decomposed at room temperature, it underwent 1,3-dipolar cycloadditions in dry solvents with several types of acetylenic and olefinic dipolarophiles.

Thioisomünchnones are known to react with acetylenic dipolarophiles to form either pyrid-2-ones or thiophenes,[10]

Keywords: 1,3-Dipolar cycloaddition; Mesoionic heterocycle; C-nucleoside; Pyridone; Thioisomünchnone.
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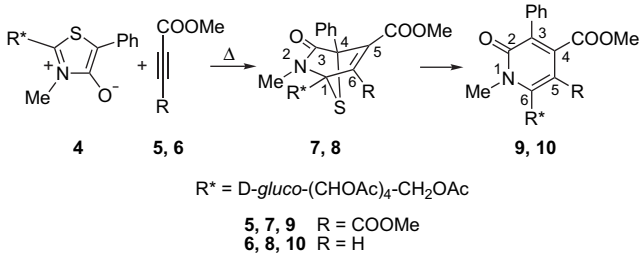
by extrusion of sulfur or isocyanate, respectively, from the initially generated cycloadducts, which to the best of our knowledge have never been isolated. However, the thioisomünchnone **4** reacted with acetylenic dipolarophiles such as dimethyl acetylenedicarboxylate (**5**) and methyl propiolate (**6**) in refluxing toluene and CH_2Cl_2, respectively, to afford single products, which were identified as cycloadducts **7** and **8** (Scheme 2).



Scheme 2.

The main structural features of these initial bicyclic systems were established by NMR spectroscopy and combustion analysis. Particularly, in the ^{13}C NMR spectra of **7**, the resonances at δ 83.3 and 69.4 ppm were attributed to the bridgehead carbons C-4 and C-1, respectively. The (1*R*,4*R*) configuration proposed for **7** was established on the basis of its ^1H NMR spectrum, having a close similarity to those of **23b** and **25b** (see below). On the other hand, cycloadduct **8** was not stable enough when it was subjected to chromatographic purification on SiO_2 and spontaneously evolved into **10** after sulfur extrusion.

Desulfuration of **7** and **8** by $Hg(OAc)_2$ in acetic acid–acetone at room temperature also afforded the C-nucleosides **9** and **10**, respectively. ^{13}C NMR data supported the pyrid-2-one structure and NOE experiments on compound **10** confirmed the regiochemistry suggested for the methyl propiolate reaction. Both H-1′ and H-2′, located at the sugar moiety, showed NOEs with H-5 (Fig. 1).

The bimolecular cycloaddition of 2-phenylthioisomünchnones with electron-deficient olefins provides a series of bicyclic adducts, which were further reacted with $NaOCH_3$ to yield pyrid-2-one derivatives.[11] However, the 2-(*N*,*N*′-dialkylamino)thioisomünchnones showed a different behavior leading to 4,5-dihydrothiophenes by opening of the initial 1:1 cycloadduct.[12]

Thioisomünchnone **4** was found to undergo dipolar cycloaddition with asymmetric and symmetrically substituted olefinic dipolarophiles. Stable cycloadducts (**14**–**16**) were obtained after reaction with methyl acrylate (**11**), methyl vinyl ketone (**12**), and acrylonitrile (**13**) (Scheme 3).

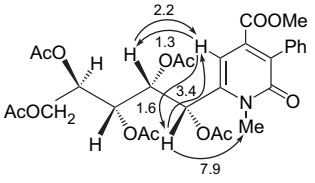
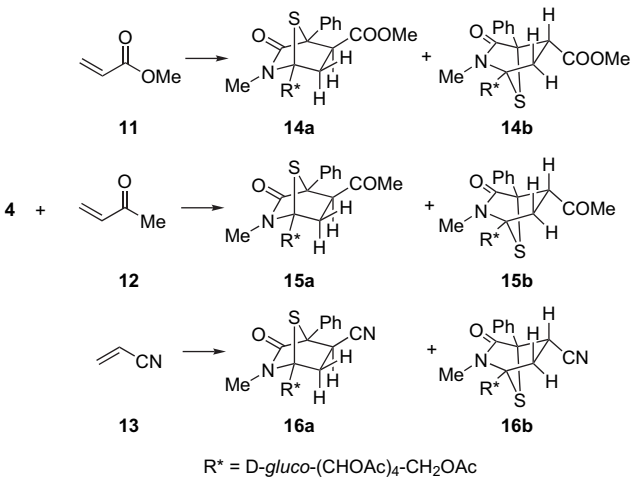


Figure 1. NOEs measured for compound **10**.



Scheme 3.

The structure of **16a** could unequivocally be established by single-crystal X-ray analysis,[6] which shows the *exo* disposition of the cyano group. In the ^1H NMR spectrum of **16a**, the resonances of H-5$_{endo}$, H-6$_{endo}$, and H-6$_{exo}$ appeared as double doublets. The more deshielding signal centered at δ 3.56 ppm contains a trans coupling (J=3.6 Hz) and a cis coupling (J=8.0 Hz) and it is therefore assigned to H-5$_{endo}$. The signal at δ 2.85 ppm showed a trans coupling as above and a geminal one (J=12.7 Hz), consistent with the H-6$_{exo}$ proton. Finally, the resonance at 2.74 ppm with cis and geminal couplings was attributed to H-6$_{endo}$. Although H-5$_{endo}$, H-6$_{endo}$, and H-6$_{exo}$ of the cycloadduct **16b** isolated from the same reaction, resonated at slightly different chemical shifts: δ 3.51 ppm (H-5$_{endo}$) and 2.80 ppm (H-6$_{exo}$ and H-6$_{endo}$), they showed a similar coupling pattern, thus allowing us to suggest that **16b** was obtained from the approach of the dipolarophile to the opposite face of the dipole. Moreover, the chemical shifts for C-5 and C-6 of **16a** and **16b** proved that the CN group is located at C-5 in both cases. The regio- and stereochemistry of the cycloadducts **14** and **15**, assigned by analogy with the NMR data of **16a** and **16b** (Tables 1 and 2) was confirmed by the existence of NOEs between the H-6$_{endo}$ proton and the *N*-CH_3 groups in these compounds. This evidence together with the cis coupling observed for the signal of the H-6$_{endo}$ proton suggest that the H-5 proton lies in an *endo* disposition in all cases.

Likewise, the optical rotatory power can be helpful for the assignment of the configuration of the bridgehead carbon atoms in these cycloadducts. Compound **16a** showed an optical rotation (+6.0°) as low as they were found for **14a** (−0.5°) and **15a** (+4.0°). However, higher values were measured for the cycloadducts **14b**–**16b** ($+56.0<[\alpha]_D<+67.5$).[13]

None of these reactions showed appreciable facial diastereoselectivity and diastereomeric mixtures (ca. 1:1 ratio) of *exo* cycloadducts arose from the approach of the dipolarophile to both faces of the dipole (Scheme 4). However, these cycloadditions proceeded with complete regioselectivity, which was in turn opposite to that observed in the case of 2-(*N*,*N*′-dialkylamino)thioisomünchnones, largely explored by our research group.[5,12,14] Although this distinctive behavior could be attributed to the presence of an amino substituent in the latter mesoionics, exerting a profound

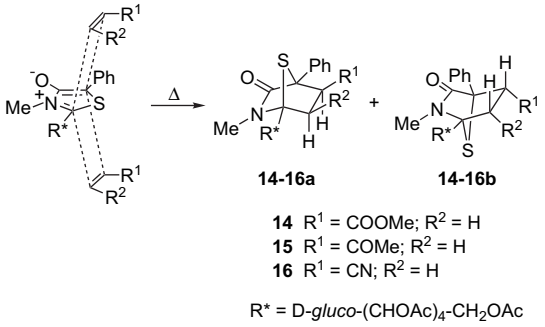
Table 1. ^{1}H NMR chemical shift (ppm) data of compounds **14–16** ($CDCl_3$)

Compound	H-5$_{endo}$	H-6$_{exo}$	H-6$_{endo}$	H-1′	H-2′	H-3′	H-4′	H-5′	H-5″
14a	3.30	2.70	2.60	5.76	5.62	5.44	5.12	4.37	4.15
14b	3.28	2.78	2.56	5.84	5.51	5.42	5.15	4.38	4.19
15a	3.44	2.70	2.50	5.75	5.63	5.45	5.15	4.38	4.17
15b	3.39	2.76	2.44	5.82	5.51	5.42	5.15	4.37	4.19
16a	3.56	2.85	2.74	5.77	5.60	5.44	5.13	4.39	4.17
16b	3.51	2.80	2.80	5.82	5.46	5.41	5.14	4.38	4.19

Table 2. ^{13}C NMR chemical shift (ppm) data of compounds **14–16** ($CDCl_3$)

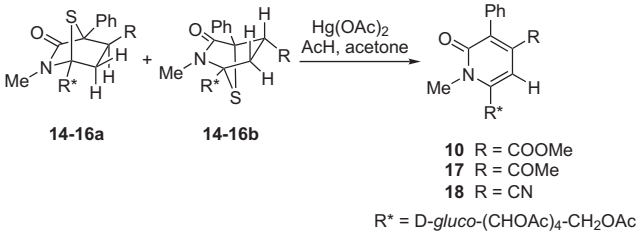
Compound	C-1	C-3	C-4	C-5	C-6	C-1′	C-2′	C-3′	C-4′	C-5′
14a	70.63	174.73	79.40	50.39	40.69	67.50	68.26	69.56	69.11	61.66
14b	70.91	174.48	78.21	49.31	40.72	67.57	67.66	69.42	69.42	61.47
15a	70.16	174.79	79.53	56.95	39.68	67.24	68.12	69.57	69.03	61.71
15b	70.50	174.55	78.22	55.59	39.76	67.53	67.53	69.35	69.35	61.45
16a	69.90	173.12	80.09	69.41	42.45	66.84	67.93	69.65	69.15	61.73
16b	70.24	172.72	78.79	69.22	42.45	67.05	67.42	69.22	69.22	61.43

stereodirecting effect, a satisfactory rationale has not yet been provided and additional studies will be required.



Scheme 4.

Cycloadducts **14–16** were transformed into the corresponding pyrid-2-one C-nucleosides **10**, **17**, and **18**, by elimination of hydrogen sulfide using mercury(II) acetate in acetic acid–acetone (Scheme 5). The formation of **10**, previously obtained from **4** and methyl propiolate, evidences the regiochemical control of these cycloadditions. The structures for pyrid-2-ones **17** and **18** were assigned on the basis of their analytical data and by comparison of their NMR spectra with those of **10** (Table 3).

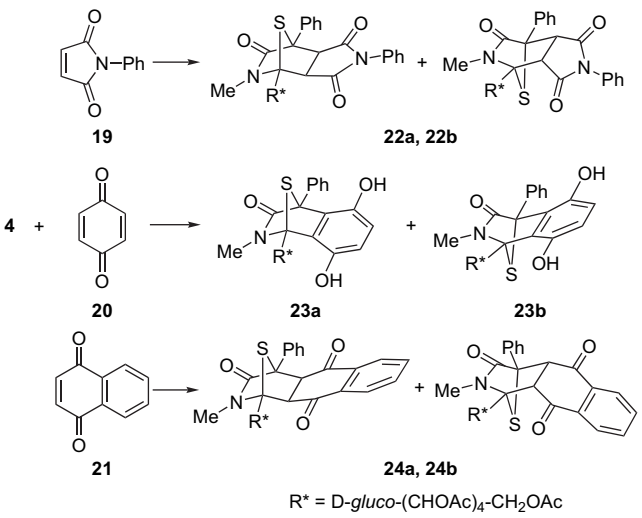


Scheme 5.

Table 3. Selected ^{13}C NMR chemical shift (ppm) data of compounds **10**, **17**, and **18** ($CDCl_3$)

Compound	C-2	C-3	C-4	C-5	C-6
10	162.41	134.88	142.67	105.11	138.57
17	162.48	134.41	146.40	104.57	142.73
18	160.93	132.62	144.31	105.73	137.31

Diastereomeric mixtures of cycloadducts **22–24** were obtained when **4** was reacted with symmetrically substituted cyclic olefins such as *N*-phenylmaleimide (**19**), 1,4-benzoquinone (**20**), and 1,4-naphthoquinone (**21**) (Scheme 6).



Scheme 6.

Suitable crystals for X-ray diffraction analysis could also be obtained in the case of **23a** (Fig. 2).[15] It is interesting to note that the tricyclic aglycon of **23a**, unlike **22** and **24**, contains only two stereogenic centers due to aromatization of the quinone moiety. This structural simplification proves that diastereomers **23a** and **23b** do not emerge from *endo*/*exo* approaches of the dipolarophile to the same face of the dipole, but rather by *exo* attack of the dipolarophile to both faces of the thioisomünchnone.

The nature of the rings fused to the 2-aza-7-thiabicyclo[2.2.1]-heptane system of **22** and **24** has a remarkable influence on their spectroscopic data, and prevents the unequivocal assignment of their configurations by means of ^{1}H- and ^{13}C-chemical shift correlations with those of **14–16**. However, aromatization of the naphthoquinone system of **24a** and **24b**, easily achieved by treatment of such a diastereomeric mixture with SiO_2 (Scheme 7), led to a mixture of

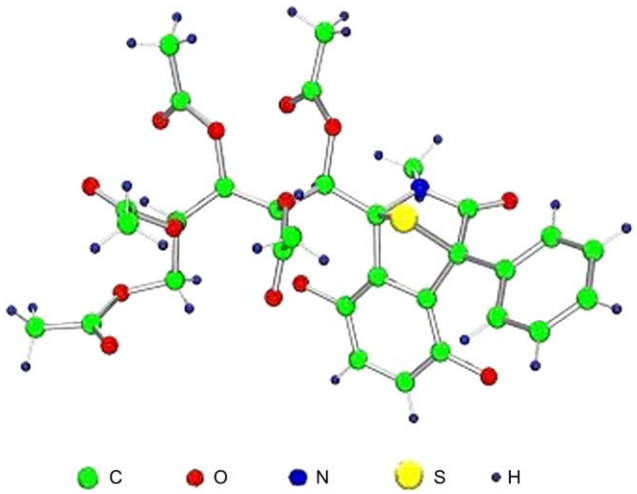
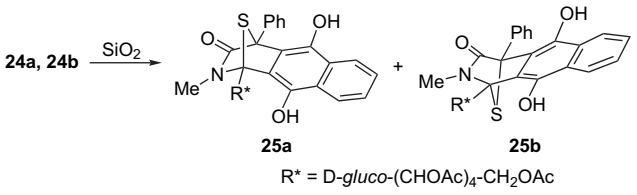


Figure 2. Perspective view of the structure of **23a**.

25a and **25b**, whose spectroscopic data were very similar to those of **23a** and **23b**, respectively. Moreover, the ^{1}H NMR spectrum of **7**, which also contains an endocyclic double bond between C-5 and C-6 atoms, exhibits the same proton pattern of ^{1}H NMR of **23b** and **25b**. This fact points to a (1*R*,4*R*) configuration for **7** (Table 4).

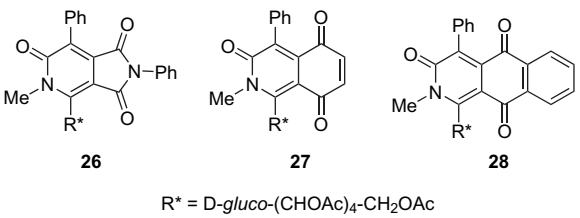


Scheme 7.

Table 4. ^{1}H NMR chemical shift (ppm) data of compounds **7**, **23**, and **25** ($CDCl_3$)

Compound	H-1′	H-2′	H-3′	H-4′	H-5′	H-5″
7	6.14	5.54	5.37	5.20	4.41	4.14
23a	6.51	5.89	5.33	5.64	4.99	4.01
23b	6.27	5.61	5.41	5.27	4.43	4.14
25a	6.62	5.82	5.59	5.33	4.76	4.30
25b	6.47	5.58	5.49	5.30	4.40	4.18

As above, cycloadducts **22** and **23** gave rise to pyrid-2-one C-nucleosides **26** and **27** upon treatment with $Hg(OAc)_2$ in acetic acid at room temperature. However, desulfuration of **24** to give **28** could only be carried out using Raney nickel in refluxing 2-butanol.



3. Conclusions

In conclusion, this paper reports a rapid access to enantiomerically pure acyclic C-nucleosides containing a pyrid-2-one moiety based on the 1,3-dipolar cycloadditions of a carbohydrate-derived 1,3-thiazolium-4-olate system with acetylenic and olefinic dipolarophiles. To the best of our knowledge, this is the first time stable cycloadducts have been isolated in the reaction of activated triple bonds (e.g., dimethyl acetylenedicarboxylate) with thioisomünchnones. Despite these [3+2] cycloadditions processes were found to be regiospecific, no appreciable facial selectivity was induced by appended chiral carbohydrate substituent. Efforts to understand this stereochemical outcome by theoretical studies as well as further pursuits to improve the diastereoselection are currently under way in our laboratories.

4. Experimental

4.1. General methods

Melting points were determined on a capillary apparatus and are uncorrected. Optical rotations were measured at the sodium line at 18±2 °C. Analytical and preparative TLC were performed on silica gel with monitoring by means of UV light at 254 and 360 nm and iodine vapors. Flash chromatography was performed with silica gel (400–230 mesh). IR spectra were recorded on KBr pellets. ^{1}H and ^{13}C NMR spectra were obtained at 400 and 100 MHz, respectively, in $CDCl_3$ (Me_4Si as internal standard) unless otherwise specified. Compounds **2** and **3** were prepared according to literature procedures.[9]

4.2. Synthesis and characterization

4.2.1. 2-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-3-methyl-5-phenyl-1,3-thiazolium-4-olate (4). To a solution of *N*-methyl-D-thiogluconamide (**3**) (1.0 g, 2.3 mmol) in dry chloroform (10 mL) was added dropwise a solution of α-chlorophenylacetyl chloride (0.7 mL, 4.6 mmol) in dry chloroform (5 mL). After stirring at room temperature for 15 min and refluxing for 30 min, the reaction mixture was washed with water. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was washed with petroleum ether and treated with a mixture of chloroform–diethyl ether–petroleum ether to give **4** (0.8 g, 63%) as a yellowish solid; mp 65–70 °C (dec); $[\alpha]_D$ +128 (*c* 0.5, chloroform); IR (KBr, cm^{-1}): ν_{max} 1751, 1624, 1371, 1217; ^{1}H NMR ($CDCl_3$) δ 7.90–7.16 (m, 5H), 6.30 (d, 1H, *J*=6.3 Hz), 5.69 (dd, 1H, *J*=4.3 and 6.2 Hz), 5.34 (dd, 1H, *J*=4.3 and 6.6 Hz), 5.02 (m, 1H), 4.38 (dd, 1H, *J*=2.5 and 12.7 Hz), 4.09 (dd, 1H, *J*=5.6 and 12.7 Hz), 3.81 (s, 3H), 2.18 (s, 3H), 2.15 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H), 2.05 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.72, 169.72, 169.51, 169.26, 169.01, 159.78, 143.60, 132.60, 128.62, 125.66, 124.07, 99.87, 68.95, 68.50, 68.24, 67.06, 61.38, 33.08, 20.62, 20.49, 20.35, 20.25.

4.2.2. (1*R*,4*R*)-1-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-2-aza-2-methyl-5,6-dimethoxycarbonyl-3-oxo-4-phenyl-7-thiabicyclo[2.2.1]hept-5-ene (7). To a solution of **4** (1.0 g, 1.8 mmol) in dry toluene (15 mL) dimethyl

acetylenedicarboxylate (0.3 mL, 2.2 mmol) was added, and the mixture was refluxed for 5 h. After removal of the solvent, the crude product was purified by flash chromatography (diethyl ether) to give **7** (0.5 g, 40%); mp 60–65 °C (dec); $[\alpha]_D$ +66 (*c* 0.5, chloroform); IR (KBr, cm^{-1}): ν_{max} 2959, 1750, 1624, 1440, 1373, 1213, 1128, 1044, 976; ^1H NMR ($CDCl_3$) δ 7.66–7.37 (m, 5H), 6.14 (d, 1H, *J*=2.9 Hz), 5.54 (dd, 1H, *J*=5.9 and 5.4 Hz), 5.37 (t, 1H, *J*=5.7 Hz), 5.20 (m, 1H), 4.41 (dd, 1H, *J*=3.5 and 12.4 Hz), 4.14 (dd, 1H, *J*=5.3 and 12.4 Hz), 3.79 (s, 3H), 3.51 (s, 3H), 3.04 (s, 3H), 2.17 (s, 3H), 2.13 (s, 3H), 2.09 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 178.52, 170.49, 169.75, 169.69, 169.23, 169.12, 163.01, 162.50, 150.31, 149.80, 130.93, 128.96, 128.29, 128.11, 83.28, 69.36, 68.08, 67.81, 65.29, 52.94, 52.45, 33.08, 20.76, 20.59, 20.33. Anal. Calcd for $C_{31}H_{35}NO_{15}S$: C, 53.68; H, 5.08; N, 2.02; S, 4.62. Found: C, 53.96; H, 5.06; N, 1.82; S, 4.47.

4.2.3. 6-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-4,5-dimethoxycarbonyl-1-methyl-3-phenylpyrid-2-one (9). To a suspension of $Hg(OAc)_2$ (0.1 g, 0.3 mmol) in acetic acid (3 mL) compound **7** (0.1 g, 0.2 mmol) was added and the reaction mixture was stirred at room temperature. Acetone (3 mL) was mixed with the resultant gel and the insoluble material was filtered off and washed with acetone. The filtrate was diluted with water, filtered, adjusted to pH 5 with sodium hydrogen carbonate, and extracted with chloroform. The organic layer was washed with sodium hydrogen carbonate solution (1 M) followed by water, dried ($MgSO_4$), and concentrated in vacuo. Purification of the residue by thin layer preparative chromatography (diethyl ether) afforded **9**, which crystallized as a white solid from diethyl ether–petroleum ether (0.02 g, 30%); mp 75 °C (dec); $[\alpha]_D$ +74.5 (*c* 0.5, chloroform); IR ν_{max} (KBr, cm^{-1}) 3418, 2955, 1751, 1655, 1541, 1439, 1371, 1304, 1219, 1045; ^1H NMR ($CDCl_3$) δ 7.41–7.22 (m, 5H), 6.49 (m, 1H), 5.91 (dd, 1H, *J*=3.2 and 5.7 Hz), 5.31 (dd, 1H, *J*=3.4 and 6.2 Hz), 5.09 (m, 1H), 4.29 (dd, 1H, *J*=3.7 and 12.3 Hz), 4.10 (dd, 1H, *J*=6.0 and 12.2 Hz), 3.78 (s, 3H), 2.72 (s, 3H), 3.46 (s, 3H), 2.09 (s, 9H), 2.02 (s, 3H), 1.98 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 169.30, 168.79, 168.58, 165.33, 164.99, 160.66, 143.13, 139.52, 133.83, 128.76, 127.71, 127.24, 110.79, 70.33, 69.70, 68.82, 68.32, 60.97, 52.23, 51.60, 33.73, 19.84, 19.68. Anal. Calcd for $C_{31}H_{35}NO_{15}$: C, 56.28; H, 5.33; N, 2.12. Found: C, 55.50; H, 5.20; N, 2.07.

4.2.4. 6-(1′,2′,3′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-4-methoxycarbonyl-2-methyl-3-phenylpyrid-2-one (10). *Method A*: A solution of **4** (1.0 g, 1.81 mmol) and methyl propiolate (0.2 mL, 2.17 mmol) in dry dichloromethane (15 mL) was heated at reflux for 10 h. The solvent was then evaporated under reduced pressure and the crude product was purified by flash chromatography (diethyl ether) and then poured into a suspension of $Hg(OAc)_2$ (0.1 g, 0.3 mmol) in acetic acid (3 mL) at room temperature and processed as described for **9** to give **10** (0.2 g, 19%) as a white solid; mp 80 °C; $[\alpha]_D$ 56.5 (*c* 0.5, chloroform); IR (KBr, cm^{-1}) ν_{max} 3472, 2960, 1749, 1653, 1555, 1454, 1373, 1217, 1049; ^1H NMR ($CDCl_3$) δ 7.40–7.27 (m, 5H), 6.41 (s, 1H), 6.07 (d, 1H, *J*=4.6 Hz), 5.60 (t, 1H, *J*=4.7 Hz), 5.42 (t, 1H, *J*=5.3 Hz), 5.07 (m, 1H), 4.36 (dd, 1H, *J*=2.9 and 12.6 Hz), 4.10 (dd, 1H, *J*=6.2 and 12.6 Hz), 3.75 (s, 3H), 3.54 (s, 3H), 2.20 (s, 3H), 2.13 (s, 6H), 2.08 (s, 3H), 2.07 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.63, 169.80, 169.49, 167.36, 162.41, 142.67, 138.57, 134.88, 131.62, 129.12, 128.10, 127.87, 105.11, 70.11, 69.19, 68.95, 68.41, 61.48, 52.31, 31.90, 20.65, 20.68, 20.62, 20.22. Anal. Calcd for $C_{29}H_{33}NO_{13}$: C, 57.71; H, 5.51; N, 2.32. Found: C, 57.54; H, 5.53; N, 2.23. *Method B*: A mixture of cycloadducts **14a** and **14b** (0.13 g, 0.2 mmol) was poured into a suspension of $Hg(OAc)_2$ (0.1 g, 0.3 mmol) in acetic acid (3 mL) at room temperature and processed as described for **9** to give **10** (0.3 g, 35%).

4.2.5. (1*S*,4*R*,5*R*)-1-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-2-aza-5-methoxycarbonyl-2-methyl-3-oxo-4-phenyl-7-thiabicyclo[2.2.1]heptane (14a) and (1*R*,4*S*,5*S*)-1-(1′,2′,3′,4′,5′-penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-2-aza-5-methoxycarbonyl-2-methyl-3-oxo-4-phenyl-7-thiabicyclo[2.2.1]heptane (14b). To a solution of **4** (1.0 g, 1.8 mmol) in dry chloroform (15 mL) methyl acrylate (0.2 mL, 2.2 mmol) was added, and the mixture was refluxed for 12 h. After removal of the solvent, the crude product was purified by flash chromatography (diethyl ether) and the two diastereomeric cycloadducts **14a** (0.2 g, 12%) and **14b** (0.2 g, 12%) were separated by thin layer preparative chromatography (diethyl ether). **14a**: mp 83 °C (dec); $[\alpha]_D$ −0.5 (*c* 0.5, chloroform); IR (KBr, cm^{-1}): ν_{max} 2965, 1750, 1447, 1373, 1213, 1045; ^1H NMR ($CDCl_3$) δ 7.42–7.26 (m, 5H), 5.76 (d, 1H, *J*=5.1 Hz), 5.62 (t, 1H, *J*=4.9 Hz), 5.44 (t, 1H, *J*=4.9 Hz), 5.12 (m, 1H), 4.37 (dd, 1H, *J*=3.3 and 12.4 Hz), 4.15 (dd, 1H, *J*=5.3 and 12.4 Hz), 3.30 (m, 1H, *J*=4.3 and 8.0 Hz), 3.25 (s, 3H), 2.84 (s, 3H), 2.70 (dd, 1H, *J*=4.4 and 12.3 Hz), 2.60 (dd, 1H, *J*=8.0 and 12.3 Hz), 2.19 (s, 3H), 2.15 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.02 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 174.73, 170.57, 170.39, 169.80, 169.42, 169.27, 131.75, 128.39, 127.85, 79.40, 70.63, 69.56, 69.11, 68.26, 67.50, 61.66, 51.76, 50.39, 40.69, 28.75, 20.96, 20.65, 20.55. Anal. Calcd for $C_{29}H_{35}NO_{13}S$: C, 54.62; H, 5.53; N, 2.20; S, 5.03. Found: C, 54.57; H, 5.58; N, 2.14; S, 5.07. **14b**: mp 80 °C (dec); $[\alpha]_D$ +56.0 (*c* 0.5, chloroform); IR (KBr, cm^{-1}) ν_{max} 2955, 1751, 1447, 1373, 1213, 1043; ^1H NMR ($CDCl_3$) δ 7.43–7.27 (m, 5H), 5.84 (d, 1H, *J*=3.3 Hz), 5.51 (dd, 1H, *J*=3.7 and 4.9 Hz), 5.42 (t, 1H, *J*=4.9 Hz), 5.15 (m, 1H), 4.38 (dd, 1H, *J*=2.9 and 12.5 Hz), 4.19 (dd, 1H, *J*=5.8 and 12.4 Hz), 3.28 (m, 1H), 3.26 (s, 3H), 2.88 (s, 3H), 2.78 (dd, 1H, *J*=4.4 and 12.8 Hz), 2.56 (dd, 1H, *J*=8.2 and 12.7 Hz), 2.25 (s, 3H), 2.17 (s, 3H), 2.13 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 174.48, 170.78, 170.63, 169.96, 169.72, 169.39, 131.85, 128.52, 128.31, 127.93, 78.21, 70.91, 69.42, 67.66, 67.57, 61.47, 51.80, 49.31, 40.72, 28.22, 20.89, 20.71, 20.57. Anal. Calcd for $C_{29}H_{35}NO_{13}S$: C, 54.62; H, 5.53; N, 2.20; S, 5.03. Found: C, 54.63; H, 5.47; N, 2.28; S, 4.84.

4.2.6. (1*S*,4*R*,5*R*)-5-Acetyl-1-(1′,2′,3′,4′,5′-penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-2-aza-2-methyl-3-oxo-4-phenyl-7-thiabicyclo[2.2.1]heptane (15a) and (1*R*,4*S*,5*S*)-5-acetyl-1-(1′,2′,3′,4′,5′-penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-2-aza-2-methyl-3-oxo-4-phenyl-7-thiabicyclo[2.2.1]-heptane (15b). To a solution of **4** (1.0 g, 1.8 mmol) in dry chloroform (15 mL) methyl vinyl ketone (0.3 mL, 2.2 mmol) was added, and the mixture was refluxed for 12 h. After removal of the solvent, the crude product was purified by flash chromatography (eluant: diethyl ether) and the two

diastereomeric cycloadducts **15a** (0.2 g, 18%) and **15b** (0.2 g, 18%) were separated by preparative thin layer chromatography (diethyl ether). **15a**: mp 100 °C (dec); $[\alpha]_D$ +4.0 (*c* 0.5, chloroform); IR (KBr, cm^{-1}): ν_{max} 2980, 1751, 1707, 1371, 1215, 1043; ^1H NMR ($CDCl_3$) δ 7.51–7.27 (m, 5H), 5.75 (d, 1H, *J*=5.3 Hz), 5.63 (t, 1H, *J*=4.9 Hz), 5.45 (dd, 1H, *J*=4.6 and 6.5 Hz,), 5.15 (m, 1H), 4.38 (dd, 1H, *J*=3.1 and 12.5 Hz), 4.17 (dd, 1H, *J*=5.3 and 12.5 Hz), 3.44 (dd, 1H, *J*=4.3 Hz), 2.85 (s, 3H), 2.70 (dd, 1H, *J*=4.3 and 12.3 Hz), 2.50 (dd, 1H, *J*=8.0 and 12.3 Hz), 2.20 (s, 3H), 2.18 (s, 3H), 2.15 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 1.68 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 204.02, 174.79, 170.60, 170.48, 169.82, 169.42, 169.34, 131.92, 128.76, 128.41, 79.53, 70.16, 69.57, 69.03, 68.12, 67.24, 61.71, 56.95, 39.68, 30.19, 28.62, 20.69, 20.55. Anal. Calcd for $C_{29}H_{35}NO_{12}S$: C, 56.03; H, 5.67; N, 2.25; S, 5.16. Found: C, 55.85; H, 5.70; N, 2.49; S, 5.18. **15b**: mp 80 °C (dec); $[\alpha]_D$ +62.5 (*c* 0.5, chloroform); IR (KBr, cm^{-1}) ν_{max} 2961, 1744, 1707, 1373, 1215, 1043; ^1H NMR ($CDCl_3$) δ 7.49–7.28 (m, 5H), 5.82 (d, 1H, *J*=3.5 Hz), 5.51 (t, 1H, *J*=4.8 Hz), 5.42 (dd, 1H, *J*=5.2 and 6.3 Hz), 5.15 (m, 1H), 4.37 (dd, 1H, *J*=2.9 and 12.5 Hz), 4.19 (dd, 1H, *J*=5.8 and 12.4 Hz), 3.39 (dd, 1H, *J*=4.3 and 8.0), 2.87 (s, 3H), 2.76 (dd, 1H, *J*=4.4 and 12.8 Hz), 2.44 (dd, 1H, *J*=8.1 and 12.8 Hz), 2.25 (s, 3H), 2.17 (s, 3H), 2.14 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H), 1.69 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 204.36, 174.55, 170.60, 169.89, 169.85, 169.75, 169.40, 131.97, 128.77, 128.44, 128.26, 78.22, 70.50, 69.35, 67.53, 61.45, 55.59, 39.76, 30.50, 28.15, 20.85, 20.65, 20.59. Anal. Calcd for $C_{29}H_{35}NO_{12}S$: C, 56.03; H, 5.67; N, 2.25; S, 5.16. Found: C, 55.94; H, 5.83; N, 2.32; S, 5.18.

4.2.7. (1*S*,4*R*,5*R*)-1-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-2-aza-5-cyano-2-methyl-3-oxo-4-phenyl-7-thiabicyclo[2.2.1]heptane (16a) and (1*R*,4*S*,5*S*)-1-(1′,2′,3′,4′,5′-penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-2-aza-5-cyano-2-methyl-3-oxo-4-phenyl-7-thiabicyclo[2.2.1]-heptane (16b). To a solution of **4** (1.0 g, 1.8 mmol) in dry chloroform (15 mL) acrylonitrile (0.1 mL, 2.2 mmol) was added, and the mixture was refluxed for 12 h. After removal of the solvent, the crude product was purified by flash chromatography (diethyl ether) and the two diastereomeric cycloadducts **16a** (0.1 g, 9%) and **16b** (0.1 g, 9%) were separated by preparative thin layer chromatography (diethyl ether). **16a**: mp 97 °C (dec); $[\alpha]_D$ +6.0 (*c* 0.5, chloroform); IR (KBr, cm^{-1}) ν_{max} 2949, 1753, 1715, 1448, 1373, 1215, 1047; ^1H NMR ($CDCl_3$) δ 7.47–7.43 (m, 5H), 5.77 (d, 1H, *J*=5.4 Hz), 5.60 (t, 1H, *J*=4.8 Hz), 5.44 (dd, 1H, *J*=4.6 and 6.5 Hz), 5.13 (m, 1H), 4.39 (dd, 1H, *J*=3.0 and 12.6 Hz), 4.17 (dd, 1H, *J*=5.1 and 12.6 Hz), 3.56 (dd, 1H, *J*=3.6 and 8.0 Hz), 2.85 (dd, 1H, *J*=8.0 and 12.7 Hz), 2.83 (s, 3H), 2.74 (dd, 1H, *J*=3.7 and 12.7 Hz), 2.22 (s, 3H), 2.18 (s, 3H), 2.14 (s, 3H), 2.11 (s, 3H), 2.09 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 173.12, 171.15, 170.69, 170.55, 169.78, 169.32, 130.71, 129.44, 128.77, 128.26, 118.28, 80.09, 69.90, 69.65, 69.41, 69.15, 67.93, 66.84, 61.73, 42.45, 39.09, 28.54, 20.72, 20.60, 20.52, 20.46. Anal. Calcd for $C_{28}H_{32}N_2O_{11}S$: C, 55.62; H, 5.33; N, 4.63; S, 5.30. Found: C, 55.31; H, 5.28; N, 4.64; S, 5.48. **16b**: mp 93.2 °C (dec); $[\alpha]_D$ +67.5° (*c* 0.5, chloroform); IR (KBr, cm^{-1}): ν_{max} 2976, 1755, 1719, 1448, 1373, 1213, 1047; ^1H NMR ($CDCl_3$) δ 7.48–7.43 (m, 5H), 5.82 (d, 1H, *J*=3.8 Hz), 5.46 (t, 1H, *J*=4.5 Hz), 5.41 (dd, 1H, *J*=4.9 and 6.3 Hz), 5.14 (m, 1H), 4.38 (dd, 1H, *J*=2.92 and 12.5 Hz, H-5′), 4.19 (dd, 1H, *J*=5.6 and 12.5 Hz), 3.51 (dd, 1H, *J*=3.9 and 8.0 Hz), 2.85 (s, 3H), 2.80 (m, 2H), 2.25 (s, 3H), 2.18 (s, 3H), 2.15 (s, 3H), 2.09 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 172.72, 170.62, 169.85, 169.66, 169.36, 130.78, 129.45, 128.77, 128.16, 118.19, 78.79, 70.24, 69.22, 67.42, 67.05, 61.43, 42.45, 37.87, 28.02, 20.99, 20.76, 20.67, 20.52. Anal. Calcd for $C_{28}H_{32}N_2O_{11}S$: C, 55.62; H, 5.33; N, 4.63; S, 5.30. Found: C, 55.33; H, 5.43; N, 4.77; S, 4.81.

4.2.8. 4-Acetyl-6-(1′,2′,3′,4′,5′-penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-1-methyl-3-phenylpyrid-2-one (17). A mixture of cycloadducts **15a** and **15b** (0.12 g, 0.2 mmol) was poured into a suspension of $Hg(OAc)_2$ (0.1 g, 0.3 mmol) in acetic acid (3 mL) at room temperature and processed as described for **9** to give **17** (0.05 g, 53%); mp 72 °C (dec); $[\alpha]_D$ +118.0 (*c* 0.5, chloroform); IR (KBr, cm^{-1}) ν_{max} 3472, 2964, 1751, 1719, 1659, 1501, 1447, 1373, 1215, 1045; ^1H NMR ($CDCl_3$) δ 7.42–7.30 (m, 5H), 6.22 (s, 1H), 6.05 (d, 1H, *J*=4.7 Hz), 5.61 (t, 1H, *J*=4.5 Hz), 5.39 (t, 1H, *J*=5.1 Hz), 5.08 (m, 1H), 4.35 (dd, 1H, *J*=2.8 and 12.4 Hz), 4.09 (dd, 1H, *J*=6.1 and 12.4 Hz), 3.77 (s, 3H), 2.19 (s, 3H), 2.15 (s, 3H), 2.09 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 1.79 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 203.05, 170.58, 170.43, 169.76, 169.57, 169.52, 162.48, 146.40, 142.73, 134.41, 130.02, 129.15, 128.89, 128.41, 104.57, 70.36, 69.14, 68.87, 68.39, 61.47, 31.88, 29.72, 20.67, 20.25. Anal. Calcd for $C_{29}H_{33}NO_{12}$: C, 59.28; H, 5.66; N, 2.38. Found: C, 59.14; H, 5.61; N, 2.19.

4.2.9. 6-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-4-cyano-1-methyl-3-phenylpyrid-2-one (18). A mixture of cycloadducts **16a** and **16b** (0.12 g, 0.2 mmol) was poured into a suspension of $Hg(OAc)_2$ (0.1 g, 0.3 mmol) in acetic acid (3 mL) at room temperature and processed as described for **9** to give **18** (0.03 g, 33%); mp 86.5 °C; $[\alpha]_D$ +114.0 (*c* 0.5, chloroform); IR (KBr, cm^{-1}) ν_{max} 2353, 1732, 1695, 1454, 1373, 1217, 1049; ^1H NMR ($CDCl_3$) δ 7.55–7.44 (m, 5H), 6.34 (s, 1H), 6.06 (d, 1H, *J*=4.0 Hz), 5.57 (t, 1H, *J*=4.6 Hz), 5.45 (t, 1H, *J*=5.5 Hz), 5.06 (m, 1H), 4.38 (dd, 1H, *J*=2.8 and 12.5 Hz), 4.11 (dd, 1H, *J*=5.9 and 12.5 Hz), 3.76 (s, 3H), 2.23 (s, 3H), 2.14 (s, 6H), 2.08 (s, 6H), 2.06 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.71, 169.81, 169.48, 160.93, 144.31, 137.31, 132.62, 129.62, 128.29, 119.18, 116.12, 105.73, 69.62, 69.24, 69.02, 68.20, 61.46, 32.14, 20.64, 20.22. Anal. Calcd for $C_{28}H_{30}N_2O_{11}$: C, 58.94; H, 5.30; N, 4.91. Found: C, 58.93; H, 5.27; N, 5.03.

4.2.10. (3a*S*,4*S*,7*R*,7a*R* and 3a*R*,4*R*,7*S*,7a*S*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-4,7-epithio-2,3a,4,5,7,7a-hexahydro-5-methyl-2,7-diphenyl-1*H*-pyrrolo[3,4-*c*]pyridine-1,3,6-trione (22a and 22b). To a suspension of **4** (1.0 g, 1.8 mmol) in dry toluene (15 mL) *N*-phenylmaleimide (0.4 g, 2.2 mmol) was added, and the mixture was refluxed for 12 h. After removal of the solvent, the crude product was purified by flash chromatography (diethyl ether) and the two diastereomeric cycloadducts were separated by preparative thin layer chromatography (diethyl ether). Fast-moving diastereomer: 0.4 g (30%), mp 175–6 °C (dec); $[\alpha]_D$ −33.5 (*c* 0.5, chloroform); IR (KBr, cm^{-1}) ν_{max} 2980, 1723, 1499, 1373, 1217, 1044, 955; ^1H NMR ($CDCl_3$) δ 7.43–7.19 (m, 10H), 6.35 (m, 1H), 6.10

(d, 1H, *J*=2.0 Hz), 5.56 (t, 1H, *J*=2.0 Hz), 5.10 (m, 1H), 4.50 (dd, 1H, *J*=2.6 and 12.5 Hz), 4.19 (dd, 1H, *J*=6.8 and 12.5 Hz), 4.03 (d, 1H, *J*=6.8 Hz), 4.03 (d, 1H, *J*=6.8 Hz), 3.79 (d, 1H, *J*=6.8 Hz), 3.10 (s, 3H), 2.20 (s, 3H), 2.18 (s, 3H), 2.10 (s, 3H), 2.04 (s, 3H), 1.99 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 174.58, 171.75, 170.53, 170.43, 169.99, 169.75, 169.55, 164.46, 131.19, 129.99, 128.99, 128.67, 128.17, 126.33, 80.67, 70.62, 69.55, 69.25, 68.51, 61.45, 55.91, 51.05, 30.69, 21.05, 20.73, 20.60. Anal. Calcd for $C_{35}H_{36}N_2O_{13}S$: C, 58.00; H, 5.01; N, 3.87; S, 4.42. Found: C, 57.81; H, 4.81; N, 3.63; S, 4.01. Slow-moving diastereomer: 0.4 g (30%), mp 120–1 °C (dec); $[\alpha]_D$ +3.0 (*c* 0.5, chloroform); IR (KBr, cm^{-1}) ν_{max} 2994, 1719, 1499, 1373, 1215, 1051; ^{1}H NMR ($CDCl_3$) δ 7.50–7.21 (m, 10H), 5.71–5.63 (m, 3H), 5.10 (m, 1H), 4.28 (dd, 1H, *J*=2.4 and 12.5 Hz), 4.17 (dd, 1H, *J*=4.2 and 12.5 Hz), 3.92 (d, 1H, *J*=6.7 Hz), 3.77 (d, 1H, *J*=6.7 Hz), 3.09 (s, 3H), 2.26 (s, 3H), 2.17 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 175.05, 171.12, 170.85, 170.48, 169.87, 169.68, 167.27, 131.20, 129.84, 129.11, 128.96, 128.77, 128.26, 126.44, 79.06, 70.33, 68.96, 68.13, 66.80, 66.72, 61.66, 53.86, 51.04, 30.57, 20.83, 20.64, 20.45, 20.37. Anal. Calcd for $C_{35}H_{36}N_2O_{13}S$: C, 58.00; H, 5.01; N, 3.87; S, 4.42. Found: C, 57.70; H, 4.85; N, 3.73; S, 4.21.

4.2.11. (1*S*,4*S*)-1-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-1,4-epithio-1,2,4-trihydro-5,8-dihydroxy-2-methyl-4-phenylisoquinolin-3-one (23a) and (1*R*,4*R*)-1-(1′,2′,3′,4′,5′-penta-*O*-acetyl-D-gluco-pentitol-1-yl)-1,4-epithio-1,2,4-trihydro-5,8-dihydroxy-2-methyl-4-phenyl-isoquinolin-3-one (23b). From 1,4-benzoquinone (0.2 g, 2.2 mmol) compounds **23** were obtained as white solids as described for **22**. **23a**: 0.2 g (20%); mp 210 °C (dec); $[\alpha]_D$ +1.0 (c 0.5, chloroform); IR (KBr, cm^{-1}) ν_{max} 2920, 1744, 1696, 1493, 1435, 1375, 1287, 1213, 1065, 955; ^{1}H NMR ($CDCl_3$) δ 8.09–7.43 (m, 5H), 7.23 (s, 1H), 6.58 (d, 1H, *J*=8.9 Hz), 6.51 (s, 1H), 6.42 (d, 1H, *J*=8.9 Hz), 5.88 (d, 1H, *J*=8.5 Hz), 5.64 (dd, 1H, *J*=2.2 and 7.7 Hz), 5.33 (dd, 1H, *J*=2.2 and 8.5 Hz), 4.99 (dd, 1H, *J*=2.5 and 12.4 Hz), 4.38 (s, 1H), 4.01 (dd, 1H, *J*=10.0 and 12.4 Hz), 2.62 (s, 3H), 2.27 (s, 3H), 2.14 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 192.45, 191.92, 177.91, 172.77, 171.03, 170.04, 169.63, 169.21, 145.34, 141.67, 132.77, 130.38, 129.51, 128.57, 128.27, 119.40, 118.82, 81.80, 70.54, 68.96, 68.17, 66.26, 63.71, 62.16, 30.84, 21.31, 21.07, 20.83, 20.46. Anal. Calcd for $C_{31}H_{33}NO_{13}S$: C, 56.44; H, 5.04; N, 2.12; S, 4.86. Found: C, 56.29; H, 5.16; N, 2.03; S, 4.65. **23b**: 0.09 g (7%); mp 115 °C; $[\alpha]_D$ +4.5 (*c* 0.5, chloroform); IR (KBr, cm^{-1}): ν_{max} 3430, 1753, 1493, 1371, 1217, 1047, 955; ^{1}H NMR ($CDCl_3$) δ 8.13–7.46 (m, 5H), 6.56 (d, 1H, *J*=8.9 Hz), 6.43 (d, 1H, *J*=8.9 Hz), 6.27 (d, 1H, *J*=2.4 Hz), 5.61 (dd, 1H, *J*=2.4 and 5.8 Hz), 5.41 (dd, 1H, *J*=5.8 Hz), 5.27 (m, 1H), 4.43 (dd, 1H, *J*=3.8 and 12.3 Hz), 4.14 (dd, 1H, *J*=5.5 and 12.3 Hz), 2.78 (s, 3H), 2.14 (s, 3H), 2.12 (s, 6H), 2.10 (s, 3H), 2.02 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.69, 170.08, 169.87, 169.08, 145.25, 143.02, 132.00, 129.74, 129.56, 128.62, 127.44, 119.31, 119.13, 81.51, 69.58, 68.73, 63.44, 61.42, 30.47, 21.00, 20.85, 20.66. Anal. Calcd for $C_{31}H_{33}NO_{13}S$: C, 56.44; H, 5.04; N, 2.12; S, 4.86. Found: C, 56.22; H, 5.25; N, 2.05; S, 4.58.

4.2.12. (1*S*,4*R*,4a*R*,10a*S* and 1*R*,4*S*,4a*S*,10a*R*)-1-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-1,4-epithio-1,2,4,4a,10a-pentahydro-2-methyl-4-phenylbenzo[*h*]isoquinolin-3,5,10-trione (24a and 24b). From 1,4-naphtoquinone (0.3 g, 2.2 mmol) compounds **24** were obtained as white solids as described for **22**. Fast-moving diastereomer: 0.2 g (10%); mp 105–110 °C; $[\alpha]_D$ +47 (*c* 0.5, chloroform), IR (KBr, cm^{-1}): ν_{max} 2955, 1750, 1686, 1449, 1371, 1215, 1049; ^{1}H NMR ($CDCl_3$) δ 7.89–7.39 (m, 9H), 5.56 (dd, 1H, *J*=1.2 and 8.2 Hz), 5.47 (dd, 1H, *J*=1.3 and 9.1 Hz), 5.24 (d, 1H, *J*=8.2 Hz), 55.02 (m, 1H), 4.22 (dd, 1H, *J*=2.6 and 12.5 Hz), 4.00 (m, 2H), 3.63 (d, 1H, *J*=7.3 Hz), 3.11 (s, 3H), 2.30 (s, 3H), 2.23 (s, 3H), 2.12 (s, 3H), 1.98 (s, 3H), 1.97 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 192.45, 191.92, 175.12, 170.60, 170.42, 169.87, 169.57, 168.15, 137.42, 137.12, 134.46, 129.87, 129.23, 128.84, 128.08, 126.89, 126.20, 79.43, 71.69, 69.11, 68.08, 67.14, 67.01, 61.68, 58.34, 56.79, 30.75, 20.82, 20.61, 20.47. Anal. Calcd for $C_{35}H_{35}NO_{13}S$: C, 59.23; H, 4.97; N, 1.97; S, 4.52. Found: C, 58.76; H, 4.86; N, 1.64; S, 4.55. Slow-moving diastereomer: 0.06 g (3%); mp 135 °C; $[\alpha]_D$ −32 (*c* 0.25, chloroform); IR (KBr, cm^{-1}) ν_{max} 2930, 1760, 1684, 1446, 1371, 1213, 1045; ^{1}H NMR ($CDCl_3$) δ 7.94–7.36 (m, 9H), 5.93 (d, 1H, *J*=2.9 Hz), 5.80 (t, 1H, *J*=3.1 Hz), 5.46 (dd, 1H, *J*=4.9 and 6.2 Hz), 5.15 (m, 1H), 4.44 (dd, 1H, *J*=3.1 and 12.4 Hz), 4.14 (dd, 1H, *J*=5.6 and 12.4 Hz), 3.91 (d, 1H, *J*=7.4 Hz), 3.66 (d, 1H, *J*=7.3 Hz), 3.11 (s, 1H), 2.13 (s, 6H), 2.08 (s, 6H), 2.03 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 192.30, 191.30, 175.42, 170.60, 170.09, 169.75, 169.15, 168.57, 137.41, 136.21, 134.60, 134.23, 130.26, 129.04, 128.90, 127.98, 126.73, 81.73, 69.91, 69.66, 69.18, 67.90, 67.72, 61.48, 58.93, 56.62, 30.53, 20.83, 20.70, 20.59.

4.2.13. 1-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-1,4-epithio-1,2,4-trihydro-5,10-dihydroxy-2-methyl-4-phenylbenzo[*h*]isoquinoline-3-one (25a) and 1-(1′,2′,3′,4′,5′-penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-1,4-epithio-1,2,4-trihydro-5,10-dihydroxy-2-methyl-4-phenylbenzo[*h*]isoquinoline-3-one (25b). A mixture of diastereomers **24a** and **24b** (0.1 g, 0.14 mmol) was treated with silica gel (3.0 g) for 10 days. The reaction mixture was filtered and after washing three times the silica gel with ethyl acetate, combined solutions were concentrated in vacuo to give a mixture of **25a** and **25b**, which were separated by preparative thin layer chromatography (diethyl ether). **25a**: 0.03 g (25%), mp 85 °C (dec); $[\alpha]_D$ −216 (*c* 0.25, chloroform); IR (KBr, cm^{-1}) ν_{max} 1753, 1667, 1593, 1371, 1049; ^{1}H NMR ($CDCl_3$) δ 8.12–7.42 (m, 10H), 6.62 (d, 1H, *J*=0.8 Hz), 5.82 (dd, 1H, *J*=0.8 and 7.1 Hz), 5.59 (dd, 1H, *J*=4.3 and 7.1 Hz), 5.33 (m, 1H), 4.76 (dd, 1H, *J*=2.7 and 12.4 Hz), 4.30 (dd, 1H, *J*=7.9 and 12.5 Hz), 2.84 (s, 3H), 2.23 (s, 3H), 2.15 (s, 3H), 2.11 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 183.04, 179.04, 177.70, 170.75, 170.32, 170.03, 169.70, 169.45, 156.75, 153.07, 134.69, 134.11, 132.25, 131.50, 131.02, 128.93, 128.68, 128.32, 127.98, 126.89, 126.73, 82.57, 70.45, 69.93, 69.08, 65.80, 66.04, 61.44, 32.57, 21.39, 20.78, 20.55. Anal. Calcd for $C_{35}H_{35}NO_{13}S$: C, 59.23; H, 4.97; N, 1.97; S, 4.52. Found: C, 59.45; H, 4.82; N, 1.82; S, 4.48. **25b**: 0.04 g (40%), $[\alpha]_D$ +45 (*c* 0.25, chloroform); IR (KBr, cm^{-1}) ν_{max} 1755, 1666, 1593, 1371, 1049; ^{1}H NMR ($CDCl_3$) δ 8.03–7.26 (m, 10H), 6.47 (d, 1H, *J*=3.8 Hz),

5.58 (t, 1H, J=4.2 Hz), 5.49 (dd, 1H, J=4.8 and 6.1 Hz), 5.30 (m, 1H), 4.40 (dd, 1H, J=3.4 and 12.4 Hz), 4.18 (dd, 1H, J=5.2 and 12.4 Hz), 2.97 (s, 3H), 2.22 (s, 3H), 2.09 (s, 9H), 2.05 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 181.79, 179.03, 178.74, 170.54, 170.27, 169.75, 169.36, 168.90, 156.81, 153.50, 134.45, 134.08, 132.25, 131.70, 131.08, 128.98, 128.75, 128.02, 126.77, 126.35, 82.49, 69.50, 68.99, 68.69, 65.60, 61.51, 30.89, 21.01, 20.75, 20.68, 20.49.

4.2.14. 4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-2,5-dihydro-5-methyl-2,7-diphenyl-1*H*-pyrrolo [3,4-*c*]pyridine-1,3,6-trione (26). A mixture of cycloadducts **22a** and **22b** (0.1 g, 0.2 mmol) was poured into a suspension of $Hg(OAc)_2$ (0.1 g, 0.3 mmol) in acetic acid (3 mL) at room temperature and processed as described for **9** to give **26** (0.03 g, 30%) as a white solid; mp 95 °C (dec); $[\alpha]_D$ +47.0 (*c* 0.5, chloroform); IR (KBr, cm^{-1}) ν_{max} 3472, 2964, 1751, 1719, 1659, 1501, 1447, 1373, 1215, 1045; ^{1}H NMR ($CDCl_3$) δ 7.52–7.35 (m, 5H), 7.59 (d, 1H, J=8.6 Hz), 6.00 (dd, 1H, J=2.3 and 8.7 Hz), 5.19 (dd, 1H, J=2.5 and 7.6 Hz), 5.08 (m, 1H), 4.25 (dd, 1H, J=3.0 and 12.6 Hz), 4.03 (dd, 1H, J=5.6 and 12.6 Hz), 3.88 (s, 3H), 2.16 (s, 6H), 2.08 (s, 3H), 2.05 (s, 3H), 2.00 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.48, 170.24, 169.99, 169.63, 168.66, 164.56, 163.81, 163.69, 142.97, 132.78, 131.50, 131.08, 130.15, 129.95, 129.53, 128.86, 128.59, 127.71, 126.89, 126.50, 108.09, 68.70, 68.60, 67.44, 66.96, 61.35, 35.38, 21.01, 20.73, 20.62, 20.46. Anal. Calcd for $C_{35}H_{34}N_2O_{13}$: C, 60.13; H, 4.96; N, 4.06. Found: C, 60.11; H, 5.02; N, 4.09.

4.2.15. 1-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-2-methyl-4-phenyl-2*H*-isoquinoline-3,5,6-trione (27). A mixture of cycloadducts **23a** and **23b** (0.1 g, 0.2 mmol) was poured into a suspension of $Hg(OAc)_2$ (0.1 g, 0.3 mmol) in acetic acid (3 mL) at room temperature and processed as described for **9** to give **27** (0.02 g, 20%) as a yellowish solid; mp 85 °C (dec); $[\alpha]_D$ −17.0 (*c* 0.25, chloroform); IR (KBr, cm^{-1}) ν_{max} 3480, 2980, 1751, 1643, 1510, 1447, 1373, 1217, 1074; ^{1}H NMR ($CDCl_3$) δ 7.46–7.75 (m, 5H), 7.53 (d, 1H, J=4.1 Hz), 6.01 (t, 1H, J=4.5 Hz), 5.62 (t, 1H, J=5.6 Hz), 5.19 (m, 1H), 4.53 (dd, 1H, J=2.4 and 12.5 Hz), 4.32 (dd, 1H, J=6.7 and 12.5 Hz), 3.81 (s, 3H), 2.71 (s, 3H), 2.14 (s, 3H), 2.09 (s, 3H), 2.08 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 184.22, 183.71, 170.64, 170.02, 169.69, 169.30, 169.21, 163.45, 150.44, 141.72, 138.18, 134.87, 134.75, 133.44, 111.88, 70.07, 69.73, 69.32, 69.24, 61.56, 37.20, 20.77, 20.55. Anal. Calcd for $C_{31}H_{31}NO_{13}$: C, 59.52; H, 4.99; N, 2.24. Found: C, 59.14; H, 4.91; N, 2.19.

4.2.16. 1-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*gluco*-pentitol-1-yl)-2-ethoxy-5-(1,2-diethoxycarbonyl hydrazine)-5-phenyl-3-methylthiazolidin-4-one (28). A suspension of Raney nickel (0.03 g) in acetone (5 mL) was refluxed for 2 h. After cooling at room temperature and decanting the solvent, a solution of cycloadducts **24a** and **24b** (0.1 g, 0.1 mmol) in 2-butanol was added and the reaction mixture was heated at reflux for 2 h. After three washings of the catalyst with 2-butanol, the combined solutions were filtered and the solvent was concentrated in vacuo. The crude mixture was purified by preparative thin layer chromatography (acetonitrile–chloroform 1:9 as eluent) to give **28** (0.03 g, 32%); mp 95 °C; $[\alpha]_D$ −9.5 (*c* 0.25, chloroform); IR (KBr, cm^{-1}) ν_{max} 2970, 1751, 1641, 1447, 1371, 1217, 1049; ^{1}H NMR ($CDCl_3$) δ 8.08–6.88 (m, 9H), 8.17 (d, 1H, J=4.0 Hz), 629.55 (t, 1H, J=4.5 Hz), 6.07 (t, 1H, J=5.7 Hz), 5.59 (m, 1H), 4.83 (d, 1H, J=12.3 Hz), 4.48 (dd, 1H, J=6.5 and 12.3 Hz), 3.84 (s, 3H), 1.74 (s, 6H), 1.68 (s, 3H), 1.60 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 183.31, 182.61, 170.61, 170.02, 169.66, 169.27, 150.79, 136.81, 135.75, 135.23, 134.51, 133.93, 133.78, 128.32, 127.83, 127.36, 126.67, 113.40, 70.61, 69.97, 69.50, 69.33, 61.67, 37.65, 21.01, 20.78. Anal. Calcd for $C_{35}H_{33}NO_{13}$: C, 62.22; H, 4.92; N, 2.07. Found: C, 61.85; H, 4.98; N, 2.19.

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15. Crystal data for compound **23a**: monoclinic, space group $P2_1$, a=13.137(2), b=7.9233(8), c=15.190(2) Å, V=1580.9(4) Å^3, Z=2, d_{calcd}=1.382 Mg/m^3, θ range for data collection=3.00–25.02°, index ranges=$-15\leq h\leq 15$, $-9\leq k\leq 9$, $-14\leq l\leq 17$, (Mo Kα)=0.171 mm^{-1}. For a total of 5779 collected reflections, 4481 were independent reflections [R_{int}=0.0755]. The final R indices were R_1=0.0697, wR_2=0.1330 [$F^2>2\sigma(F^2)$], R_1=0.1312, wR_2=0.1624 (all data). The final difference electron density map contains maximum and minimum peak heights of 0.303 and −0.387 e/Å^3. These data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 146528. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB12 1EZ, UK [fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].