Fluoronucleosides, Isothiocyanato *C*-Nucleosides, and Thioureylene Di-*C*-nucleosides via Cyclic Sulfates

José Fuentes,* Manuel Angulo, and M. Angeles Pradera

Departamento de Química Orgánica, Facultad de Química, Universidad de Sevilla, E-41071 Sevilla, Spain

jfuentes@cica.es

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Cyclic sulfates of *N*- and *C*-nucleosides (D-*ribo* and D-*erythro* configurations, respectively) are used to prepare 3′-fluoro and 3′-azido D-*xylo N*-nucleosides and L-*threo C*-nucleosides. The reduction of the 3′-azido *C*-nucleosides (furan, imidazoline-2-thione, and pyrrole derivatives) gives 3′-amino *C*-nucleosides, which, by reaction with thiocarbonyldiimidazole, are transformed into 3′-isothiocyanato *C*-nucleosides. Reaction of the 3′-amino with the 3′-isothiocyanato *C*-nucleosides gives thioureylene di-*C*-nucleosides, a type of nucleotide analogue with a nonionic bridge isosteric of the phosphate group.

Introduction

In the past decade, the chemistry of cyclic sulfates of diols has been strongly developed.[1] Although some of these cyclic esters had been known for many years, their applications in organic syntheses were very limited, probably due to the lack of a good method of preparation. In 1988, Sharpless[2] reported the oxidation of cyclic sulfites of diols with sodium periodate catalyzed by ruthenium chloride as a new and efficient method for the preparation of cyclic sulfates of diols. The same author also reported several nucleophilic opening reactions of the cyclic sulfates, showing that these compounds have a similar chemical behavior to those of epoxides, although frequently they are more reactive than the latter compounds. Cyclic sulfates are also useful in organic synthesis because they activate a position for nucleophilic attack, simultaneously serving as a protecting group of a second position, frequently adjacent to the first one. In comparison with the corresponding acyclic derivatives, the carbon atoms of the cyclic sulfates exhibit a higher reactivity toward nucleophiles due to the ring strain and the partial double-bond character between the sulfur atom and the ring oxygen atoms.[1] The increase in the synthetic uses of cyclic sulfates has provoked not only the development of new preparation methods but also the revival of described methods. Thus, currently, cyclic sulfates of diols, including sugar derivatives, are prepared mainly in three ways. (a) From cyclic sulfites following the Sharpless method. The starting sulfites are prepared by reaction of the diols with thionyl chloride or *N*,*N*′-thionyldiimidazole.[3,4] (b) Reaction of the diol with sulfuryl chloride. This method, useful in the cases of diol substrates that can react with ruthenium chloride,[5,6] gives good yields with cis rigid cyclic diols and recently has been used with acyclic diols having an electron-withdrawing group.[7,8] (c) Reaction of the diol with *N*,*N*′-sulfuryl diimidazole in the presence of sodium hydride.[9] Following one of these procedures has allowed preparation of different 1,2 and 1,3 sugar derivative cyclic sulfates.[2,10] The data on cyclic sulfates of nucleosides are scarce and limited to *N*-nucleosides.[11]

Azidonucleosides and fluoronucleosides are compounds of pharmaceutical interest, especially due to the success of their use in the treatment of diseases such as AIDS.[12,13] The substitution of a hydroxyl group by a fluorine atom in a sugar derivative can give information on carbohydrate−protein interactions,[14] as the fluorine can act as an acceptor in a hydrogen bond but not as a donor.[15] At the same time, azidonucleosides are the most frequent precursors of aminonucleosides. Several efforts have recently been directed toward the introduction of azido and fluoro groups into the carbohydrate moiety of nucleosides;[16] however, the data on this functionalization using

* Corresponding Author. Phone: 34 95 4557150. Fax: 34 95 4624960.

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cyclic sulfates as intermediates are very few and restricted to *N*-nucleosides.[11b] It has been demonstrated that modifications of the sugar moiety of nucleosides are compatible with their biological activity.[17]

The isothiocyanates are synthetic intermediates of wide versatility. The strong electrophilicity of the NCS group gives the isothiocyanates facility to participate in addition and cycloaddition reactions, and these heterocumulenes are especially useful in heterocycle syntheses.[18] In the last two decades, isothiocyanato derivatives of sugars, mainly glycosyl isothiocyanates, have been widely used in the syntheses of different glycoconjugates[19] such as thioureidosugars,[20] *N*-glycopeptides,[21] nucleoside analogues,[22] and spironucleosides.[23] They have also been employed in the preparation of macrocycles with thiourea spacers.[24] In the field of *N*-nucleosides, the synthesis and chemical and biological properties of 3′-deoxy-3′-isothiocyanatothymidine have been reported.[25] Other 3′- and 5′-isothiocyanato derivatives of thymidine have been used in the preparation of thymidine oligomers with *S*-methylthioureido[26] and guanidino[27] bridges. Isothiocyanato derivatives of uridine, 3′-deoxyuridine,[25b] and adenosine derivatives having the NCS group on the adenine moiety[28] have also been prepared. To the best of our knowledge, there are no bibliographic data on isothiocyanato derivatives of *C*-nucleosides.

The synthesis of analogues of natural oligonucleotides (antisense oligonucleotides) has been a growing research area in the past few years due to the therapeutic activity of these compounds[29,30] as inhibitors of the protein biosynthesis. Several analogues changing the phosphate bridge by positively charged and nonionic isosteric spacers such as guanidino,[27,31] *S*-methylthioureido,[26] amide,[32] carbamate,[33] and fosforamidate[34] have been reported. Some analogues modifying the structure of the heterocyclic base have also been described.[29,30] No data on thioureido derivatives of *C*-nucleosides have been found.

In this paper, we report on the introduction of the fluoro, azido, amino, and isothiocyanato groups into D-erythrofuranosyl *C*-nucleosides of furan, pyrrole, and imidazoline via cyclic sulfates. Some data on similar functionalizations in a 5-*O*-trityladenosine are also reported. 3,3′-Thioureylene di-*C*-nucleosides are obtained by reaction of aminonucleosides and isothiocyanatonucleosides.

Results and Discussion

Cyclic Sulfates. With the aim of studying the regio- and stereoselectivity of the opening reactions of nucleoside cyclic sulfates, we have started from the erythrofuranosyl *C*-nucleosides of furan (**1**, **2**), of imidazoline-2-thione (**3**, **4**), of pyrrole (**6**), and of the dityrityl derivative (**5**) of adenosine, all compounds having a cis diol group. Compounds **1** and **2** were obtained by reaction of D-glucose with ethyl acetoacetate[35] followed by cyclodehydration of the tetritolyl chain.[36] The imidazoline-2-thione *C*-nucleosides **3** and **4** were obtained by cyclodehydration[37] of the acyclic *C*-nucleoside from the reaction of 1-deoxy-1-*p*-tolylamino-D-fructose with methyl isothiocyanate.[38] As the separation of the pairs of anomers **1**,**2** and **3**,**4** is more difficult than the resolution of the corresponding cyclic sulfates (**7**−**10**), we have used the anomeric mixtures to prepare these esters. The *N*-nucleoside derivative **5** was prepared by tritylation of adenosine.[39] The pyrrole derivative β-*C*-nucleoside **6** was prepared from D-glucose and 2,4-pentanedione, followed by cyclodehydration of the resulting product.[40] The reaction of the pairs of anomers **1**,**2** and **3**,**4** gives the corresponding cyclic sulfates **7**,**8** and **9**,**10**, respectively, as pairs of anomers, and the reaction of **5** with sulfuryl chloride and triethylamine at 0 °C gives **11** as sole product (Scheme 1). The mixture of **7** and **8** could be easily resolved, whereas in the case of the mixture of **9** and **10**, the β-anomer **9** was the major product and the minor product, the α-anomer **10**, of easy decomposition, could be characterized only by NMR and FAB MS data. From the reaction of the pyrrole derivative **6** with sulfuryl chloride originated a complex mixture of products, among which small amounts of the cyclic sulfate **12** and of the chloro derivative in position 4 of the pyrrole ring were identified. The formation of HCl in the reaction medium

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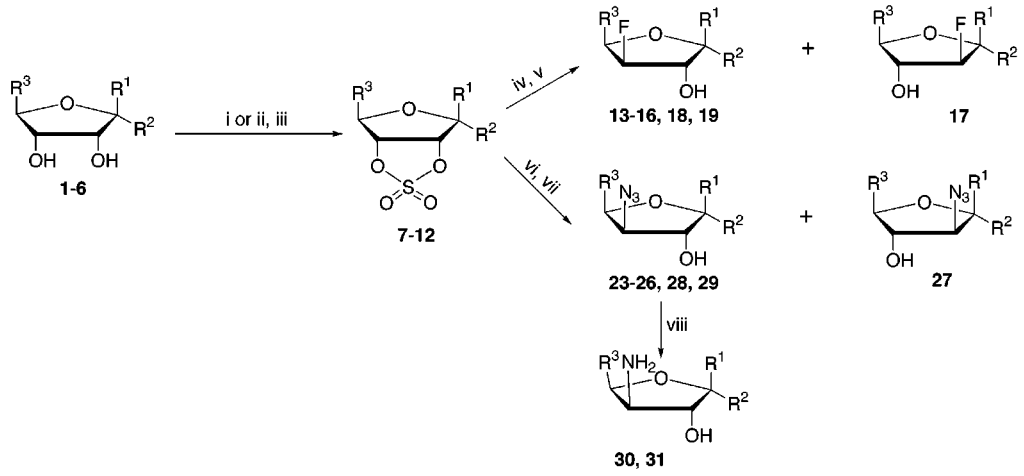
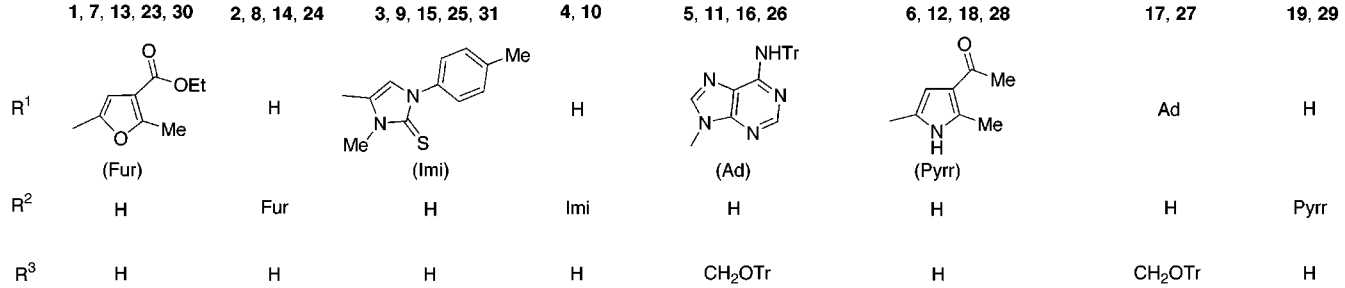
Scheme 1[a]





[a] Reagents: For compounds **7**−**11**, (i) Cl_2SO_2/Et_3N, 0 °C, yields 70−85%. For compound **12**, (ii) NaH, DMF, 0 °C; (iii) Im_2SO_2, DMF, −40 °C; (iv) $Et_4NF{\cdot}2H_2O$, Me_2CO, rt; (v) H_2SO_4/H_2O, THF, rt, yields 40−71%; (vi) NaN_3/DMF, 30 °C; (vii) H_2SO_4/H_2O, THF, rt, yields 72−88%; (viii) H_2, Pd/C (10%), MeOH, rt, yields 81−93%.

produces the fast decomposition of the mixture, probably through acid-catalyzed anomeric equilibria of chlorinated and non-chlorinated products.[41] To avoid these difficulties, the esterification reaction was performed using NaH in dry DMF and after sulfuryl diimidazole at −40 °C. In these conditions, the cyclic sulfate **12** was isolated in 87% yield. The resonance signals[42] of H-2′, H-3′, C-2′, and C-3′ were deshielded with respect to the same signals for the parent compounds, supporting the formation of the cyclic esters. The $J_{1',2'}$ value in tetrahydrofuran derivatives is not indicative of the anomeric configuration.[43] We proposed the β-configuration for compounds **7**, **9**, **11**, and **12** because in the starting materials, the β-product was the major (in the case of **1** and **3**) or the only (in the case of **5** and **6**) product and the reaction conditions (basic medium) do not favor anomeric equilibria.[35,41,44,45] Moreover, the ^{13}C resonance for C-1′ in all the studied compounds (α- and β-anomers) appeared at a lower field when the substituents on C-1′ and C-2′ were in a trans relationship than when these substituents are in a cis relationship. This observation coincides with reported data for related *C*- and *N*-nucleoside derivatives.[43,46]

Fluoronucleosides. The reaction of the cyclic sulfates **7**−**9**, **11**, and **12** with tetraethylammonium fluoride dihydrate[47] in acetone (for **7**−**9**) or DMF (for **11**−**12**) at room temperature and subsequent aqueous H_2SO_4 hydrolysis give the corresponding fluoronucleosides **13**−**19** (Scheme 1). In the case of the β-furyl *C*-nucleoside **7**, the regioselection was complete and the 3′-fluoro derivative **13** was the only product isolated; this regioselection is attributable to the steric hindrance on position 2′ of the β-furyl group. In the case of the corresponding α-anomer **8**, the 3′-fluoro derivative **14** was isolated as the major product, together with the furyl-furan derivative **20** as a minor compound. Chromatographic data reveal that the formation of **20** takes place during the first step of the reaction, that is, in the treatment with the fluoride anion, and not in the subsequent hydrolysis. The fluoride anion is a hard base, easily promoting E2 reactions. Thus, the attack of fluoride (Figure 1) on H-1′ produces the conjugate intermediate **21**, which undergoes a new β-elimination to give the aromatic compound **20**. The formation of **20** is an additional support for the α-anomeric configuration of **8** and indirectly in support of that for **7**, as only the α-anomer can adopt conformations such as $^3T_2$ and E_2 (Figure 1), with a trans relationship between the groups participating in E2 elimination to give a conjugate product (**21**). Nevertheless, the substitution on C-3′, to produce **14**, predominates over this elimination. The NMR data of **20** showed no signals for tetrahydrofuran protons and carbons.

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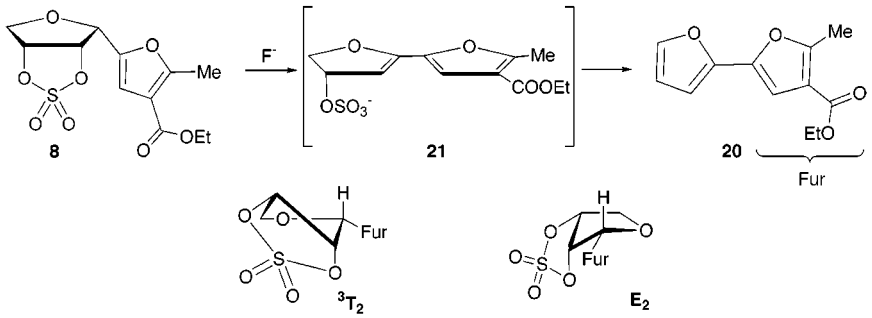

Figure 1.

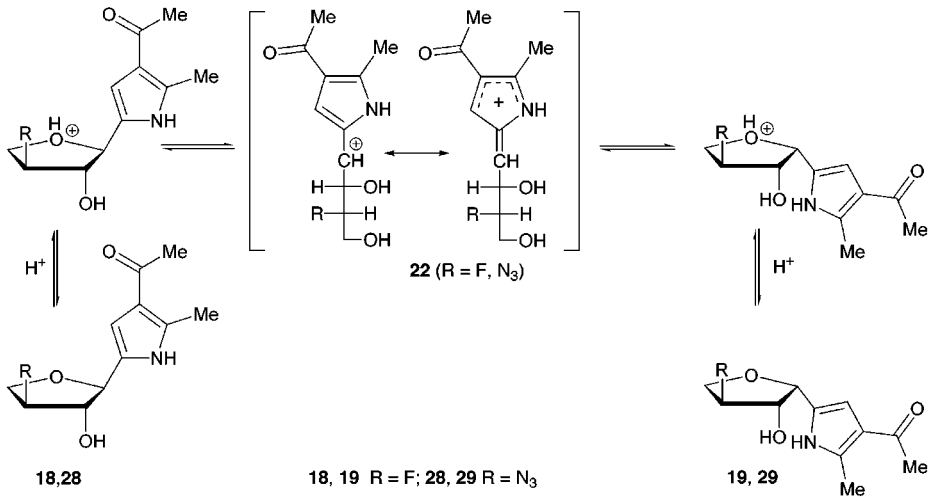

Figure 2.

The reaction of the imidazoline *C*-nucleoside cyclic sulfate **9** with tetraethylammonium fluoride was parallel to that for **7**, and only the 3′-fluoroderivative **15** was isolated.

Starting from the *β*-erythrofuranosylpyrrole derivative **12**, in the conditions described above, the α(**18**) and *β*-(**19**) 3′-fluoro *C*-nucleosides were obtained.[48] The regioselection for the introduction of the fluoro group was complete, but acid-catalyzed anomerization took place. It is reported[40] that tetrahydroxybutylpyrroles undergo reversible cyclodehydration in acid medium more easily than similar derivatives of the other heterocycles. We think that the first product of the fluorination of **12** is the α-L-treofuranosyl derivative **18**, which in the acid medium of the step of hydrolysis (see Scheme 1) undergoes partial anomerization through the strongly stabilized cation **22** (Figure 2) to produce the mixture of anomers. Under the conditions of the opening reaction, the α-anomer **18** is the major product. However, treatment of this product in slightly acidic medium at 40 °C for 7 days produces a 1:2 ratio of **18** to **19**. Consequently, **18** is the product of kinetic control, and **19** is the more thermodynamically stable. No similar equilibria were observed in the cases of the furan and imidazoline derivatives, probably due to the low stabilization of a carbocation similar to **22**.

The opening reaction of the cyclic sulfate of the adenosine derivative **11** produced the two regioisomers **16** and **17**, the 3′-fluoroderivative **16** being the major product (11:1 ratio roughly). This difference of behavior with respect to *C*-nucleosides **7**−**10** and **12** is due to the steric hindrance of the bulky CH_2OTr group on the C-3′ position and the increase in electrophilicity of position C-2′, originating from the neighboring nitrogen atom.

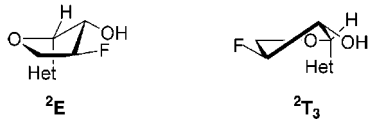

Figure 3.

The NMR data of the fluoro derivatives **13**−**16**, **18**, and **19** confirmed the proposed structures. The resonances of C-3′ ($95.2 < \delta_{C-3'} < 98.1$ ppm) and H-3′ ($5.04 < \delta_{H-3'} < 5.16$ ppm) appeared to be deshielded with respect to the corresponding signals for C-2′ and H-2′. The coupling constant values $J_{H3'-F}$ ($50.8 < J_{H3'-F} < 52.7$ Hz) and $J_{C3'-F}$ ($180.2 < J_{C3'-F} < 188.6$ Hz) are in the range for $^2J_{HF}$ and $^1J_{CF}$ couplings.[49] The ^{1}H NMR spectra of the 3-fluoro-*β*-L-threofuranosyl *C*-nucleosides **14** and **19** showed $^4J_{H1',F}$ in the range of 3.1−3.4 Hz, indicative of a W arrangement between the corresponding nuclei and, consequently, of ^2E and $^2T_3$ conformations (Figure 3). This is a confirmation of the *β*-L-anomeric configuration for these compounds, as only *β*-L-*threo* anomers can adopt conformations with a W arrangement between H-1′ and F-3′.

The NMR data of compound **17** were indicative of the presence of the fluorine atom in the position C-2′. The ^5J

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Table 1. Selected Spectroscopic Data (*ν*/cm, *δ* ppm)[a,b] for Compounds 23−51

compd	$\nu(N_3)$[c]	ν(NCS)[c]	δH-3′	δC-2′	δC-3′	δNCS	Δδ(C-3′)[d]
23	2103		4.06	79.5	67.0		
24	2106		4.21	76.4	66.9		
25	2101		4.02	79.5	67.6		
26	2108		4.20	79.4	65.4		
27	2110		4.31[f]	67.9	75.6		
28[g]	2103		4.10	80.8	68.0		
29[g]	2103		4.23	77.0	67.3		
30			3.43	81.9	59.7		
31			3.47	81.5	59.7		
32	2103		4.08	86.3	65.6		
33			3.57	89.6	57.8		
34		2077	4.20	87.3	61.2	134.9	−4.4
35	2101		4.11	86.2	65.5		
36	2099		4.12	85.6	65.7		
37	2103		4.10	80.7	65.8		
38	2104		4.30	77.8	64.8		
39	2104		4.15	80.0	65.8		
40	2104		4.15	82.4	65.8		
41	2104		4.22	78.4	65.5		
42			3.51	84.4	58.6		
43			3.73	80.7	57.1		
44			3.60	83.5	58.5		
45			3.68	83.7	57.4		
46			3.65	82.0	57.9		
47		2060	4.23	80.8	61.1	135.7	−4.7
48		2070	4.44	79.9	60.1	137.1	−4.7
49		2074	4.26	79.9	61.1	137.3	−4.7
50		2076	4.20	83.1	61.1	136.9	−4.7
51		2070	4.69	77.4	60.5	132.5	−5.0

[a] For NMR frequencies, see Experimental Section. [b] NMR data are obtained in $CDCl_3$ except for the indicated compounds. [c] KBr disks. [d] Δδ(C-3′) = δC-3′ (isothiocyanate) − δC-3′ (azide). [e] In Me_2SO-d_6. [f] H-2′ in this case. [g] Data for **28** and **29** were obtained from a mixture of these regioisomers.

value between H-8 (adenine ring) and C2′−F, described[50] for other 2′-fluoroadenosine derivatives, was observed.

Azido-, Amino-, and Isothiocyanato-Nucleosides. The treatment of the cyclic sulfates **7**−**9**, **11**, and **12** with sodium azide in DMF at 30 °C and subsequent aqueous H_2SO_4 hydrolysis gives the azidonucleosides **23**−**29** (Scheme 1). In the cases of the compounds **7**−**9**, the opening of the cyclic ester ring was, as in the cases of the fluorination reactions, completely regioselective and only the 3′-azido derivatives **23**−**25** were isolated. For compound **8**, the high nucleophilicity of the azido anion favored the substitution reaction to produce **24**, and no formation of the elimination product **20** was observed (see above). For the same respective reasons discussed for fluorination reactions, the opening of the cyclic sulfates **11** and **12** produces separable mixtures of regioisomers **26**,**27** and of anomers **28**,**29** (Figure 2), respectively. In the case of the adenine derivative **11** the major product is the 3′-azido derivative **26**, whereas in the case of **12**, the major compound is the α-anomer[48] **28** (**28**:**29** ratio of roughly 5:1). NMR and IR spectroscopic data of **23**−**29** (Table 1) supported the proposed structures. All the cases showed the IR absorption at ≅ 2100 cm^{-1} corresponding to the azido group. The presence of this group was also confirmed by the *δ* values of H-3′, C-3′, and C-2′.

Catalytic (Pd/C) hydrogenation of the azido *C*-nucleosides **23** and **25** gave the 3′-amino-α-L-*C*-nucleosides **30** and **31**, respectively. For **23**, the reaction time was 15 min and **30** was obtained in a virtually quantitative yield; however, for **25**, due to the presence of the sulfur atom, 28 h of reaction time and several additions of catalyst were necessary, the yield being 81%.

The simultaneous presence in a sugar derivative of *β*- and *γ*-located hydroxyl and isothiocyanato groups easily produces cyclic thiocarbamates.[23] Consequently, and with the aim of preparing isothiocyanato derivatives of nucleosides and after thioureylene-dinucleosides, the protection of the hydroxyl group was necessary. This protection was carried out on the azido derivatives, and protecting groups easy to remove in the presence of thiourea groups were convenient. The first attempt was to use benzyl bromide as a protecting reagent and to carry out the azido→amino transformation in conditions compatible with the presence of a benzyloxy group. Thus, treatment of the furan azido *C*-nucleoside **23** with benzyl bromide in the presence of a soft base that does not affect the ester group[51] gave the benzyl derivative **32** (Scheme 2), which was further manipulated until transformation into the isothiocyanate **34** (see below), but the overall yield (**23**→**34**) was 34%.

The benzylation of the imidazoline-2-thione-*C*-nucleoside **25** gave (Scheme 2) the expected product **35** in low yield, the main compound being the oxoderivative **36** ($\nu_{C=O}$ 1690 cm^{-1}, $\delta_{C=O}$ 152.4 ppm), coming from the hydrolysis of the thiocarbonyl group. Related desulfuration has been observed during S-benzylation reactions of N-monosubstituted imidazoline-2-thiones.[52]

Taking these results into account, we attempted to use the acetyl as an O-protecting group, which is easy to remove, use reaction conditions that minimize the O→N acetyl migration, and avoid the thiocarbonyl hydrolysis.

The acetylation of the azido *C*-nucleosides **23**−**25**, **28**, and **29** with acetic anhydride and pyridine gave the corresponding O-acetylderivatives **37**−**41** (Scheme 2). In the case of the pyrrole derivatives, we started with the mixture of anomers **28**,**29**, which was conducted to a mixture of **40** and **41**, which could be chromatographically separated for characterization.

Catalytic hydrogenation at room temperature for different times (see Experimental Section) of the azido derivatives **32** and **37**−**41** produced the corresponding 3′-amino-3′-deoxy-*C*-nucleosides **33** and **42**−**46** (Scheme 2). The reduction of the 3′-azido pyrrole derivatives was carried out on the mixture of anomers **40**,**41** (α:*β* ratio of 5:2), but the resulting products **45** and **46** were isolated as pure compounds by chromatography. The reduction time for the imidazoline-2-thione **39** was longer than that for the rest of the azido compounds, and a major amount of catalyst was necessary; under these conditions, some deacetylation took place and a small amount of **31** was detected. Related de-O-acetylations have been reported. No significant O→N transacylation for **42**−**46** was observed.

Reaction of the 3′-amino *C*-nucleosides **33** and **42**−**46** with *N*,*N*′-thiocarbonyldiimidazole in dichloromethane at room temperature gave (Scheme 2) the corresponding 3′-deoxy-3′-isothiocyanato *C*-nucleosides **34** and **47**−**51**, respectively, in good yields. The use of *N*,*N*′-thiocarbonyldiimidazole[53] as a isothiocyanatation reagent is especially useful in the case of pyrrole derivatives **50** and **51**, as the basic character of the imidazole avoids anomeric

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(51) Mori, S.; Ohno, T.; Harada, H.; Aoyama, T.; Shioiri, T. *Tetrahedron* **1991**, *47*, 5051−5070.

(52) Fuentes, J.; Molina, J. L.; Caballero, A.; Pradera, M. A. *J. Carbohydr. Chem.* **1997**, *16*, 93−107.

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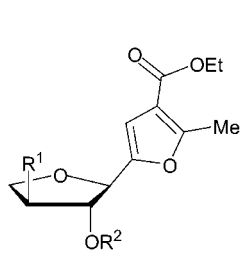
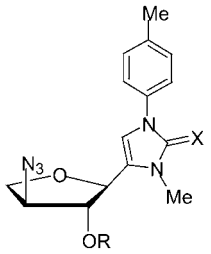
Scheme 2[a]



23-34



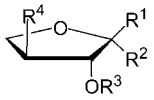
25

23 $\xrightarrow{i}$ **32** $\xrightarrow{ii}$ **33** $\xrightarrow{iii}$ **34**

2 5 $\xrightarrow{iv}$ **35** + **36**

	23	**32**	**33**	**34**
R^1	N_3	N_3	NH_2	NCS
R^2	H	Bn	Bn	Bn

	25	**35**	**36**
R	H	Bn	Bn
X	S	S	O



23-25, **28**, **29** $\xrightarrow{v}$ **37-41** $\xrightarrow{vi}$ **42-46** $\xrightarrow{vii}$ **47-51**

	23	**24**	**25**	**28**	**29**	**37**	**38**	**39**	**40**	**41**
R^1	Fur[b]	H	Imi	Pyrr	H	Fur	H	Imi	Pyrr	H
R^2	H	Fur	H	H	Pyrr	H	Fur	H	H	Pyrr
R^3	H	H	H	H	H	Ac	Ac	Ac	Ac	Ac
R^4	N_3	N_3	N_3	N_3	N_3	N_3	N_3	N_3	N_3	N_3

	42	**43**	**44**	**45**	**46**	**47**	**48**	**49**	**50**	**51**
R^1	Fur	H	Imi	Pyrr	H	Fur	H	Imi	Pyrr	H
R^2	H	Fur	H	H	Pyrr	H	Fur	H	H	Pyrr
R^3	Ac	Ac	Ac	Ac	Ac	Ac	Ac	Ac	Ac	Ac
R^4	NH_2	NH_2	NH_2	NH_2	NH_2	NCS	NCS	NCS	NCS	NCS

[a] Reagents: (i) BrBn/Ag_2O, DMF, yields 70%; (ii) H_2, Pd/C(10%), MeOH, yields 96%; (iii) Im_2CS, CH_2Cl_2, yields 69%; (iv) BrBn/NaH, DMF, rt, yields 29% (**35**), 41% (**36**); (v) Ac_2O/Py, 0 °C, yields 81−88%; (vi) H_2, Pd/C (10%), yields 66−89%; (vii) Im_2CS, CH_2Cl_2, rt, yields 72−90%. [b] See Scheme 1.

equilibria such as that discussed for **18**, **19**, **28**, and **29** (Figure 2). Nevertheless, the NMR data for **51** have to be obtained in Me_2SO-d_6, as in deuteriochloroform anomerization took place.

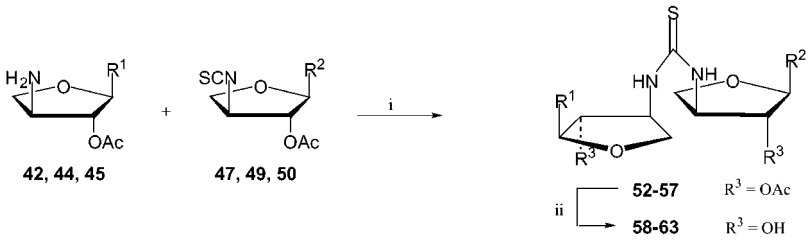
It is interesting to note that the overall yield for the sequence **23** → **37** → **42** → **47** (acetyl derivatives) is 65%, instead of the 34% of the parallel sequence **23** → **32** → **33** → **34** (benzyl derivatives).

The structure of the acetyl derivatives **37**−**41** was supported on analytical and spectroscopic data. The resonance of H-2′ (see Experimental Section) appeared ≈1 ppm deshielded with respect to the same signal for the parent compounds **23**−**25**, **28**, and **29**, indicating the esterification of OH-2 and, consequently, confirming the position of the azido group. This conclusion was also supported on the basis of the *β*-effects for the resonances of C-1′ and C-3′ (Table 1 and Experimental Section). The amino group of **33** and **42**−**46** was evident from a strong shielding (7−8 ppm) in the resonance of C-3′ and small changes in the resonances of C-2′ and C-4′ (deshielding of ≈3 ppm) and of H-3′ (shielding of ≈0.6 ppm). The isothiocyanato group of **34** and **47**−**51** was supported on the basis of the IR absorption at 2060−2077 cm^{-1} and the ^{13}C resonance at 132.5−137.1 ppm. The introduction of the NCS group in position C-3′ produced an increase in the *δ* values for H-3′ and C-3′ (see Table 1) with respect to the same signal in the amino precursors **33** and **42**−**46**. When the resonance of C-3′ for the isothiocyanates **34** and **47**−**51** is compared with the same signal for the azido derivatives **32** and **37**−**41**, an almost constant shielding of 4.7 ppm is observed (Table 1).

Thioureylene Di-*C*-nucleosides. With the aim of having dinucleotide analogues with a thiourea bridge, we have prepared (Scheme 3) symmetric (**52**−**54**) and nonsymmetric (**55**−**57**) thioureylene di-*C*-nucleosides. Thus, the reaction of the amino *C*-nucleosides **42**, **44**, and **45** with the corresponding 3′-isothiocyanatoerythrofuranosides **47**, **49**, and **50** in acetone (for **52**, **53**, and **55**) or DMF (for **54**, **56**, and **57**), and under stringently anhydrous conditions, yielded the thiourea derivatives **52**−**57**, whose structures were based on analytical and spectroscopic data. In all the cases, the FAB MS showed pseudomolecular ions $(M + H)^+$ or $(M + Na)^+$. The C═S of the thiourea spacer resonated at 182 ppm, as in related di-, tri-, and tetrasaccharides with one thioureylene group.[20c] Broad NMR signals for the resonances of H-3 (*δ* 4.70−4.76 ppm) and C-3 (*δ* 59.6−60.2 ppm) of the sugar moieties also supported the presence of the thiourea group. This group was also evident from the EI MS, which showed the cleavages of the N−CS bonds as main fragmentations.

Deacylation with NaOMe of compounds **52**−**57**, under conditions that do not affect the thioamido group,[22] gave the corresponding hydroxyl derivative **58**−**63** in almost

Scheme 3[a]



	42	44	45	47	49	50
R^1	Fur[b]	Imi	Pyrr	-	-	-
R^2	-	-	-	Fur	Imi	Pyrr

	52	53	54	55	56	57	58	59	60	61	62	63
R^1	Fur	Imi	Pyrr	Imi	Pyrr	Pyrr	Fur	Imi	Pyrr	Imi	Pyrr	Pyrr
R^2	Fur	Imi	Pyrr	Fur	Fur	Imi	Fur	Imi	Pyrr	Fur	Fur	Imi

[a] Reagents: (i) Me_2CO or DMF, 40 °C, yields 80−100%; (ii) NaOMe/MeOH, yields 100%. [b] See Scheme 1.

quantitative yield. The structures **58**−**63** were supported on the basis of NMR and MS data.

Conclusions

The nucleophilic opening of nucleoside cyclic sulfates is a regio- and stereoselective method for preparing 3′-fluoro and 3′-azido nucleosides, particularly L-*threo C*-nucleosides and D-*xylo N*-nucleosides. The reaction of 3-amino-3-deoxy *C*-nucleosides (derived from furan, imidazole, and pyrrole) with thiocarbonyldiimidazole is an experimentally easy and high-yielding procedure for preparing isothiocyanato *C*-nucleosides, which by reaction with amino *C*-nucleosides give access to thioureylene di-*C*-nucleosides, a new type of dinucleotide analogue.

Experimental Section

General Procedures. Melting points are uncorrected. Tubes of 1 cm and solutions in CH_2Cl_2 were used for measurement of specific rotations. IR spectra were recorded for KBr disks on a FTIR spectrophotometer. ^1H (and ^{13}C NMR) spectra were recorded at 500 (125.7) and/or 300 (75.5) MHz. Chemical shifts are given in parts per million, and tetramethylsilane was the internal standard. Proton assignments were confirmed by homonuclear 2D COSY correlated experiments. Heteronuclear 2D correlated spectra were obtained in order to assist in carbon resonance assignments. Mass spectra (EI and FAB) were recorded with a resolution of 1000 or 10 000 (10% valley definition). For the FAB spectra, ions were produced by a beam of xenon atoms (6−7 keV), using 3-nitrobenzyl alcohol and thioglycerol as a matrix and NaI as a salt. The MS, IR, and NMR (^1H and ^{13}C) data of all the prepared compounds are given in Supporting Information. TLC was performed on silica gel HF_{254}, with detection by UV light or charring with H_2SO_4. Silica gel 60 (70−230 and 230−400 mesh) was used for preparative chromatography. The term "conventional acetylation" means treatment with Ac_2O−pyridine (1:1 v/v, 10 mL for 1 g of sample) overnight. The reaction mixture is then poured into ice−water and extracted with CH_2Cl_2, and the organic layer is washed with 2N H_2SO_4 and saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated.

General Procedure for the Preparation of Compounds 7−12. To a cooled (0 °C) stirred solution of Et_3N (*x* mL) and the corresponding erythronucleoside **1**−**6** (*m* g) in EtOAc (*y* mL) under argon was added a solution of Cl_2SO_2 (*z* mL) in EtOAc (*y* mL). The reaction was controlled by TLC. After *t* min, the reaction mixture was washed with water, dried ($MgSO_4$), filtered, and evaporated to dryness. The residue was purified by column chromatography.

3-Ethoxycarbonyl-2-methyl-5-(2′,3′-*O*-sulfonyl-*β*-D-erythrofuranosyl)furan (7): From **1** + **2** (9:2); *x* = 12.5 mL, 88.75 mmol; *y* = 90 mL; *z* = 2.75 mL, 33.87 mmol; *m* = 1.720 g, 5.434 mmol; *t* = 3 h and 30 min; TLC, dichloromethane. Column chromatography, ether/petroleum ether (1:2 → 2:1), yielded **7** and **8**. Compound **7** was an amorphous solid (1.48 g, 85%); mp 74−77 °C from ether/petroleum ether; $[\alpha]^{25}_D$ −77 (*c* 1.2, dichloromethane). Anal. Calcd for $C_{12}H_{14}O_8S$: C, 45.28; H, 4.43. Found: C, 45.49; H, 4.39.

3-Ethoxycarbonyl-2-methyl-5-(2′,3′-*O*-sulfonyl-α-D-erythrofuranosyl)furan (8) was an amorphous solid (280 mg, 72%); mp 78−80 °C from ether/petroleum ether; $[\alpha]^{20}_D$ −87 (*c* 1.6 dichloromethane). Anal. Calcd for $C_{12}H_{14}O_8S$: C, 45.28; H, 4.43. Found: C, 45.50; H, 4.45.

1,3-Dihydro-3-methyl-4-(2′,3′-*O*-sulfonyl-*β*-D-erythrofuranosyl)-1-*p*-tolyl-2*H*-imidazole-2-thione (9): From **3** + **4** (7:1); *x* = 3.5 mL, 24.85 mmol; *y* = 35 mL; *z* = 0.75 mL, 9.24 mmol; *m* = 0.79 g, 2.258 mmol; *t* = 3 h and 30 min; TLC, dichloromethane/methanol (40:1). Column chromatography, dichloromethane/methanol (100:1→60:1), yielded **9** and **10**. Compound **9** was as an amorphous solid (585 mg, 70%); $[\alpha]^{25}_D$ −133 (*c* 1.1, dichloromethane). Anal. Calcd For $C_{15}H_{16}N_2O_5S_2$: C, 48.90; H, 4.38; N, 7.60. Found: C, 48.94; H, 4.44; N, 7.62.

1,3-Dihydro-3-methyl-4-(2′,3′-*O*-sulfonyl-α-D-erythrofuranosyl)-1-*p*-tolyl-2*H*-imidazole-2-thione (10): FAB MS *m*/*z* 391 ([M + Na]$^+$).

***N*^{6},5′-*O*-Dirityladenosine 2′,3′-cyclic Sulfate (11):** From *N*,^{6}5′-*O*-dirityladenosine (**5**); *x* = 4.2 mL (29.82 mmol); *y* = 25 mL; *z* = 0.8 mL (9.85 mmol); *m* = 1.36 g (1.757 mmol); *t* = 6 h; TLC, ether/petroleum ether (3:1). Column chromatography, dichloromethane:methanol (100:1→60:1), yielded **11** as an amorphous solid (1.20 g, 70%): mp 201−205 °C from acetonitrile; $[\alpha]^{20}_D$ −1.7 (*c* 1.2 dichloromethane). Anal. Calcd for $C_{48}H_{39}N_5O_6S$: C, 70.83; H, 4.83; N, 8.61. Found: C, 70.91; H, 4.94; N, 8.88.

3-Acetyl-2-methyl-5-(2′,3′-*O*-sulfonyl-*β*-D-erythrofuranosyl)pyrrole (12). To a cooled (0°C), stirred solution of 3-acetyl-5-(*β*-D-erythrofuranosyl)-2-methylpyrrole (**6**) (513 mg, 2.280 mmol) in DMF (11 mL) under argon was added sodium hydride (80% in liquid paraffin). The reaction mixture was stirred for 10 min at 0°C and then 20 min at room temperature. The mixture was cooled to −40°C, and a solution of *N*,*N*′-sulfuryldiimidazole (0.685 g, 3.46 mmol) in DMF (7 mL) was added dropwise; the mixture was stirred for 1 h, and the reaction was controlled by TLC (3:1 EtOAc/petroleum ether). The reaction mixture was diluted with EtOAc and washed with water. The aqueous layer was extracted with EtOAc, and the combined organic layers were dried ($MgSO_4$), filtered, and evaporated to dryness. The residue was purified by column chromatography (3:1 EtOAc/petroleum ether). The yield was 570 mg (87%) as an amorphous solid: $[\alpha]^{25}_D$ −120 (*c* 1.3,

dichloromethane). Anal. Calcd for $C_{11}H_{13}NO_6S$: C, 45.99; H, 4.56; N, 4.88. Found: C, 46.23; H, 4.57; N, 5.13.

General Procedure for the Preparation of Fluoronucleosides 13−19. To a solution of the corresponding cyclic sulfate **7**−**9**, **11**, or **12** (*m* g) in DMF or acetone (*x* mL) at room temperature was added tetraethylammonium fluoride dihydrate (*y* mg). The reaction mixture was stirred for t_1 h, and the reaction was controlled by TLC. The solvent was removed in vacuo, and the residue was stirred with THF (*x* mL), H_2SO_4 (50 μL/mmol), and H_2O (18 μL/mmol) at room temperature for t_2 h, diluted with EtOAc, and washed with saturated aqueous sodium hydrogencarbonate. The organic layer was washed with water, dried ($MgSO_4$), filtered, and evaporated to dryness. The residue was purified by column chromatography.

5-(3′-Deoxy-3′-fluoro-α-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (13): From **7**; *m* = 98 mg (0.308 mmol); acetone, *x* = 1.6 mL; *y* = 88 mg (0.474 mmol); t_1 = 9 h; t_2 = 3 h; TLC, dichloromethane/methanol (4:1). Column chromatography, ether/petroleum ether (1:1), yielded 50 mg (63%) as an amorphous solid: $[\alpha]^{26}_D$ −60 (*c* 1.2, dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.63 (s, 1 H), 5.08 (ddt, 1 H, *J* = 1.4, 4.0, 52.7 Hz), 4.69−4.61 (m, 2 H), 4.27 (q, 2 H, *J* = 7.1 Hz), 4.22 (ddd, 1 H, *J* = 11.4, 22.2 Hz), 4.10 (ddd, 1 H, *J* = 34.4 Hz), 2.56 (s, 3 H), 1.33 (t, 3 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.9, 159.6, 148.9, 114.2, 109.4, 97.9, 80.4, 79.3, 71.8, 60.2, 14.2, 13.7; HREI MS *m*/*z* calcd for $C_{12}H_{15}FO_5$ 258.0903 ($[M]^{\bullet+}$), found 258.0902.

5-(3′-Deoxy-3′-fluoro-β-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (14): From **8**; *m* = 83 mg (0.261 mmol); acetone, *x* = 1.3 mL; *y* = 75 mg (0.404 mmol); t_1 = 6 h; t_2 = 0.5 h; TLC, dichloromethane/methanol (4:1). Column chromatography, ether/petroleum ether (1:1), yielded **14** (27 mg, 40%) and **20** (11 mg, 20%). Compound **14** was an amorphous solid: $[\alpha]^{23}_D$ −15 (*c* 0.9, dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.71 (s, 1 H), 5.14 (dd, 1 H, *J* = 3.5, 51.8 Hz), 5.02 (bt, 1 H, *J* = 3.1 Hz), 4.38 (dd, 1 H, *J* = 11.0 Hz), 4.34 (ddd, 1 H, *J* = 11.3, 40.2 Hz), 4.28 (c, 2 H, *J* = 7.1 Hz), 4.05 (dd, 1 H, *J* = 27.8 Hz), 2.56 (s, 3 H), 1.32 (t, 3 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.7, 159.8, 146.9, 114.5, 110.8, 96.4, 76.7, 75.3, 71.7, 60.2, 14.2, 13.7. Anal. Calcd for $C_{12}H_{15}FO_5$: C, 55.81; H, 5.85. Found: C, 55.80; H, 5.78.

3-Ethoxycarbonyl-5-(fur-2′-yl)-2-methylfuran (20): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, 1 H, *J* = 1.7 Hz), 6.77 (s, 1 H), 6,54 (d, 1 H, *J* = 3.3 Hz), 6.45 (dd, 1 H), 4.30 (q, 2 H, *J* = 7.1 Hz), 2.63 (s, 3 H), 1.36 (t, 3 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.8, 158.4, 145.7, 144.3, 142.0, 115.1, 111.3, 105.5, 60.2, 14.3, 13.8; HREI MS *m*/*z* calcd for $C_{12}H_{12}O_4$ 220.0736 ($[M]^{\bullet+}$), found 220.0735.

4-(3′-Deoxy-3′-fluoro-α-L-threofuranosyl)-1,3-dihydro-3-methyl-1-*p*-tolyl-2*H*-imidazole-2-thione (15): From **9**; *m* = 100 mg (0.271 mmol); acetone, *x* = 1.4 mL; *y* = 76 mg (0.409 mmol); t_1 = 3 h; t_2 = 2 h; TLC, dichloromethane/methanol (20:1). Column chromatography, dichloromethane/methanol (40:1), yielded 50 mg (60%) as an amorphous solid: $[\alpha]^{27}_D$ −15 (*c* 1.0, dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.25 (m, 4 H), 6.83 (s, 1 H), 5.04 (dd, 1 H, *J* = 3.4, 51.9 Hz), 4.67 (d, 1 H, *J* = 4.1 Hz), 4.45 (bd, 1 H, *J* = 18.0 Hz), 4.22 (dd, 1 H, *J* = 11.5, 21.9 Hz), 4.07 (ddd, 1 H, *J* = 3.4, 37.0 Hz), 3.68 (s, 3 H), 3.43 (bs, 1 H), 2.38 (s, 3 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.7, 138.5−125.7, 127.7, 116.3, 97.9, 79.1, 78.8, 71.9, 32.8, 21.0; HREI MS *m*/*z* calcd for $C_{15}H_{17}FN_2O_2S$ 308.0995 ($[M]^{\bullet+}$), found 308.0983.

9-(3′-Deoxy-3′-fluoro-5′-*O*-trityl-β-D-xylofuranosyl)-*N*^{6}-trityladenine (16) and 9-(2′-Deoxy-2′-fluoro-5′-*O*-trityl-β-D-arabinofuranosyl)-*N*^{6}-trityladenine (17): From **11**; *m* = 100 mg (0.123 mmol); DMF, *x* = 0.8 mL; *y* = 35 mg (0.188 mmol); t_1 = 1.5 h; t_2 = 4.5 h; TLC, dichloromethane/methanol (4:1). Column chromatography, dichloromethane/methanol (100:1), yielded **16** (72 mg, 72%) and **17** (6 mg, 6.5%) as amorphous solids. Compound **16**: $[\alpha]^{23}_D$ −33 (*c* 1.1, dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 1 H), 7.82 (s, 1 H), 7.50−7.22 (m, 30 H), 7.13 (s, 1 H), 6.07 (s, 1 H), 5.04 (m, 1 H, *J* = 50.8 Hz), 4.66 (m, 1 H, *J* = 29.7 Hz), 4.58 (bd, 1 H, *J* = 14.5 Hz), 3.63 (m, 1 H), 3.49 (dd, 1 H, *J* = 5.2, 10.0 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 154.2, 151.5, 147.3,144.8, 143.5, 137.6, 129.0−127.0, 121.2, 95.2, 91.3, 87.2, 81.8, 79.4, 71.6, 60.9. Anal. Calcd for $C_{48}H_{40}N_5O_3F$: C, 76.47; H, 5.35; N, 9.29. Found C, 76.01; H, 5.79; N, 8.98. Compound **17**: $[\alpha]^{26}_D$ 0 (*c* 0.6, dichloromethane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1 H), 7.96 (d, 1 H, *J* = 3.4 Hz), 7.47−7.23 (m, 30 H), 7.03 (s, 1 H), 6.48 (dd, 1 H, *J* = 3.1, 20.9 Hz), 4.95 (m, 1 H, *J* = 51.3 Hz), 4.51 (m, 1 H, *J* = 16.9 Hz), 4.11 (m, 1 H), 3.48 (m, 1 H), 3.37 (dd, 1 H, *J* = 5.0, 10.1 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 154.1, 152.1, 148.3,144.8, 143.5, 139.3, 128.9−126.8, 120.2, 94.6, 86.9, 83.3, 82.7, 75.4, 71.4, 63.3. HRFAB MS *m*/*z* calcd for $C_{48}H_{40}N_5O_3F$ + Na: 776.3013. Found: 776.3023.

3-Acetyl-5-(3′-deoxy-3′-fluoro-α-L-threofuranosyl)-2-methylpyrrole (18) and 3-Acetyl-5-(3′-deoxy-3′-fluoro-β-L-threofuranosyl)-2-methylpyrrole (19): From **12**; *m* = 100 mg (0.348 mmol); DMF, *x* = 1.8 mL; *y* = 98 mg (0.527 mmol); t_1 = 12 h; t_2 = 3 h; TLC, dichloromethane/methanol (15:1). Column chromatography, dichloromethane/methanol (15:1), yielded **18** (33 mg 41%) and **19** (25 mg, 31%) as amorphous solids. Compound **18**: $[\alpha]^{23}_D$ −56 (*c* 0.8, dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (bs, 1 H), 6.43 (d, 1 H, *J* = 2.6 Hz), 5.09 (m, 1 H, *J* = 52.1 Hz), 4.73 (d, 1 H, *J* = 3.3 Hz), 4.40 (bd, 1 H, *J* = 16.9 Hz), 4.26 (dd, 1 H, *J* = 11.4, 21.9 Hz), 4.06 (ddd, 1 H, *J* = 3.0, 38.7 Hz), 3.37 (bs, 1 H), 2.48 (s, 3 H), 2.35 (s, 3 H).^{13}C NMR (75.4 MHz, $CDCl_3$) δ 195.4, 135.9 (C-5), 127.0, 120.7, 108.9, 98.1, 81.6, 80.1, 71.8, 28.2, 14.0; HREI MS *m*/*z* calcd for $C_{11}H_{14}NO_3F$ 227.0958 ($[M]^{\bullet+}$), found 227.0957. Compound **19**: $[\alpha]^{25}_D$ −53 (*c* 0.7, dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.91 (bs, 1 H), 6.46 (d, 1 H, *J* = 2.6 Hz), 5.16 (dd, 1 H, *J* = 3.8, 51.7 Hz), 5.00 (dd, 1 H, *J* = 3.2, 3.4 Hz), 4.35 (bd, 1 H, *J* = 8.7 Hz), 4.35 (ddd, 1 H, *J* = 11.3, 40.7 Hz), 4.04 (dd, 1 H, *J* = 30.7 Hz), 3.03 (bs, 1 H), 2.46 (s, 3 H), 2.35 (s, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 195.1, 135.8 (C-5), 123.7, 120.7, 110.0, 96.7, 76.8, 75.9, 71.4, 28.2, 13.9; HREI MS *m*/*z* calcd for $C_{11}H_{14}NO_3F$ 227.0958 ($[M]^{\bullet+}$), found 227.0962.

General Procedure for the Preparation of the Azido Compounds 23−29. To a solution of the corresponding cyclic sulfate **7**−**9**, **11**, or **12** (*m* g) in DMF (*x* mL) under argon and at room temperature was added sodium azide (*y* mg). The reaction mixture was stirred for t_1 min and controlled by TLC (dichloromethane). The solvent was removed in vacuo, and the residue was stirred with 36 N H_2SO_4 (40 μL/mmol) and H_2O (16 μL/mmol) at room temperature for t_2 min, diluted with EtOAc, and washed with saturated aqueous sodium hydrogencarbonate. The organic layer was washed with water, dried ($MgSO_4$), filtered, and evaporated to dryness. The residue was purified by column chromatography.

5-(3′-Azido-3′-deoxy-α-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (23): From **7**; t_1 = 90 min; t_2 = 15 min; *m* = 750 mg (2.358 mmol); *x* = 13.3 mL; *y* = 305 mg (4.753 mmol). Column chromatography, ether/petroleum ether (1:1), yielded 583 mg (88%) as an amorphous solid; $[\alpha]^{29}_D$ −43 (*c* 1.0, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{12}H_{15}N_3O_5$: C, 51.24; H, 5.38; N, 14.94. Found: C, 51.20; H, 5.35; N, 14.81.

5-(3′-Azido-3′-deoxy-β-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (24): From **8**; t_1 = 45 min; t_2 = 15 min; *m* = 125 mg (0.393 mmol); *x* = 2.2 mL; *y* = 51 mg (0.794 mmol). Column chromatography, ether/petroleum ether (1:1→3:1), yielded 97 mg (88%) as an amorphous solid; $[\alpha]^{29}_D$ −43 (*c* 1.0, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{12}H_{15}N_3O_5$: C, 51.24; H, 5.38; N, 14.94. Found: C, 51.12; H, 5.37; N, 14.64.

4-(3′-Azido-3′-deoxy-α-L-threofuranosyl)-1,3-dihydro-3-methyl-1-*p*-tolyl-2*H*-imidazole-2-thione (25): From **9**; TLC, dichloromethane/methanol (20:1); t_1 = 120 min; t_2 = 30 min; *m* = 675 mg (1.833 mmol); *x* = 10.0 mL; *y* = 196 mg (3.023 mmol). Column chromatography, dichloromethane/methanol (60:1), yielded 449 mg (74%) as an amorphous solid; $[\alpha]^{29}_D$ −39 (*c* 1.0, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{15}H_{17}N_5O_2S$: C, 54.36; H, 5.17; N, 21.13. Found: C, 54.21; H, 5.34; N, 20.60.

9-(3′-Azido-3′-deoxy-5′-*O*-trityl-β-D-xylofuranosyl)-*N*^{6}-trityladenine (26) and 9-(2′-Azido-2′-deoxy-5′-*O*-trityl-β-

D-arabinofuranosyl)-N^6-trityladenine (27): From **11**; TLC, dichloromethane/methanol (15:1); $t_1 = 135$ min; $t_2 = 120$ min; $m = 450$ mg (0.553 mmol); $x = 10.0$ mL; $y = 72$ mg (1.108 mmol). Column chromatography, ether/petroleum ether (1:1), yielded **26** and **27** as amorphous solids. Compound **26** (257 mg, 60%): $[\alpha]^{29}_D$ −49 (*c* 1.0, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. HRCIMS *m*/*z* calcd for $C_{48}H_{41}N_8O_3$ 777.3302 ($[M + H]^+$), found 777.3273. Compound **27** (17 mg, 4%): $[\alpha]^{29}_D$ −13 (*c* 0.8, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. HRCIMS *m*/*z* calcd for $C_{48}H_{41}N_8O_3$ 777.3302 ($[M + H]^+$), found 777.3265.

3-Acetyl-5-(3′-azido-3′-deoxy-α-L-threofuranosyl)-2-methylpyrrole (28) and 3-Acetyl-5-(3′-azido-3′-deoxy-β-L-threofuranosyl)-2-methylpyrrole (29): From **12**; TLC, EtOAc/petroleum ether (3:1); $t_1 = 90$ min; $t_2 = 15$ min; $m = 500$ mg (1.742 mmol); $x = 9.0$ mL; $y = 150$ mg (1.108 mmol). Column chromatography, EtOAc/petroleum ether (1:1→3:1), yielded 314 mg (72%) of **28** and **29** as a mixture of anomers (α:β ratio of 2.7:1); FAB MS *m*/*z* 251 ($[M + H]^+$). For IR, and NMR data, see Table 1 and Supporting Information.

5-(3′-Azido-2′-*O*-benzyl-3′-deoxy-α-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (32). To a stirred solution of **23** (100 mg, 0.356 mmol) in DMF (1.4 mL) under argon and at 0 °C was added silver oxide (165 mg, 0.712 mmol). Then, benzyl bromide (106 μL, 0.890 mmol) was added dropwise, and the reaction mixture was kept at 0 °C for 5 min, stirred at room temperature for 24 h, and controlled by TLC (2:1 ether/petroleum ether). The mixture was diluted with ether (30 mL), filtered, washed with a solution of citric acid (10%), water, saturated aqueous sodium hydrogencarbonate, and saturated aqueous sodium chloride, dried ($MgSO_4$), filtered, and evaporated to dryness. The residue was purified by column chromatography (1:4 ether/petroleum ether). Yield: 92 mg (70%) as an amorphous solid; $[\alpha]^{23}_D$ −5 (*c* 1.3); FAB MS *m*/*z* 394 ($[M + Na]^+$). For IR and NMR data, see Table 1 and Supporting Information.

4-(3′-Azido-2′-*O*-benzyl-3′-deoxy-α-L-threofuranosyl)-1,3-dihydro-3-methyl-1-*p*-tolyl-2-*H*-imidazole-2-thione (35) and 4-(3′-azido-2′-*O*-benzyl-3′-deoxy-α-L-threofuranosyl)-1,3-dihydro-3-methyl-1-*p*-tolyl-2-*H*-imidazole-2-one (36). To a solution of **25** (220 mg, 0.665 mmol) and NaH (50 mg, 80% in paraffin liquid) in DMF (4.2 mL) at room temperature was added benzyl bromide (140 μL). The reaction mixture was stirred for 24 h, and then MeOH (0.9 mL) and Et_3N (0.05 mL) were added. The resulting mixture was stirred for 30 min, diluted with EtOAc (10 mL), dried ($MgSO_4$), filtered, and evaporated to dryness. The residue was purified by column chromatography (dichloromethane→20:1 dichloromethane/methanol) to yield **35** (82 mg, 29%) and **36** (110 mg, 41%) as amorphous solids. Compound **35**: $[\alpha]^{20}_D$ −55 (*c* 2.4, dichloromethane); FAB MS *m*/*z* 444 ($[M + Na]^+$). Compound **36**: $[\alpha]^{20}_D$ −9 (*c* 2.2, dichloromethane); FAB MS *m*/*z* 428 ($[M + Na]^+$). For IR and NMR data, see Table 1 and Supporting Information.

Acetyl derivatives **37**−**41** were obtained in virtually quantitative yields by conventional acetylation of the corresponding azidonucleoside (**23**−**25**, **28**, or **29**) with acetic anhydride and pyridine.

5-(2′-*O*-Acetyl-3′-azido-3′-deoxy-α-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (37): From **23**; TLC, EtOAc/petroleum ether (1:2). Column chromatography, ether/petroleum ether (1:2), yielded an amorphous solid; $[\alpha]^{24}_D$ −69 (*c* 1.3, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{14}H_{17}N_3O_6$: C, 52.01; H, 5.30; N, 12.99. Found: C, 52.16; H, 4.86; N, 12.52.

5-(2′-*O*-Acetyl-3′-azido-3′-deoxy-β-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (38): From **24**; column chromatography, ether/petroleum ether (1:1), yielded an amorphous solid; $[\alpha]^{27}_D$ −70 (*c* 1.0). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{14}H_{17}N_3O_6$: C, 52.01; H, 5.30; N, 12.99. Found: C, 51.68; H, 5.29; N, 12.58.

4-(2′-*O*-Acetyl-3′-azido-3′-deoxy-α-L-threofuranosyl)-1,3-dihydro-3-methyl-1-*p*-tolyl-2-*H*-imidazole-2-thione (39): From **25**; column chromatography, ether/petroleum ether (2:1). Compound **39** was an amorphous solid: $[\alpha]^{23}_D$ −106 (*c*, 1.1). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{17}H_{19}N_5O_3S$: C, 54.68; H, 5.13. Found: C, 54.34; H, 5.13.

3-Acetyl-5-(2′-*O*-acetyl-3′-azido-3′-deoxy-α-L-threofuranosyl)-2-methylpyrrole (40) and 3-Acetyl-5-(2′-*O*-acetyl-3′-azido-3′-deoxy-β-L-threofuranosyl)-2-methylpyrrole (41): From a mixture of **28** and **29** (2.7:1); column chromatography, dichloromethane/methanol (100:1), yielded **40** and **41**. Compound **40** crystallized from ether/petroleum ether: mp 154−156 °C; $[\alpha]^{23}_D$ −52 (c 1.0, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{13}H_{16}N_4O_4$: C, 53.42; H, 5.52; N, 19.17. Found: C, 53.36; H, 5.36; N, 19.55. Compound **41** was an amorphous solid: $[\alpha]^{23}_D$ −9 (*c* 0.8, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{13}H_{16}N_4O_4$: C, 53.42; H, 5.52; N, 19.17. Found: C, 53.29; H, 5.44; N, 18.90.

General Procedure for the Preparation of Amino Compounds 30, 31, 33, and 42−46. The corresponding azido compound **23**, **25**, **32**, or **37**−**41** (*m* mg) was dissolved in MeOH (*x* mL) and hydrogenated at 1 atm of pressure and room temperature for *t* min in the presence of 10% Pd/C (*y* mg). The catalyst was filtered off; the solvent was evaporated, and the corresponding residue was purified by column chromatography (dichloromethane/methanol (20:1→9:1)).

5-(3′-Amino-3′-deoxy-α-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (30): From **23**; $t = 15$ min; $m = 65$ mg (0.231 mmol); $x = 6$ mL; $y = 7$ mg. Compound **30** (55 mg, 93%) was an amorphous solid: $[\alpha]^{20}_D$ −41 (*c*, 1.3, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{12}H_{17}NO_5$: C, 56.46; H, 6.71. Found: C, 56.56; H, 6.68.

4-(3′-Amino-3′-deoxy-α-L-furanosyl)-1,3-dihydro-3-methyl-1-*p*-tolyl-2-*H*-imidazole-2-thione (31): From **25**; $t = 15$ h; $m = 100$ mg (0.302 mmol); $x = 7.8$ mL; $y = 10$ mg. Compound **31**, (75 mg, 81%) was an amorphous solid: $[\alpha]^{20}_D$ −68 (*c* 0.8, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. HREI MS *m*/*z* calcd for $C_{15}H_{19}N_3O_2S$ 305.1198 ($[M]^{+\bullet}$), found 305.1193.

5-(3′-Amino-2′-*O*-benzyl-3′-deoxy-α-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (33): From **32**; $t = 60$ min; $m = 78$ mg (0.210 mmol); $x = 7.0$ mL; $y = 3.9$ mg. Compound **33** (50 mg, 69%) was an amorphous solid: $[\alpha]^{23}_D$ −50 (*c* 1.3, dichloromethane); FAB MS *m*/*z* 346 ($[M + H]^+$). For IR and NMR data, see Table 1 and Supporting Information.

5-(2′-*O*-Acetyl-3′-amino-3′-deoxy-α-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (42): From **37**; $t = 15$ min; $m = 140$ mg (0.433 mmol); $x = 11.0$ mL; $y = 14$ mg. Compound **42** (75 mg, 81%) was an amorphous solid: $[\alpha]^{28}_D$ −57 (*c* 1.3, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{14}H_{19}NO_6$: C, 56.56; H, 6.44; N, 4.71. Found: C, 56.44; H, 6.25; N, 4.85.

5-(2′-*O*-Acetyl-3′-amino-3′-deoxy-β-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (43): From **38**; $t = 15$ min; $m = 148$ mg (0.498 mmol); $x = 11.0$ mL; $y = 15$ mg. Compound **43** (123 mg, 83%) was an amorphous solid: $[\alpha]^{28}_D$ −68 (*c* 1.0, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{14}H_{19}NO_6$: C, 56.56; H, 6.44; N, 4.71. Found: C, 56.46; H, 6.47; N, 4.46.

4-(2′-*O*-Acetyl-3′-amino-3′-deoxy-α-L-furanosyl)-1,3-dihydro-3-methyl-1-*p*-tolyl-2-*H*-imidazole-2-thione (44): From **39**; $t = 6$ h; $m = 250$ mg (0.670 mmol); $x = 17.0$ mL; $y = 50$ mg. Compound **44** (154 mg, 66%) was an amorphous solid: $[\alpha]^{27}_D$ −97 (*c* 1.1, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{17}H_{21}N_3O_3S$: C, 58.77; H, 6.09; N, 12.09. Found: C, 58.34; H, 5.92; N, 12.23.

3-Acetyl-5-(2′-*O*-acetyl-3′-amino-3′-deoxy-α-L-threofuranosyl)-2-methylpyrrole (45) and 3-Acetyl-5-(2′-*O*-acetyl-3′-amino-3′-deoxy-β-L-threofuranosyl)-2-methylpyrrole (46): From a mixture of **40** and **41**; $t = 30$ min; $m = 248$ mg (0.849 mmol); $x = 22.0$ mL; $y = 25$ mg. Compound **45** (119

mg, 88%) was an amorphous solid: $[\alpha]^{25}_D$ −57 (*c* 0.9, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. HREI MS *m*/*z* calcd for $C_{13}H_{18}N_2O_4$ 266.1267 ($[M]^{\bullet+}$), found 266.1260. Compound **46** (48 mg, 85%) was an amporphous solid: $[\alpha]^{26}_D$ +7 (*c* 1.4, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. HREI MS *m*/*z* calcd for $C_{13}H_{18}N_2O_4$ 266.1267 ($[M]^{\bullet+}$), found 266.1266.

General Procedure for the Preparation of Compounds 34 and 47−51. To a solution of the corresponding amino compound **33** or **42**−**46** (*m* mg) in dichloromethane (*x* mL) was added *N*,*N*′-thiocarbonyldiimidazole (*y* mg). The mixture was stirred at room temperature for *t* h or min. When monitoring of the reaction by TLC indicated that all the starting material had been consumed, the solvent was evaporated to dryness, and the residue was purified by column chromatography.

5-(2′-*O*-Benzyl-3′-deoxy-3′-isothiocyanato-α-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (34): From **33**; *t* = 10 h; *m* = 40 mg (0.116 mmol); *x* = 1.2 mL; *y* = 62 mg (0.348 mmol, 3 equiv). TLC, dichloromethane/methanol (15:1). Column chromatography, dichloromethane, yielded **34** (31 mg, 69%) as an amorphous solid: $[\alpha]^{28}_D$ +79 (*c* 1.4, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. HRCIMS *m*/*z* calcd for $C_{20}H_{22}NO_5S$ 388.1219 ($[M + H]^{\bullet+}$), found 388.1214.

5-(2′-*O*-Acetyl-3′-deoxy-3′-isothiocyanato-α-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (47): From **42**; *t* = 60 min; *m* = 420 mg (1.414 mmol); *x* = 13.0 mL; *y* = 677 mg (3.799 mmol, 2.7 equiv). TLC, ether/petroleum ether (3:1) and dichloromethane/methanol (25:1); column chromatography, ether/petroleum ether (1:1). Compound **47** (410 mg, 86%) was an amorphous solid: $[\alpha]^{28}_D$ +117 (*c* 0.8, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{15}H_{17}NO_6S$: C, 53.08; H, 5.05; N, 4.13. Found: C, 52.92; H, 4.82; N, 4.23.

5-(2′-*O*-Acetyl-3′-deoxy-3′-isothiocyanato-β-L-threofuranosyl)-3-ethoxycarbonyl-2-methylfuran (48): From **43**; *t* = 60 min; *m* = 98 mg (0.330 mmol); *x* = 3.0 mL; *y* = 200 mg (1.122 mmol, 3.4 equiv). TLC, dichloromethane/methanol (25:1); column chromatography, dichloromethane. Compound **48** (80 mg, 72%) was an amorphous solid: $[\alpha]^{20}_D$ +139 (*c* 0.6, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. HRCIMS *m*/*z* calcd for $C_{15}H_{18}NO_6S$ 340.0855 ($[M + H]^+$), found 340.0858.

4-(2′-*O*-Acetyl-3′-deoxy-3′-isothiocyanato-α-L-threofuranosyl)-1,3-dihydro-3-methyl-1-*p*-tolyl-2*H*-imidazole-2-thione (49): From **44**; *t* = 120 min; *m* = 122 mg (0.351 mmol); *x* = 3.2 mL; *y* = 169 mg (1.01 mmol, 2.7 equiv). TLC, dichloromethane/methanol (25:1); column chromatography, ether/petroleum ether (1:1), yielded **49** (123 mg, 90%) as an amorphous solid: $[\alpha]^{26}_D$ +33 (*c* 0.7, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{18}H_{19}N_3O_3S_2$: C, 55.51; H, 4.92; N, 10.79. Found: C, 55.66; H, 4.82; N, 10.88.

3-Acetyl-5-(2′-*O*-acetyl-3′-deoxy-3′-isothiocyanato-α-L-threofuranosyl)-2-methylpyrrole (50): From **45**; *t* = 120 min; *m* = 56 mg (0.210 mmol); *x* = 1.9 mL; *y* = 112 mg (0.629 mmol, 3.0 equiv). TLC, EtOAc/petroleum ether (3:1) and dichloromethane/methanol (25:1); column chromatography, EtOAc/petroleum ether (1:3→1:1), yielded **50** (51 mg, 79%) as an amorphous solid: $[\alpha]^{25}_D$ +63 (*c* 1.1, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. HREI MS *m*/*z* calcd for $C_{14}H_{16}N_2O_4S$ 308.0831 ($[M]^{\bullet+}$), found 308.0834.

3-Acetyl-5-(2′-*O*-acetyl-3′-deoxy-3′-isothiocyanato-β-L-threofuranosyl)-2-methylpyrrole (51): From **46**; *t* = 120 min; *m* = 55 mg (0.207 mmol); *x* = 2 mL; *y* = 108 mg (0.606 mmol, 2.9 equiv). TLC, ether/petroleum ether (6:1) and dichloromethane/methanol (15:1); column chromatography, ether/petroleum ether (1:2→3:1), yielded **51** (50 mg, 78%) as an amorphous solid: $[\alpha]^{25}_D$ +186 (*c* 0.8, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{14}H_{16}N_2O_4S$: C, 54.53; H, 5.23; N, 9.08; S, 10.40. Found: C, 54.82; H, 5.17; N, 8.71; S, 10.96.

General Procedure for the Preparation of Thioureas 52−57. A solution of the corresponding isothiocyanatonucleoside **47**, **49**, or **50** (m_1 mg) and the aminonucleoside **42**, **44**, or **45**, respectively, (m_2 mg) in acetone or DMF (*x* mL) at 40°C was stirred for *t* h. When monitoring of the reaction by TLC indicated that all starting material had been consumed, the solvent was evaporated to dryness. The residue was purified as described.

***N*,*N*′-Bis-[2-*O*-acetyl-1,3-dideoxy-1-(3′-ethoxycarbonyl-2′-methylfur-5′-yl)-α-L-threofuranos-3-yl]thiourea (52):** From **47** (isothiocyanate) and **42** (aminonucleoside); *t* = 7 h; m_1 = 52 mg (0.153 mmol); m_2 = 52 mg (0.175 mmol); *x* = 0.5 mL. TLC, dichloromethane/methanol (25:1); column chromatography, dichloromethane/methanol (50:1), yielded **52** (95 mg, 98%) as an amorphous solid: $[\alpha]^{27}_D$ +78 (*c* 1.0, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{29}H_{36}N_2O_{12}S$: C, 54.71; H, 5.70; N, 4.40. Found: C, 54.39; H, 5.66; N, 4.51.

***N*,*N*′-Bis-[2-*O*-acetyl-1,3-dideoxy-1-(1′,3′-dihydro-3′-methyl-1′-*p*-tolyl-2′*H*-imidazole-2′-thioxo-4′-yl)-α-L-threofuranos-3-yl]thiourea (53):** From **49** (isothiocyanate) and **44** (aminonucleoside); *t* = 12 h; m_1 = 37 mg (0.095 mmol); m_2 = 41 mg (0.118 mmol); *x* = 0.7 mL. TLC, dichloromethane/methanol (25:1); column chromatography, dichloromethane/methanol (50:1), yielded **53** (73 mg, 93%) as an amorphous: $[\alpha]^{24}_D$ −188 (*c* 0.8, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{35}H_{40}N_6O_6S_3$: C, 57.04; H, 5.47; N, 11.40. Found: C, 56.44; H, 5.56; N, 11.57.

***N*,*N*′-Bis-[2-*O*-acetyl-1-(3′-acetyl-2′-methylpyrrole-5′-yl)-1,3-dideoxy-α-L-threofuranos-3-yl]thiourea (54):** From **50** (isothiocyanate) and **45** (aminonucleoside); *t* = 4 h; m_1 = 37 mg (0.120 mmol); m_2 = 33 mg (0.124 mmol); *x* = 1.2 mL; TLC, dichloromethane/methanol (25:1); column chromatography dichloromethane/methanol (50:1), yielded **54** (62 mg, 90%) as an amorphous solid: $[\alpha]^{29}_D$ −75 (*c* 0.2, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. HREI MS *m*/*z* calcd for $C_{27}H_{34}N_4O_8S$ 574.2097 ($[M]^{\bullet+}$), found 574.2102.

***N*-[2-*O*-Acetyl-1,3-dideoxy-1-(1′,3′-dihydro-3′-methyl-2′-thioxo-1′-*p*-tolyl-2′*H*-imidazole-4′-yl)-α-L-threofuranos-3-yl]-*N*′-[2″-*O*-acetyl-1″,3″-dideoxy-1″-(3‴-ethoxycarbonyl-2‴-methylfur-5‴-yl)-α-L-threofuranos-3″-yl]thiourea (55):** From **47** (isothiocyanate) and **44** (aminonucleoside); *t* = 12 h; m_1 = 28 mg (0.083 mmol); m_2 = 35 mg (0.101 mmol); *x* = 0.6 mL. TLC, dichloromethane/methanol (25:1); column chromatography, dichloromethane/methanol (15:1), yielded **55** (44 mg, 80%) as an amorphous solid: $[\alpha]^{27}_D$ −121 (*c* 1.0, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{32}H_{38}N_4O_9S_2$: C, 55.96; H, 5.58; N, 8.16. Found C, 55.42; H, 5.63; N, 7.98.

***N*-[2-*O*-Acetyl-1,3-dideoxy-1-(3′-acetyl-2′-methylpyrrole-5′-yl)-α-L-threofuranos-3-yl]-*N*′-[2″-*O*-acetyl-1″,3″-dideoxy-1″-(3‴-ethoxycarbonyl-2‴-methylfur-5‴-yl)-α-L-threofuranos-3″-yl]thiourea (56):** From **47** (isothiocyanate) and **45** (aminonucleoside); *t* = 1 h; m_1 = 31 mg (0.091 mmol); m_2 = 25 mg (0.094 mmol); *x* = 0.7 mL. TLC, dichloromethane/methanol (25:1); column chromatography, dichloromethane/methanol (15:1), yielded **56** (49 mg, 100%) as an amorphous solid: $[\alpha]^{27}_D$ −76 (*c* 1.0, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{28}H_{35}N_3O_{10}S$: C, 55.53; H, 5.82; N, 6.94. Found: C, 55.43; H, 5.82; N, 6.91.

***N*-[2-*O*-Acetyl-(3′-acetyl-2′-methylpyrrole-5′-yl)-1,3-dideoxy-1-α-L-threofuranos-3-yl]-*N*′-[2″-*O*-acetyl-1″,3″-dideoxy-1″-(1‴,3‴-dihydro-3‴-methyl-2‴-thioxo-1‴-*p*-tolyl-2‴-*H*-imidazole-4‴-yl)-α-L-threofuranos-3″-yl]thiourea (57):** From **49** (isothiocyanate) and **45** (aminonucleoside); *t* = 4.5 h; m_1 = 36 mg (0.092 mmol); m_2 = 28 mg (0.105 mmol); *x* = 0.7 mL. TLC, dichloromethane/methanol (25:1); column chromatography, dichloromethane/methanol (40:1), yielded **57** (53 mg, 88%) as an amorphous solid: $[\alpha]^{27}_D$ −128 (*c* 1.2, dichloromethane). For FAB MS, IR, and NMR data, see Table 1 and Supporting Information. Anal. Calcd for $C_{31}H_{37}$-

$N_5O_7S_2$: C, 56.78; H, 5.69; N, 10.68; S, 9.78. Found: C, 56.32; H, 5.39; N, 10.32; S, 10.23.

General Procedure for the Preparation of Compounds 58−63. To a solution of the corresponding thioureylene derivative **52**−**57** (*m* mg) in anhydrous methanol (*x* mL) at room temperature was added 1 M NaOMe in methanol (*y* μL). The process was controlled by TLC ether/petroleum ether (12:1), until total deacylation of the starting material was achieved. After *t* min, the reaction mixture was neutralized with acid resin Amberlite IR-120(H) and filtered and the solvent evaporated under reduced pressure. The products were obtained pure and with quantitative yields.

***N*,*N*′-Bis-[1,3-dideoxy-1-(3′-ethoxycarbonyl-2′-methylfur-5′-yl)-α-L-furanos-3-yl]thiourea (58):** From **52**; *t* = 15 min; *m* = 15 mg (0.024 mmol); *x* = 3 mL; *y* = 12 μL. TLC, ether/petroleum ether (12:1). For FAB MS and NMR data, see Table 1 and Supporting Information. HRFAB MS *m*/*z* calcd for $C_{25}H_{32}N_2O_{10}S$ + Na: 575.1675. Found: 575.1676.

***N*,*N*′-Bis-[1,3-dideoxy-1-(1′,3′-dihydro-3′-methyl-2′-thioxo-1′-*p*-tolyl-2′-*H*-imidazole-4′-yl)-α-L-threofuranos-3-yl]thiourea (59):** From **53**; *t* = 5 min; *m* = 10 mg (0.015 mmol); *x* = 1.6 mL; *y* = 7 μL. TLC, dichloromethane/methanol (25:1). For FAB MS and NMR data, see Table 1 and Supporting Information. HRFAB MS *m*/*z* calcd for $C_{31}H_{36}N_6O_4S_3$ + Na: 675.1858. Found: 675.1857.

***N*,*N*′-Bis-[1,3-dideoxy-1-(3′-acetyl-2′-methylpyrrol-5′-yl)-α-L-threofuranos-3-yl]thiourea (60):** From **54**; *t* = 15 min; *m* = 3 mg (0.006 mmol); *x* = 1.0 mL; *y* = 4 μL. TLC, dichloromethane/methanol (15:1). For FAB MS and NMR data, see Table 1 and Supporting Information. HRFAB MS *m*/*z* calcd for $C_{23}H_{30}N_4O_6S$ + Na: 513.1784. Found: 513.1782.

***N*-[1,3-Dideoxy-1-(1′,3′-dihydro-3′-methyl-2′-thioxo-1′-*p*-tolyl-2′*H*-imidazole-4′-yl)-α-L-threofuranos-3-yl]-*N*′-[1″,3″-dideoxy-1″-(3‴-ethoxycarbonyl-2‴-methylfur-5‴-yl)-α-L-threofuranos-3″-yl]thiourea (61):** From **55**; *t* = 15 min; *m* = 10 mg (0.017 mmol); *x* = 1.8 mL; *y* = 4 μL. TLC, dichloromethane/methanol (40:1). For FAB MS and NMR data, see Table 1 and Supporting Information. HRFAB MS *m*/*z* calcd for $C_{28}H_{34}N_4O_7S_2$ + Na: 625.1767. Found: 625.1764.

***N*-[1,3-Dideoxy-1-(3′-acetyl-2′-methylpyrrole-5′-yl)-α-L-threofuranos-3-yl]-*N*′-[1″,3″-dideoxy-1″-(3‴-ethoxycarbonyl-2‴-methylfur-5‴-yl)-α-L-threofuranos-3″-yl]thiourea (62):** From **56**; *t* = 15 min; *m* = 10 mg (0.019 mmol); *x* = 2 mL; *y* = 8 μL. TLC, dichloromethane/methanol 25:1. For FAB MS and NMR data, see Table 1 and Supporting Information. HRFAB MS *m*/*z* calcd for $C_{24}H_{31}N_3O_8S$ + Na: 544.1730. Found: 544.1732.

***N*-[1-(3′-Acetyl-2′-methylpyrrole-5′-yl)-1,3-dideoxy-α-L-threofuranos-3-yl]-*N*′-[1″,3″-dideoxy-1″-(1‴,3‴-dihydro-3‴-methyl-2‴-thioxo-1‴-*p*-tolyl-2‴-*H*-imidazole-4‴-yl)-α-L-threofuranos-3″-yl]thiourea (63):** From **57**; *t* = 15 min; *m* = 10 mg (0.017 mmol); *x* = 1.8 mL; *y* = 5 μL. TLC, dichloromethane/methanol (25:1). For FAB MS and NMR data, see Table 1 and Supporting Information. HRFAB MS *m*/*z* calcd for $C_{27}H_{33}N_5O_5S_2$ + Na: 594.1821. Found: 594.1816.

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Supporting Information Available: MS, IR, and assigned NMR (^{1}H and ^{13}C) data for compounds **7**−**12** and **23**−**63**, MS and IR data for compounds **13**−**20**, and copies of ^{13}C NMR spectra (125.7 MHz) for compounds **10**, **13**, **15**, **17**, **18**−**20**, **26**, **31**, **34**, **45**, **46**, **48**, **50**, **54**, **58**-**63**.

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