JOC Article

Synthesis of 4-Amino-5-*H*-2,3-dihydroisothiazole-1,1-dioxide Ring Systems on Sugar Templates via Carbanion-Mediated Sulfonamide Intramolecular Cyclization Reactions (CSIC Protocols) of Glyco-α-sulfonamidonitriles

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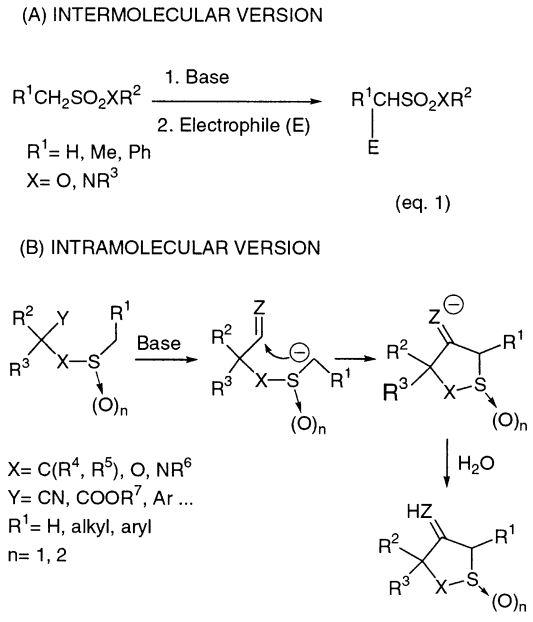
The carbanion-mediated sulfonate intramolecular cyclizations (CSIC protocols) of glyco-α-sulfonamidonitriles derived from readily available monosaccharides have been extensively investigated using potassium carbonate, cesium carbonate, *n*-BuLi, and LDA as bases. As a result, a series of enantiomerically pure spiro(4-amino-5-*H*-2,3-dihydroisothiazole-1,1-dioxide) derivatives have been prepared efficiently and isolated in good yield. The synthesis of these new bicyclic systems is key to accessing a novel range of aza analogues of TSAO nucleosides (ATSAOs).

Introduction

The reactivity of carbanions[1] stabilized by sulfur-containing functional groups is one of the most useful and recognized tools for carbon−carbon bond formation in organic synthesis. Contrary to the number of theoretical and synthetic studies on the chemistry of α-sulfinyl,[2] α-sulfonyl,[3] and α-sulfonimidoyl carbanions,[4,5] the literature regarding related α-sulfonyl carbanions derived from alkanesulfonates and alkanesulfonamides is relatively scarce.[6] From a synthetic perspective, it has been shown that a large range of bases, from *n*-BuLi to DBU, are able to abstract protons from the α-position to the sulfur atom in alkanesulfonates and alkanesulfonamides to give anions that react with various electrophiles such as alkyl halides, sulfonates, either α,*β*-unsaturated or unsaturated carbonyl compounds (ketones, esters), nitriles, and aromatic activated substrates, in inter- and intramolecular conversions, and yield substituted alkanesulfonates, alkanesulfonamides, and different types of heterocyclic ring systems (Scheme 1, eqs 1 and 2).

SCHEME 1. CSIC Reaction



We have named and typified these types of transformations as CSIC reactions, by taking the initials of the

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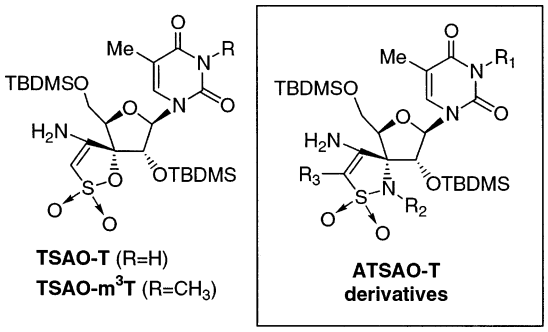

FIGURE 1. Structure of TSAO and ATSAO compounds.

keywords that describe and define the process for both intermolecular [carbanion-mediated sulfonate (or sulfonamide, sulfoxide, or sulfone) intermolecular coupling] and intramolecular [carbanion-mediated sulfonate (or sulfonamide, sulfoxide, or sulfone) intramolecular cyclization] conversions.[7]

The first example of an intramolecular CSIC reaction was reported in 1970 by Durst and Tin[8] following the pioneering studies on the intermolecular reaction of α-metalated species obtained from either alkanesulfonates or alkanesulfonamides with electrophiles described by Corey[9] and Truce.[10] Durst and Tin reported the synthesis of five- and six-membered ring sultones by the CSIC reaction with 1,2-ethylene or 1,3-propylene dimethane (diethane or diphenylmethane)sulfonates, respectively, promoted by *n*-BuLi, at −78 °C and allowing the reaction mixture to warm to 0 °C over 30 min, in THF as a solvent.[8] Since then, this reaction has been used starting from sulfonates and sulfonamides possessing an electrophilic center.

In the same year (1988) that Thompson[11] communicated the intermolecular CSIC reaction of alkanesulfonamides with nitriles, De las Heras reported[12] an intramolecular version of this reaction (Scheme 1, eq 2: X = O; Y = CN, Z = NH; R^1 = H). An anomalous reaction involving sugar-based cyanomesylate was observed in which a 4-aminosultone was formed instead of the desired *β*-elimination product. The synthesis and incorporation of the novel 3′-spiro-5″-(4″-amino-1″, 2″-oxathiole-2″,2″-dioxide) ring system in different sugar templates has afforded adducts whose subsequent transformation have provided a large family of nucleosides (named TSAO compounds), which represent a particular type of specific HIV-1 RT inhibitor (Figure 1).[13]

Subsequent studies from other laboratories[14] and, particularly those from Simig,[15] Marco,[16] and Postel[17] have been the major contribution to the expansion and exploitation of this synthetic methodology.

Recently, we have shown[16] that alkyl and benzylsulfonates, other than mesylates, may also act as the active methylene group in the CSIC reaction to give the corresponding substituted 4-amino-*γ*-sultones. In addition, we have demonstrated that the CSIC conditions can be successfully applied to many alkylsulfonyl nitriles in which the SO_2 group may be attached to either an oxygen or a nitrogen atom.[16] Our studies have revealed the scope and limitations of the CSIC intramolecular cyclization reaction to be as follows. (i) The nitrogen atom of the sulfonamido group should be fully substituted to prevent the removal of the amino hydrogen under strong basic conditions, thus giving the corresponding insoluble salt. (ii) Primary sulfonamido nitrile derivatives are unreactive under classical conditions, and the CSIC reaction can be achieved exclusively when the hydrogen atom of the methylene group is activated with an electron-withdrawing group (e.g., CN) at the α position.[16c,d]

However, the development and application of the CSIC reaction with alkanesulfonamides situated on monosaccharide backbones has never been undertaken. Only very recently, one of us approached and solved this problem, showing that this is a convenient access to a novel range of precursors for the synthesis of aza-analogues of TSAO nucleosides, which we have named ATSAO nucleosides.[17] Our interest in carbohydrate chemistry, especially that pertaining to glyco-α-aminonitriles,[18] encouraged us to extend our investigations into the CSIC reaction. Moreover, retrosynthetic analysis demonstrates that both glyco-α-aminonitrile formation and carbanion-mediated sulfonamide intramolecular cyclization are the key steps in the synthesis of ATSAO nucleosides (Chart 1). Herein we report, in full, our studies on the glycoaminocyanation and cyclization steps to afford the target 4-amino-5-*H*-2,3-dihydroisothiazole-1,1-dioxides using synthetic routes that start from either D-ribose or D-xylose.

Results and Discussion

Several glycoaminocyanation routes have been published.[19a−c] Most of them consist of catalytic (asymmetric) Strecker-type reactions using a Lewis acid as catalyst and various cyanogen reagents.[20a,b] Enantioselective ap-

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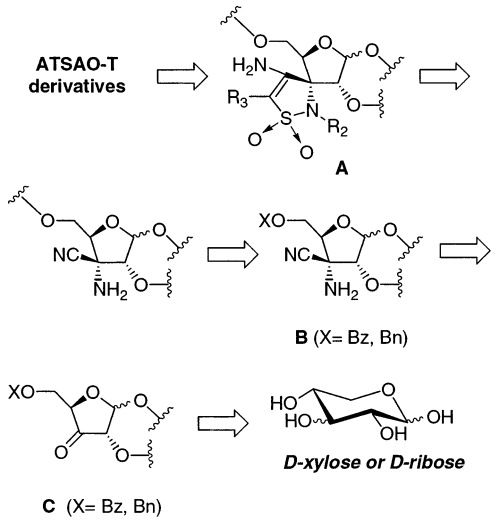
CHART 1. Key Intermediates for Access to ATSAO



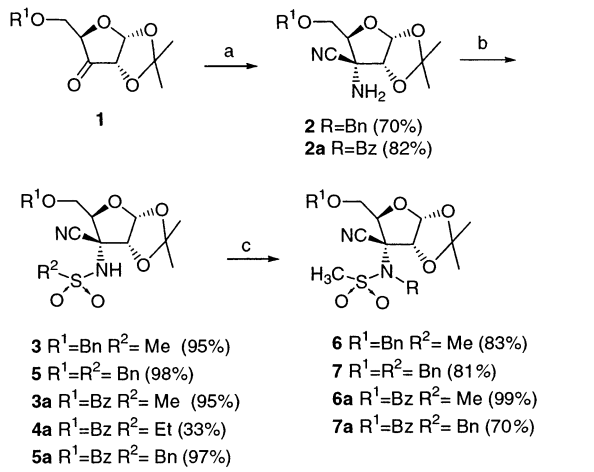
proaches to the reaction generally use a preformed imine whereby the nitrogen atom bears a chiral inducer or chiral metallic complexe as a catalyst.[20,21a−e] However, few examples have been reported on the synthesis of α-aminonitriles of sugars and rarely on uloses involving a nonanomeric carbon atom of the sugar ring at C-α.[22a−c] Steiner described the introduction of an α-aminonitrile group onto 6-deoxy-2,3-*O*-isopropylidene-α-L-lyxo-hexopyranosid-4-ulose, but all of their attempts resulted in epimeric mixtures of the target aminonitriles and a small amount of the corresponding cyanohydrine byproduct.[23a,b]

At the outset of our project, we selected derivatives **B** (Chart 1), where the choice of 5-*O*-benzyl and 5-*O*-benzoyl protecting groups was made on the basis that such groups are well-known to be readily cleaved under mild conditions. These intermediates could be derived from the substrates **C**, which are readily available from either D-ribose or D-xylose (Chart 1).

In the following sections, first we describe the results that we have obtained using the CSIC reaction and exploring the use of 5-*O*-benzyl and 5-*O*-benzoyl protecting groups, respectively.

Classical Strecker conditions applied to the protected *erythro*-pentofuranos-3-ulose derivative **1**[23a,24] and **1a**,[25a,b] which was obtained from D-xylose using PDC or a Swern-modified oxidation method, afforded the corresponding cyanohydrine. Several reaction conditions were examined, but the best results were obtained using NH_3-MeOH and $Ti(OiPr)_4$ as the Lewis acid. The 3-(*R*)-glyco-α-aminonitriles **2** and **2a** were obtained stereoselectively in 70 and 82% yields, respectively. It should be noted that these conditions represent a convenient and versatile method for the formation of a large variety of N-substituted glyco-α-aminonitriles from either alkyl- or arylamines. Moreover, $Ti(OiPr)_4$ is a mild catalyst compatible with a large variety of acid-sensitive functional groups such as lactams, *tert*-butyldimethylsilyl, ethers and acetonides. Compounds **2** and **2a** failed to react readily with RSO_2Cl-pyridine alone; however, upon addition of DMAP, the key methanesulfonamidonitriles **3** and **3a** and the phenylmethanesulfonylamidonitrile analogues **5** and **5a** were obtained in good yields (Scheme 2). The synthesis of the ethanesulfonamides **4** and **4a** were problematic. Under the usual conditions (rt, after 24 h, or after 9 days, using an excess of the sulfonyl chloride) and starting from benzyl-protected derivative **2**, the reaction was incomplete, and we obtained an inseparable mixture of the starting material **2** and the target compound **4** in variable amounts, ranging from traces of product **2** to 0.6:1 or 1:1 ratios of **2**/**4**, respectively (Scheme 3). Under more forcing conditions (pyridine, at 50 °C for 48 h), we observed a large amount of decomposition with product **4** being undetected in the reaction mixture. In short, the reaction was quite erratic, and we were unable to reproduce our own results; consequently, in the next step of the N-alkylation reaction, we were obliged to use samples of compound **4** contaminated with product **2**. Similary, the ethanesulfonamido compound **4a** was also obtained in a lower yield (33%) from **2a** (Scheme 2).

SCHEME 2[a]



[a] Reagents and conditions: (a) (i) $Ti(OiPr)_4$ (1.2 equiv), NH_3, MeOH; (ii) TMSCN. (b) RSO_2Cl (3 equiv), C_5H_5N, DMAP (0.5 equiv). (c) MeI or BnBr (2 equiv), K_2CO_3 (1.5 equiv), acetone, reflux (45 min to 8 h).

A gathering of results to assess the overall scope and limitations of the CSIC reaction on α-aminonitriles derived from commercial ketones indicated that the central nitrogen atom of the aminonitrile is required to be fully substituted to prevent removal of the amino hydrogen, thus giving an insoluble salt of the alkylsul-

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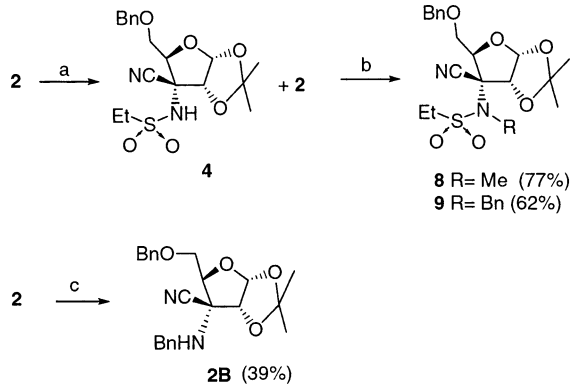
SCHEME 3[a]



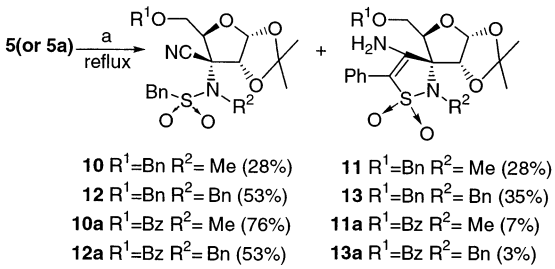
[a] Reagents and conditions: (a) RSO_2Cl (3 equiv), C_5H_5N, DMAP (0.5 equiv). (b) Mel or BnBr (2 equiv), K_2CO_3 (1.5 equiv), acetone, reflux (45 min to 8 h). (c) BnBr (3 equiv), K_2CO_3 (1.5 equiv), acetone, reflux (48 h).

fonamidonitrile.[16] Therefore, we decided, in this work, to limit our studies solely to N-methylated and N-benzylated sulfonamido derivatives. Substitution of the amino hydrogen with either a methyl or benzyl group was performed with methyl iodide and benzyl bromide (2 equiv), respectively, in the presence of potassium carbonate (1.5 equiv) in refluxing acetone. We distinguished major differences in reactivity between alkylsulfonamido and benzylsulfonamido derivatives.

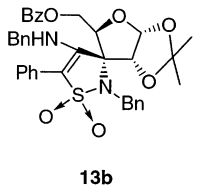
The N-methylated (**6** and **6a**) and N-benzylated derivatives (**7** and **7a**) were readily obtained in good to excellent yields (70−99%) from the precursors **3** and **3a** (Scheme 2). The ethanesulfonamido 5-O-benzylated derivative **4**, contaminated with traces of compound **2**, gave the N-substituted compounds **8** in 77% yield (Scheme 3). Similarly, a mixture of the α-aminonitrile **2** and the ethanesulfonamido 5-O-benzylated derivative **4**, in 0.6:1 ratio, gave the N-substituted compounds **9** in 62% yield (Scheme 3) and recovered starting material **2**, showing that under our reaction conditions this compound did not react with the alkylating agent. To confirm this result, an independent experiment was performed in which the pure precursor **2** was reacted with benzyl bromide using the same experimental conditions (acetone and using potassium carbonate as a base); after the same reaction time, no reaction was observed, but when the reaction time was extended to 48 h, the *N*-benzyl derivative **2B** was obtained in 39% (Scheme 3). Therefore, the increase in chain length (from methyl to ethyl) and consequential increase in inductive effect would appear to decrease the stability of the sulfonamido group to basic conditions.

In the case of the benzylsulfonamido derivatives, the N-substituted compounds **10**, **12**, **10a**, and **12a** were obtained in various yields depending on the reaction time starting from compound **5** and **5a**. In each case, we obtained the corresponding target compound (**10**, **12**, **10a**, **12a**) (28−76%) along with the dihydroisothiazole derivatives **11**, **13**, **11a**, and **13a**, which are the expected products of the CSIC reaction (Scheme 4). The presence of these *byproducts* in the N-alkylation step, compared with their absence in the similar alkylation of alcanesulfonamido compounds **3**, **3a**, **4**, and **4a**, can be explained by the higher acidity of the α-methylene group

SCHEME 4[a]



[a] Reagents and conditions: (a) Mel or BnBr (2 equiv), K_2CO_3 (1.5 equiv), acetone.



13b

FIGURE 2. Structure of **13b**.

of the phenylmethanesulfonamido derivatives **5** and **5a**. Moreover, the carbanion formed is significantly stabilized by the additive mesomeric effects of the sulfonyl and phenyl groups.

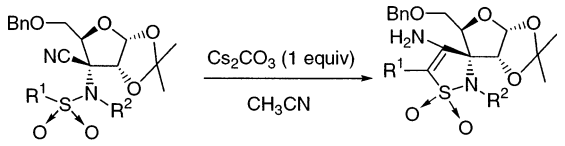
In view of these results, it was of interest to discover if an increase in the reaction time (more than 1 day) would offer an effective "one-pot reaction" protocol for accessing the target dihydroisothiazoles starting from the corresponding benzylsulfonamido precursors. Significantly, after 35 h, reaction of **5** with methyl iodide and potassium carbonate in acetone gave, exclusively, the expected CSIC product **11** in 86% yield (Scheme 4). As expected, after a longer reaction time (35 h), N-methylation of the base labile 5-*O*-benzoyl derivative **5a** gave, exclusively, the CSIC product **11a** in 85% yield. In contrast, N-benzylation of **5a** for 24 h afforded the heterocyclic derivative **13a** (66%) and the new product **13b** (14%) (Figure 2) resulting from an S_N1 reaction between benzyl bromide and **12a**.

Unfortunately, all of our attempts to achieve a one-pot CSIC reaction starting from the methanesulfonamido derivatives **3** or **3b** were unsuccessful.

The goal of converting the *N*-methyl and *N*-benzylsulfonamido derivatives **6**−**12** into the 4-amino-5-*H*-2,3-dihydroisothiazole-1,1-dioxides **14**−**17**, **11**, and **13** (59−99%) using cesium carbonate (1 equiv) as a base in acetonitrile as the solvent (Scheme 5) was successfully achieved after 1−2 h of reaction.

Interestingly, the comparative study using analogous 5-*O*-benzoyl derivatives gave some unexpected products. In each case, the *N*-methyl and *N*-benzylsulfonamido derivatives **6a** and **7a** gave a mixture of three products (**14a**−**c**, **15a**−**c**) (Scheme 6). In addition to the expected CSIC products (**14a**, **15a**), the basic conditions promoted hydrolysis of the benzoate moiety to give a free alkoxide anion on C-5 that, after Michael addition on the enamine group of the 2′,3′-dihydroisothiazole ring system and subsequent hydrolysis, gave the compounds **14b** and **15b**. The products **14c** and **15c** were probably the result of intermolecular benzoyl transfer (we cannot exclude also an intramolecular benzoyl transfer onto the amino group

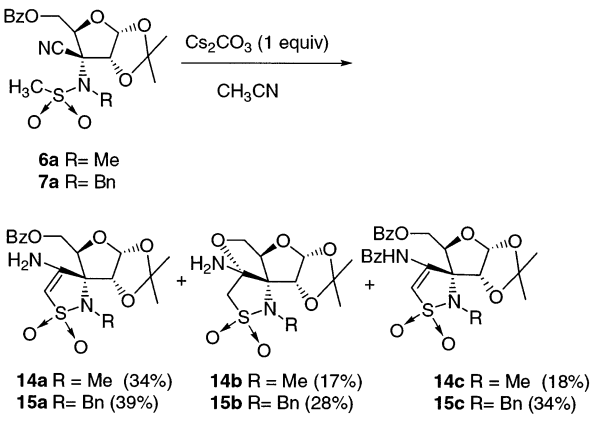
SCHEME 5. CSIC Reaction of Precursors 6−10 and 12



6 R^1, R^2= Me
7 R^1= CH_3, R^2= Bn
8 R^1= Et, R^2= Me
9 R^1= Et, R^2= Bn
10 R^1= Bn, R^2= Me
12 R^1, R^2= Bn

14 R^1= H, R^2= Me (59%)
15 R^1= H, R^2= Bn (65%)
16 R^1, R^2= Me (86%)
17 R^1= CH_3, R^2= Bn (87%)
11 R^1= Ph, R^2= Me (99%)
13 R^1= Ph, R^2= Bn (77%)

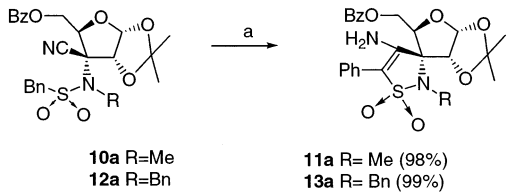
SCHEME 6. CSIC Reaction of Precursors 6a and 7a



6a R= Me
7a R= Bn

14a R = Me (34%)
15a R= Bn (39%)
14b R = Me (17%)
15b R= Bn (28%)
14c R = Me (18%)
15c R= Bn (34%)

SCHEME 7[a]



10a R=Me
12a R=Bn

11a R= Me (98%)
13a R= Bn (99%)

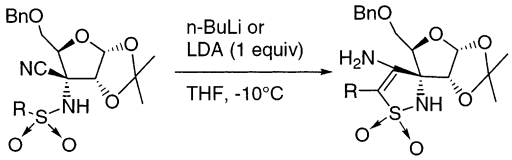
[a] Reagents and conditions: (a) Cs_2CO_3 (1 equiv), CH_3CN, reflux.

at C-5′ followed by an intermolecular benzoyl transfer onto the free alcohol at C-5) from compounds **14a** and **15a**, respectively. The interesting and stable tetracyclic derivatives **14b** and **15b** were isolated diastereomerically pure. They were assigned as having the (*S*) configuration at the newly formed stereocenter on the basis of spectroscopic analysis (see below).

Treatment of the *N*-methyl and *N*-benzylsulfonamido derivatives **10a** and **12a** with cesium carbonate afforded the compounds **11a** and **13a** (Scheme 7) in almost quantitatively yield. This result is in contrast with that observed for **6a** and **7a** which gave complex mixtures. The clean reaction observed for **10a** and **12a** is probably due to the lower basicity of the NH_2 group in the compounds **11a** and **13a** resulting from the resonance effect between the enamino group and the phenyl moiety located at the C-5′ position of these compounds.

Under similar basic CSIC conditions, no cyclization was observed with the *N*-H sulfonamides **3**−**5**, **3a** and **5a**. A plausible explanation for the lack of reactivity is that the removal of the acidic proton from the nitrogen

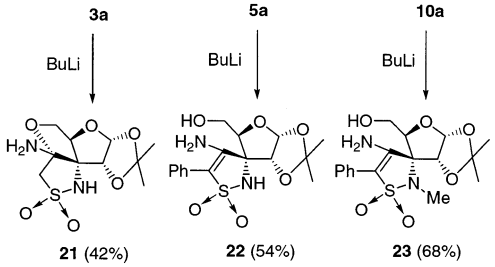
SCHEME 8. CSIC Reaction Promoted by *n*-BuLi on Precursors 3−5



3 R= Me
4 R= Et
5 R= Bn

18 R= H (99%)
19 R= Me (20%) + **2** (41%)
20 R= Ph (73%)

SCHEME 9



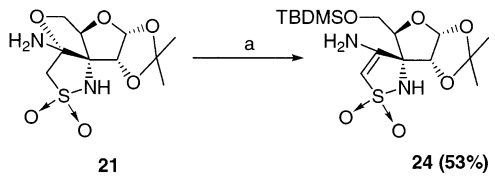
21 (42%)
22 (54%)
23 (68%)

atom of the sulfonamido group gives the corresponding insoluble salt which is unavailable for the reaction. Therefore, we chose to use a lithiated base (i.e. *n*-BuLi, LDA) with the objective of generating a lithium salt which would be expected to be sufficiently soluble in THF and therefore available to undergo a second attack to generate a carbanion for the cyclization. Thus, treatment of the 5-*O*-benzylated derivatives **3**-**5** with *n*-BuLi (3 equiv) (or with freshly prepared LDA, 3 equiv) at −10 °C provided the CSIC reaction products **18**, **19** and **20**, respectively, in good yields (Scheme 8). Compounds **4**, in addition to product **19**, afforded the aminonitrile **2** (41%), corresponding to the initial unreacted substrat. This compound has already observed in the potassium carbonate promoted benzylation of ethanesulfonamide **4** (Scheme 2).

Treatment of the 5-*O*-benzoylated derivatives **3a** and **5a** with *n*-BuLi (3 equiv) at −10 °C gave products resulting from the CSIC reaction and subsequent removal of the benzoyl group (**22**) followed by a Michael addition type reaction of the intermediate alkoxide on the enamine moiety (**21**) (Scheme 9). The interesting tetracyclic derivative **21** was isolated as a diastereomerically pure compounds whose absolute configuration at the newly formed stereocenter was established by spectroscopic analysis (see below). The formation of the hemiaminal derivatives appears to be dependent on the presence of the phenyl group in the β-position of the enamine. Similary, compound **10a** also gave a related product **23** in good yield under comparable conditions (Scheme 9). It should be noted that further introduction at the C-5 position of hemiaminal derivatives could be readily achieved with the subsequent recovery of the corresponding 4-amino-5-*H*-2,3-dihydroisothiazole-1,1-dioxide heterocycle as illustrated for compound **21** (Scheme 10).

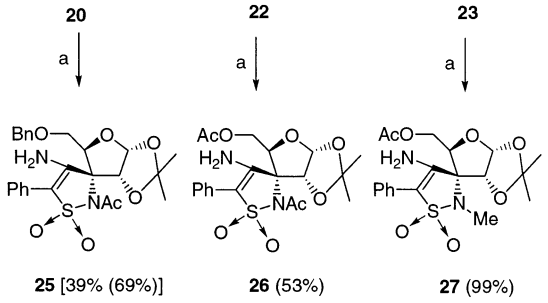
To confirm the structure of compound **20** (Scheme 8) and the alcohols **22** and **23** (Scheme 10), each was acetylated (**Experimental Part**) to give compounds **25**, **26** and **27** (Scheme 11), respectively, which were obtained

SCHEME 10[a]



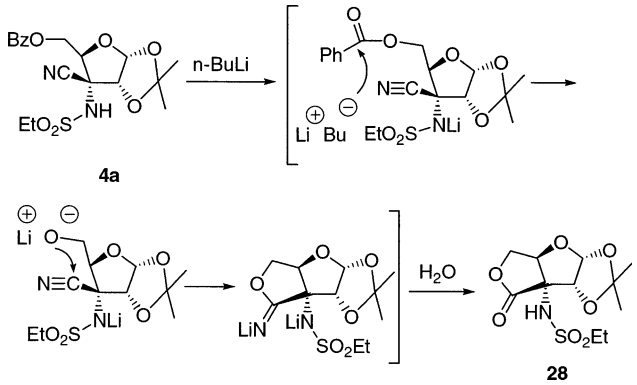
[a] Reagents and conditions: (a) TBDMSCl, imidazole, DMF, rt.

SCHEME 11[a]



[a] Reagents and conditions: (a) Ac_2O, py, rt.

SCHEME 12. Possible Mechanism for the Formation of Lactone 28

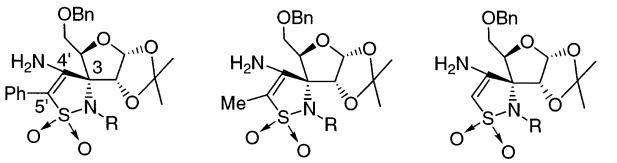


in moderate to good yields. These reactions were found to be very slow and in no case was the amino group on C-4′ acetylated under our mild and standard conditions (rt); in contrast, the free hydroxyl and NH-2′ groups reacted as expected.

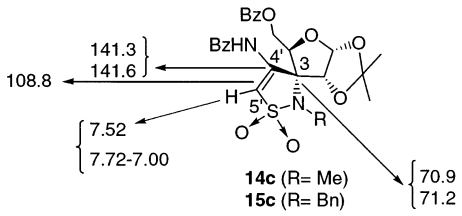
Finally, it was found that treatment of the ethanesulfonamido compound **4a** with *n*-BuLi gave lactone **28** (29%); a putative mechanism for this reaction is shown in Scheme 12. The attack of *n*-BuLi on the carbonyl group of the benzoyl at C-5 gave 1,1-dibutylbenzyl alcohol and an alcohol that after intramolecular reaction with the nitrile and subsequent by acid hydrolysis afforded the lactone **28**. It is of note that under these conditions the base was unable to deprotonate the α-hydrogen on the ethyl side chain and promote the desired CSIC reaction.

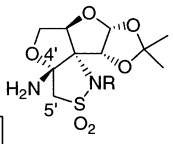
Structural Analysis and Stereochemical Considerations. The structural analysis of the products obtained in this work was achieved by NMR spectroscopy. Assignments of the chemical shifts for protons and carbons are based on a comparison of spectroscopic data with data previously reported by us[16,17] and others.[15] In the following, section we show a brief summary of the characteristic and diagnostic NMR values observed for

CHART 2. Typical NMR Values (δ) for Some the CSIC Products



	11 (R= Me); **13** (R= Bn)	**16** (R= Me); **17** (R= Bn)	**14** (R= Me); **15** (R= Bn)
C-3:	69.6 69.6	69.8	71.1
C-4′:	146.5 146.5	145.0	153.4
C-5′:	126.8 126.5	102.4	90.3





C-4′	C-5′		H-5′
96.1	58.6	**21** R= H	3.27/ 3.62 (13.2 Hz)
95.5	57.1	**14b** R = Me	3.36/ 3.58 (13.2 Hz)
93.9	58.5	**15b** R= Bn	3.27/ 3.61 (13 Hz)

the newly synthesized mixed sugar and heterocyclic derivatives.

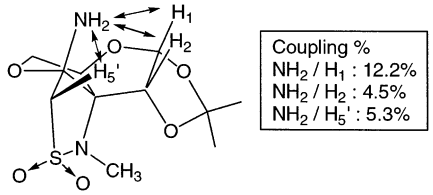
First, the exclusive formation of the products **2** and **2a** (Scheme 2) in the α-aminonitrile formation step is well established and results from the presence of the bulky isopropylidene group that prevents the cyanide attack from the α-face.

Regarding the different types of CSIC products obtained in this work (Chart 2), we have shown some of the typical chemical shifts observed in the NMR spectra. In the 5-*O*-benzyl series (products **11** and **13**−**17**), the values for C-3, C-4′, and C-5′ of the 4-amino-5-*H*-2,3-dihydroisothiazole-1,1-dioxide moiety are essentially the same for both the *N*-methyl and *N*-benzyl compounds. Similar results were observed for the 5-*O*-benzoyl derivatives (products **11a** and **13a**−**15a**).

Interestingly, the N-benzoylated CSIC products **14c** and **15c** (Scheme 7) showed data in good agreement with the presence of an extra benzoyl group at the amino function on C-4′ and in accordance with the values that we have reported in a previous publication on similar nonsugar derivatives.[16b] Particularly informative was the strong deshielding effect for H-5′ due to the presence of the *N*-benzoyl moiety at the vicinal carbon that displaces the *normal* chemical shift of the proton in compound **14a** from 5.56 to 7.52 ppm in **14c** (see Experimental Section).

For the tetracyclic compounds **21**, **14b**, and **14c** (Chart 2), the absolute configuration (*S*) at the newly formed stereocenter has been established as shown by selective

CHART 3. Coupling Value (%) for Compound 21



NOE experiments between protons NH_2 and H-1 and H-2 and H-5′, respectively (Chart 3). In fact, a simple molecular model inspection shows that the Michael addition of the lithium alkoxide to the enamine moiety is only possible from the rear part of the molecule, as the 3-spiro-(4′-amino-5′-*H*-2′,3′-dihydro-1′,1′-dioxide-isothiazolyl) residue is perpendicular to the plane of the furanose ring.

Conclusions

In summary, we have demonstrated that α-sulfonamidonitriles installed in sugar templates are key intermediates in the CSIC reaction for the synthesis of the 3-(4-amino-5-*H*-2-methyl-2,3-dihydroisothiazole-1,1-dioxide) ring system attached to a furanose ring. We have used a series of mild and basic conditions in differently substituted precursors in order to promote this reaction, and we conclude the following.

(1) The series of carbohydrate sulfonamides (**3**−**5** and **3a**−**5a**) were succefully synthesized, with only the synthesis of ethanesulfonamide **4** from α-aminonitrile **2** proving to be erratic and leading to an unsatisfactory conversion.

(2) Refluxing of the secondary methane- and ethanesulfonamides (**3** and **4**) with potassium carbonate as a base in acetone gave the N-alkylated products in good yields (62−83%). However, such conditions failed to effect the CSIC reaction in situ to give the desired 3-(4-amino-5-*H*-2-methyl-2,3-dihydroisothiazole-1,1-dioxide) ring system.

(3) Under comparable conditions as described above the benzylsulfonamide **5** gave mixtures of N-alkylated and the desired CSIC products in short reaction times. However, extended reaction times in excess of 24 h enabled the CSIC reaction product **11** to be isolated exclusively in good yield (86%).

(4) All of the N-substituted alkylsulfonamides (**6**−**12**) reacted efficiently using cesium carbonate as a base in acetonitrile to give the CSIC products (**13**−**17**) in yields ranging from 59 to 99%.

(5) *n*-BuLi (or LDA, in THF, at −10 °C) was found to be the most effective base promoting CSIC reactions in *secondary* alkylsufonamides with minimum byproduct. Only the ethanesulfonamide **4** gave a low yield of the CSIC product accompanied by a major amount of aminonitrile **2**.

(6) Similar conclusion were also found to apply to the analogous 5-*O*-benzoyl derivatives, but in addition we found that, in the cesium carbonate conditions, the benzoyl group was *partially* removed to give a complex mixture of the CSIC, *N*-benzoyl CSIC, and tetracyclic products **14c** and **15c**.

(7) Conversely, all of the alkylsulfonamides protected by the 5-*O*-benzoyl group reacted efficiently under the *n*-BuLi conditions to provide the debenzoylated CSIC products (from the benzylsulfonamides **5a** and **10a**) or the tetracyclic derivative **21** (from the methanesulfonamide **3a**). Only the ethanesulfonamide **4a** failed to afford the corresponding CSIC product, showing a different reactivity (Scheme 12).

As a result, we have found simple experimental conditions for the synthesis of a series of useful building blocks of the general structure **A** (Chart 1). The strategy reported herein provides a convenient access to precursors, in good yield, designed for the preparation of novel ranges of aza-analogues of TSAO nucleosides (ATSAOs). Further work in this field is currently in progress and will be reported in due course.

Experimental Part

Materials and Methods. Melting points are uncorrected. Optical rotations were recorded in $CHCl_3$ or MeOH solutions. ^{1}H NMR (300.13 and 200 MHz) and ^{13}C NMR (75.47 and 50 MHz) spectra were recorded in $CDCl_3$, Me_2CO-d_6, DMSO-d_6, or MeOD-d_4 (internal Me_4Si), respectively. TLC was performed on Silica F254 and detection by UV light at 254 nm or by charring with phosphomolybdic-H_2SO_4 reagent. Column chromatography was effected on Silica Gel 60 (230 mesh). Me_2CO, hexane, and ether were distilled before use. Bases and solvents were used as supplied. MeOH−NH_3 was methanol saturated with ammonia gas at room temperature.

3-Amino-5-*O*-benzyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (2). $Ti(OiPr)_4$ (4.45 mL, 14.96 mmol) was added to a solution of ulose derivative **1**[24] (3.47 g, 12.47 mmol) and NH_3 (17.8 mL, NH_3 in 7 N MeOH) in MeOH (10.0 mL). The reaction mixture was stirred at room temperature for 5 h, and then TMSCN (1.67 mL, 12.47 mmol) was added and the mixture stirred for 12 h. Water (5 mL) and EtOAc were added until oxidation of the titanium residue was complete. The solvent was evaporated to dryness and the crude product was purified by flash chromatography (EtOAc/petroleum ether, 15:85) to yield compound **2** (2.65 g, 70%) as a colorless solid: mp 111−113 °C; $[\alpha]^{25}_D$ −2 (*c* 1.1, $CHCl_3$); IR (ATR) ν 3359, 3293, 1392, 1370, 1205, 1098, 1033, 874 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.29 (m, 5 H, C_6H_5), 5.90 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 4.66 (d, 1 H, H-2), 4.59 (d, $J_{A,B}$ = 11.6 Hz, 1 H, H−A, C$H_2C_6H_5$), 4.54 (d, 1 H, H−B, C$H_2C_6H_5$), 3.99 (dd, $J_{4,5a}$ = 7.2 Hz, $J_{4,5b}$ = 5.6 Hz, 1 H, H-4), 3.90 (dd, $J_{5a,5b}$ = 9.6 Hz, 1 H, H-5a), 3.80 (dd, 1 H, H-5b), 1.93 (s, 2 H, NH_2), 1.52 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 137.1, 128.4, 127.9 (O*C*$_6$H$_5$), 113.5 [O*C*(CH$_3$)$_2$], 118.5 (CN), 104.1 (C-1), 83.0 (C-2), 79.7 (C-4), 74.0 (O*C*H$_2$C$_6$H$_5$), 69.1 (C-5), 62.4 (C-3), 26.5 (CH_3), 26.3 (CH_3); MS (ES) 305.27 [M + 1]$^+$, 327.27 [M + Na]$^+$, 343.24 [M + K]$^+$. Anal. Calcd for $C_{16}H_{20}N_2O_4$ (304.14 g/mol): C, 63.14; H, 6.62; N, 9.20. Found: C, 63.07; H, 7.00; N, 9.29.

3-Amino-5-*O*-benzoyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (2a). Likewise, **1a** (3.44 g, 12.40 mmol), NH_4Cl (3.33 g, 62.20 mmol), TEA (1.92 mL, 13.70 mmol), $Ti(OiPr)_4$ (4.45 mL, 14.90 mmol), and TMSCN (1.67 mL, 12.45 mmol) in MeOH (27.5 mL) gave, after flash chromatography (EtOAc/petroleum ether, 3:7), compound **2a** (3.10 g, 82%) as a colorless solid: mp 106−109 °C; $[\alpha]^{25}_D$ +22 (*c* 0.6, $CHCl_3$); IR (ATR) ν 1724, 1268, 1210, 1096, 1054, 1002 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.03, 7.53, 7.40 (m, 5 H, C_6H_5), 5.95 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 4.64 (d, 1 H, H-2), 4.74 (dd, $J_{4,5b}$ = 4.3 Hz, $J_{5a,5b}$ = 12.0 Hz, 1 H, H-5b), 4.60 (dd, $J_{4,5a}$ = 6.4 Hz, 1 H, H-5a), 4.04 (dd, 1 H, H-4), 1.88 (s, 2 H, NH_2), 1.52 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.0 (CO), 133.3, 129.8, 129.3, 128.4 (CO*C*$_6$H$_5$), 113.5 [O*C*(CH$_3$)$_2$], 118.0 (CN), 104.0 (C-1), 82.9 (C-2), 79.4 (C-4), 62.8 (C-5), 61.1 (C-3), 26.4, 26.2 (2 × CH_3); MS (ES) 341.15 [M + Na]$^+$, 357.19 [M + K]$^+$. Anal. Calcd for $C_{16}H_{18}N_2O_5$ (318.32 g/mol): C, 60.37; H, 5.70; N, 8.80 Found: C, 60.16; H, 5.76; N, 8.65.

General Method for the Synthesis of Compounds 3−5 and 3a−5a. Methyl-, ethyl-, or phenylmethanesulfonyl chloride (3 equiv) was added dropwise to a solution of aminonitriles **2** or **2a** and DMAP (0.5 equiv), in dry pyridine. The reaction mixture was stirred at room temperature until the disappearance of the aminonitrile (30 min to 5 h). Then, water and EtOAc were added. The organic layer was separated, dried over Na_2SO_4, and evaporated to dryness. The crude product was purified by flash chromatography to give **3**−**5** and **3a**−**5a** as indicated.

3-Amino-5-*O*-benzyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-3-*N*-methanesulfonyl-α-D-ribofuranose (3). CH_3SO_2Cl (0.76 mL, 9.90 mmol) was added dropwise to a solution of **2** (1 g, 3.30 mmol) and DMAP (0.2 g, 1.65 mmol) in dry pyridine (8.20 mL). The reaction mixture was stirred at room temperature for 3 h. Then, water and EtOAc were added. The organic layer was separated, dried over Na_2SO_4, and removed under vacuum. The crude product was submitted to flash chromatography (EtOAc/petroleum ether, 1:3) to yield compound **3** (1.20 g, 95%) as a colorless oil: $[\alpha]^{25}_D$ +14 (*c*, 2.8, $CHCl_3$); IR (ATR) ν 2986, 2926, 2866, 1452, 1378, 1348, 1155, 1092, 1034, 881 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.23 (m, 5 H, $CH_2C_6H_5$), 5.87 (s, 1 H, NH), 5.80 (d, $J_{1,2}$ = 3.4 Hz, 1 H, H-1), 4.97 (d, 1 H, H-2), 4.48 (s, 2 H, $CH_2C_6H_5$), 4.13 (m, 1 H, H-4), 3.81 (m, 2 H, 2 H-5), 2.98 (s, 3 H, SO_2CH_3), 1.44 (s, 3 H, CH_3), 1.24 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.9−128.0 (6 C, $CH_2C_6H_5$), 116.0 (CN), 113.8 [$OC(CH_3)_2$], 104.4 (C-1), 83.3 (C-2), 77.9 (C-4), 73.9 ($OCH_2C_6H_5$), 68.4 (C-5), 62.8 (C-3), 42.9 (SO_2CH_3), 26.5 (CH_3), 26.1 (CH_3); MS (ES) 382.25 $[M + 1]^+$, 405.23 $[M + Na]^+$, 421.15 $[M + K]^+$. Anal. Calcd for $C_{17}H_{22}N_2O_6S$ (382.12 g/mol): C, 53.39; H, 5.80; N, 7.33; S, 3.38. Found: C, 53.64; H, 5.92; N, 7.04; S, 8.60.

3-Amino-5-*O*-benzoyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-3-*N*-methanesulfonyl-α-D-ribofuranose (3a). Likewise, **2a** (300 mg, 18.00 mmol), DMAP (260 mg, 2.16 mmol), and CH_3SO_2Cl (1.15 mL, 11.34 mmol) in pyridine (12.4 mL) for 3 h gave, after flash chromatography (EtOAc/petroleum ether, 1:3), compound **3a** (1.80 g, 95%) as a colorless solid: mp 128−130 °C; $[\alpha]^{25}_D$ +43 (*c* 0.53, $CHCl_3$); IR (ATR) ν 1704, 1320, 1272, 1149, 710 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.01−7.54 (m, 5 H, COC_6H_5), 5.98 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 5.72 (s, 1 H, NH), 5.01 (d, 1 H, H-2), 4.84 (dd, $J_{4,5b}$ = 4.2 Hz, $J_{5a,\ 5b}$ = 12.3 Hz, 1 H, H-5b), 4.59 (dd, 1 H, H-5a), 4.24 (dd, $J_{4,5a}$ = 6.1 Hz, 1 H, H-4), 3.12 (s, 3 H, SO_2CH_3), 1.52 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.3 (CO), 136.6, 129.8, 128.9, 128.5 (6C, COC_6H_5), 115.0 (CN), 114.2 [$OC(CH_3)_2$], 104.0 (C-1), 82.4 (C-2), 78.2 (C-4), 62.4 (C-5), 61.8 (C-3), 43.0 (SO_2CH_3), 26.6 (CH_3), 26.2 (CH_3). MS (ES) 419.18 $[M + Na]^+$, 435.21 $[M + K]^+$. Anal. Calcd for $C_{17}H_{20}N_2O_7S$ (396.42 g/mol): C, 51.51; H, 5.09; N, 7.07. Found: C, 51.53; H, 5.02; N, 6.98.

3-Amino-5-*O*-benzyl-3-*C*-cyano-3-deoxy-3-*N*-ethanesulfonyl-1,2-*O*-isopropylidene-α-D-ribofuranose (4). Likewise, **2** (459 mg, 1.51 mmol), DMAP (93 mg, 0.76 mmol), and $CH_3CH_2SO_2Cl$ (0.43 mL, 4.50 mmol) in dry pyridine (10 mL) for 24 h gave, after flash chromatography (EtOAc/petroleum ether, 1:4), a mixture of compounds **2** + **4** (346 mg, 0.6:1 ratio). In the NMR spectra of this mixture we could assign specific signals for the new compound **4** {^1H NMR ($CDCl_3$, 200 MHz) δ 7.30−7.16 (m, 5 H, C_6H_5), 5.86 (d, $J_{1,2}$ = 3.6 Hz, 1 H, H-1), 5.32 (br s, 1 H, NH), 5.01 (d, 1 H, H-2), 4.50 (br s, 2 H, $CH_2C_6H_5$), (dd, $J_{4,5a}$ = 4.5 Hz, $J_{4,5b}$ = 8.5 Hz, 1 H, H-4), 3.89 (m, 2 H, 2 H-5), 3.13 (q, J = 7.5 Hz, 2 H, $CH_3CH_2SO_2$), 1.46 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 1.22 (t, 3 H, $CH_3CH_2SO_2$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 129.0−128.3 (OC_6H_5), 116.5 (CN), 114.3 [$OC(CH_3)_2$], 104.9 (C-1), 82.8 (C-2), 78.3 (C-4), 74.5 ($OCH_2C_6H_5$), 68.9 (C-5), 63.3 (C-3), 49.6 ($SO_2CH_2CH_3$), 27.0 (CH_3), 26.6 (CH_3), 8.4 ($SO_2CH_2CH_3$)}. An aliquot of this mixture was used for the synthesis of compound **9** (see below).

3-Amino-5-*O*-benzoyl-3-*C*-cyano-3-deoxy-3-*N*-ethanesulfonyl-1,2-*O*-isopropylidene-α-D-ribofuranose (4a). Likewise, **2a** (386 mg, 1.21 mmol), DMAP (70 mg, 0.61 mmol), and $CH_3CH_2SO_2Cl$ (0.35 mL, 3.63 mmol) in dry pyridine (3 mL) for 8 h gave, after flash chromatography (EtOAc/petroleum ether, 1:4), compound **4a** (165 mg, 33%) as a colorless solid: mp 85−87 °C; $[\alpha]^{25}_D$ +4 (*c* 0.53, $CHCl_3$); IR (ATR) ν 3249, 2985, 2210, 1725, 1602, 1273, 1111 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.09−7.46 (m, 5 H, COC_6H_5), 6.03 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 5.39 (s, 1 H, NH), 5.05 (d, 3 H, H-2), 4.88 (dd, $J_{4,5a}$ = 3.9 Hz, $J_{5a,5b}$ = 12.3 Hz, 1 H, H-5a), 4.65 (dd, 1 H, H-5b), 4.26 (dd, $J_{4,5b}$ = 6.1 Hz, 1 H, H-4), 3.29 (q, J = 7.3 Hz, 2 H, $CH_3CH_2SO_2$), 1.58 (s, 3 H, CH_3), 1.41 (s, 3 H, $SO_2CH_2CH_3$), 1.40 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.7 (CO), 133.9−128.9 (6 C, COC_6H_5), 115.2 (CN), 114.4 [$OC(CH_3)_2$], 104.2 (C-1), 82.6 (C-2), 78.8 (C-4), 62.9 (C-5), 62.1 (C-3), 49.8 ($SO_2CH_2CH_3$), 26.8 (CH_3), 26.5 (CH_3), 8.4 ($SO_2CH_2CH_3$); MS (ES) 428 $[M + Na]^+$, 433 $[M + K]^+$. Anal. Calcd for $C_{18}H_{22}N_2O_7S$ (410.44 g/mol): C, 52.67; H, 5.40; N, 6.83; S, 7.81. Found: C, 52.68; H; 5.61; N, 6.71; S, 7.65.

3-Amino-5-*O*-benzyl-3-*C*-cyano-3-deoxy-3-*N*-phenylmethanesulfonyl-1,2-*O*-isopropylidene-α-D-ribofuranose (5). Likewise, **2** (30 mg, 0.09 mmol), DMAP (6 mg, 0.05 mmol), and $C_6H_5CH_2SO_2Cl$ (54 mg, 0.28 mmol) in dry pyridine (0.7 mL) for 30 min gave, after flash chromatography (EtOAc/petroleum ether, 1:4), compound **5** (45 mg, 98%) as a colorless oil: $[\alpha]^{25}_D$ +5 (*c* 0.2, $CHCl_3$); IR (KBr) ν 3435, 1633, 1338, 1101 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.49−7.21 (m, 10 H, $OCH_2C_6H_5$, $SO_2CH_2C_6H_5$), 5.99 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H-1), 5.35 (s, 1 H, NH), 5.22 (d, 1 H, H-2), 4.51 (m, 2 H, $OCH_2C_6H_5$), 4.40 (m, 3 H, H-4a, $SO_2CH_2C_6H_5$), 4.21 (dd, $J_{4,5a}$ = 4.9 Hz, $J_{4,5b}$ = 8.2 Hz, 1 H, H-4), 3.86 (m, 2 H, 2 H-5), 1.63 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 136.5−128.1 ($OCH_2C_6H_5$, $SO_2CH_2C_6H_5$), 116.2 (CN), 114.3 [$OC(CH_3)_2$], 104.6 (C-1), 82.7 (C-2), 78.0 (C-4), 74.2 (C-6), 68.2 (C-5), 63.3 (C-3), 60.4 ($SO_2CH_2C_6H_5$), 26.8 (CH_3), 26.5 (CH_3); MS (ES) 459 $[M + 1]^+$, 476 $[M + NH_4]^+$, 481 $[M + Na]^+$, 939 $[2M + Na]^+$. Anal. Calcd for $C_{23}H_{26}N_2O_6S$ (458.53 g/mol): C, 60.25; H, 5.72; N, 6.11; S, 6.99. Found: C, 60.28; H; 5.81; N, 5.98; S, 7.11.

3-Amino-5-*O*-benzoyl-3-*C*-cyano-3-deoxy-3-*N*-phenylmethanesulfonyl-1,2-*O*-isopropylidene-α-D-ribofuranose (5a). Likewise, **2a** (1.60 g, 5.03 mmol), DMAP (310 mg, 2.51 mmol), and neat $C_6H_5CH_2SO_2Cl$ (2.93 g, 15.1 mmol) in pyridine (27 mL) for 30 min gave, after flash chromatography (EtOAc/petroleum ether, 1:4), compound **5a** (2.30 g, 97%) as a colorless solid: mp 69−71 °C; $[\alpha]^{25}_D$ +46 (*c* 0.07, $CHCl_3$); IR (KBr) ν 3435, 2985, 2210, 1724, 1274, 1154 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.04−7.28 (m, 10 H, $OCOC_6H_5$, $SO_2CH_2C_6H_5$), 6.05 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 5.30 (br s, 1 H, NH), 5.08 (d, 1 H, H-2), 4.84 (dd, $J_{4,5a}$ = 3.8 Hz, $J_{5a,5b}$ = 12.4 Hz, 1 H, H-5a), 4.61 (dd, $J_{4,5b}$= 6 Hz, 1 H, H-5b), 4.50 (dd, J = 14.1 Hz, 2 H, $SO_2CH_2C_6H_5$), 4.21 (dd, 1 H, H-4), 1.57 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 166.2 (CO), 133.5−128.4 ($OCOC_6H_5$, $SO_2CH_2C_6H_5$), 115.1 (CN), 114.3 [$OC(CH_3)_2$], 104.0 (C-1), 82.7 (C-2), 78.9 (C-4), 62.6 (C-5), 61.8 (C-3), 60.7 ($SO_2CH_2C_6H_5$), 26.6 (CH_3), 26.3 (CH_3); MS (ES): 490 $[M + NH_4]^+$, 495 $[M + Na]^+$, 967 $[2M + Na]^+$. Anal. Calcd for $C_{23}H_{24}N_2O_7S$ (472.54 g/mol): C, 58.46; H, 5.12; N, 5.93; S, 6.79. Found: C, 58.56; H, 4.90; N, 5.69; S, 6.57.

General Method for the Synthesis of Compounds 6−9, 6a, and 7a. To a solution of sulfonamidonitriles **3**−**5**, **3a**, and **4a** and K_2CO_3 (1.5 equiv) in acetone was added MeI or BnBr (2 equiv). The mixture was refluxed until the reaction was complete (45 min−8 h). The mixture was filtered through a silica pad and evaporated to dryness. The residue was purified by flash chromatography to give **6**−**9**, **6a**, and **7a** as indicated.

3-Amino-5-*O*-benzyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-3-*N*-methanesulfonyl-3-*N*-methyl-α-D-ribofuranose (6). To a solution of **3** (0.62 g, 1.62 mmol) and K_2CO_3 (0.33 g, 2.43 mmol) in acetone (15 mL) was added CH_3I (0.20 mL, 3.24 mmol). The reaction was refluxed for 45 min to yield, after flash chromatography through a silica pad (EtOAc/petroleum ether, 1:4), compound **6** (0.54 g, 83%) as a colorless oil: $[\alpha]^{25}_D$ +50 (*c* 2.12, $CHCl_3$); IR (ATR) ν 2986, 2932, 1347, 1154, 1032 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.27 (m, 5 H,

$CH_2C_6H_5$), 5.85 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 5.05 (d, 1 H, H-2), 4.48 (t, $J_{4,5}$ = 5.2 Hz, 1 H, H-4), 4.58 (d, $J_{A,B}$ = 11.17 Hz, 1 H, H−A, C$H_2C_6H_5$), 4.50 (d, 1 H, H−B, C$H_2C_6H_5$), 3.91 (d, 2 H, 2 H-5), 2.97 (s, 3 H, NCH_3), 2.91 (s, 3 H, SO_2CH_3), 1.50 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.9, 128.0, 127.4, (6 C, $CH_2C_6H_5$), 115.2 (CN), 112.8 [$OC(CH_3)_2$], 102.8 (C-1), 83.7 (C-2), 76.8 (C-4), 73.3 (O$CH_2C_6H_5$), 68.8 (C-5), 65.7 (C-3), 39.3 (SO_2CH_3), 34.3 (NCH_3), 25.9 (2 × CH_3); MS (ES) 397.13 $[M + 1]^+$. Anal. Calcd for $C_{18}H_{24}N_2O_6S$ (396.14 g/mol): C, 54.53; H, 6.10; N, 7.07; S, 8.09. Found: C, 54.21; H, 5.98; N, 6.84; S, 8.21.

3-Amino-5-*O*-benzoyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-3-*N*-methanesulfonyl-3-*N*-methyl-α-D-ribofuranose (6a). Likewise, **3a** (1.7 g, 4.28 mmol), K_2CO_3 (0.88 g, 6.42 mmol), and CH_3I (0.53 mL, 8.56 mmol) in acetone (50 mL) for 2 h gave, after flash chromatography (EtOAc/petroleum ether, 1:4) through a silica pad, **6a** (1.8 g, 99%) as a colorless solid: mp 115−117 °C; $[\alpha]^{25}_D$ +51 (*c* 1.31, $CHCl_3$); IR (ATR) ν 1715, 1352, 1266, 1151 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.94−7.36 (m, 5 H, COC_6H_5), 5.90 (dd, $J_{1,2}$= 3.8 Hz, 1 H, H-1), 5.07 (d, 1 H, H-2), 4.88 (dd, $J_{4,5a}$ = 7.53 Hz, $J_{5a,5b}$ = 12.2 Hz, 1 H, H-5a), 4.68 (dd, $J_{4,5b}$ = 2.5 Hz, 1 H, H-4), 4.50 (dd, 1 H, H-5b), 3.1 (s, 3 H, NCH_3), 3.00 (s, 3 H, SO_2CH_3), 1.47 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.0 (CO), 133.3, 129.6, 128.8, 128.3 (6 C, COC_6H_5), 115.0 (CN), 113.4 [O$C(CH_3)_2$], 103.1 (C-1), 83.9 (C-2), 76.1 (C-4), 65.6 (C-3), 63.3 (C-5), 39.8 (SO_2CH_3), 34.5 (NCH_3), 26.2 (CH_3), 26.0 (CH_3); MS (ES) 433.24 $[M + Na]^+$, 449.30 $[M + K]^+$, 843.31 $[2M + Na]^+$. Anal. Calcd for $C_{18}H_{22}N_2O_7S$ (410.11 g/mol): C, 52.67; H, 5.40; N, 6.83; S, 7.81. Found: C, 52.80; H, 5.69; N, 6.64; S, 8.02.

3-Amino-3-*N*-benzyl-5-*O*-benzyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-3-*N*-methanesulfonyl-α-D-ribofuranose (7). Likewise, **3** (25.9 g, 67.80 mmol), K_2CO_3 (14.72 g, 106.50 mmol), and $C_6H_5CH_2Br$ (17.4 mL, 145.28 mmol) in acetone (500 mL) for 7 h gave, after flash chromatography (EtOAc/petroleum ether, 1:9), compound **7** (21.12 g, 81%) as a colorless solid: mp 86−88 °C; $[\alpha]^{25}_D$ +58 (*c* 0.65, $CHCl_3$); IR (ATR) ν 1347, 1152, 1058, 816 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (m, 10 H, 2 × $CH_2C_6H_5$), 5.89 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 5.15 (d, 1 H, H-2), 4.69 (dd, $J_{4,5a}$ = 5.4 Hz, $J_{4,5b}$ = 4.0 Hz, 1 H, H-4), 4.66 (d, $J_{A,B}$ = 16.5 Hz, 1 H, H−A, N$CH_2C_6H_5$), 4.58 (d, 1 H, H−B, N$CH_2C_6H_5$), 4.54 (d, $J_{A,B}$= 11.7 Hz, 1 H, H−A, O$CH_2C_6H_5$), 4.46 (d, 1 H, H−B, O$CH_2C_6H_5$), 3.89 (m, 1 H, H-5a), 3.82 (m, 1 H, H-5b), 2.94 (s, 3 H, SO_2CH_3), 1.34 (s, 6 H, 2 × CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 137.4, 136.4, 129.0, 128.5 (12 C, 2 × $CH_2C_6H_5$), 70.2 (C-5), 67.8 (C-3), 51.8 (N$CH_2C_6H_5$), 41.6 (SO_2CH_3), 26.9 (CH_3), 26.4 (CH_3); MS (ES): 495.21 $[M + Na]^+$, 511.19 $[M + K]^+$. Anal. Calcd for $C_{24}H_{28}N_2O_6S$ (472.17 g/mol): C, 61.00; H, 5.97; N, 5.93; S, 6.79. Found: C: 61.13; H, 5.83; N, 6.11; S, 6.61.

3-Amino-3-*N*-benzyl-5-*O*-benzoyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-3-*N*-methanesulfonyl-α-D-ribofuranose (7a). Likewise, **3a** (30 mg, 0.07 mmol), K_2CO_3 (15 mg, 0.11 mmol), and $C_6H_5CH_2Br$ (0.02 mL, 0.11 mmol) in acetone (2 mL) for 5 h gave, after flash chromatography (EtOAc/petroleum ether, 1:4), compound **7a** (24 mg, 70%) as a colorless solid: mp 179−181 °C; $[\alpha]^{25}_D$ +3 (*c* 0.7, $CHCl_3$); IR (ATR) ν 3436, 1724, 1348, 1153 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.11−7.30 (OCOC_6H_5, $NCH_2C_6H_5$), 5.97 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 5.22 (d, 1 H, H-2), 4.79 (s, 2 H, N$CH_2C_6H_5$), 4.73 (m, 2 H, H-4, H-5a), 4.51 (dd, $J_{4,5b}$ = 7.3 Hz, $J_{5a,5b}$ = 12.6 Hz, 1 H, H-5b), 3.08 (s, 3 H, SO_2CH_3), 1.48 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 166.2 (CO), 135.7−128.4 (OCOC_6H_5, $NCH_2C_6H_5$), 115.6 (CN), 113.7 [O$C(CH_3)_2$], 103.2 (C-1), 84.4 (C-2), 76.9 (C-4), 66.7 (C-3), 64.2 (C-5), 51.7 (N$CH_2C_6H_5$), 41.9 (SO_2CH_3), 26.6 (CH_3), 26.3 (CH_3); MS (ES) 504 $[M + NH_4]^+$, 509 $[M + Na]^+$, 995 $[2M + Na]^+$. Anal. Calcd for $C_{24}H_{26}N_2O_7S$ (486.54 g/mol): C, 59.25; H, 5.39; N, 5.76; S, 6.59. Found: C, 59.68; H, 5.18; N, 5.53; S, 6.83.

3-Amino-5-*O*-benzyl-3-*C*-cyano-3-deoxy-3-*N*-ethanesulfonyl-1,2-*O*-isopropylidene-3-*N*-methyl-α-D-ribofuranose (8). A solution of α-aminonitrile **2** (241 mg, 0.79 mmol), DMAP (47 mg, 0.39 mmol), and $CH_3CH_2SO_2Cl$ (0.22 mL, 2.37 mmol) in pyridine (6 mL) at room temperature for 5 h gave, following the usual workup and flash chromatography (EtOAc/petroleum ether, 1:4), compound **4** (85 mg), which was isolated contaminated by traces of product **2**. This mixture (70 mg) refluxed with K_2CO_3 (37 mg, 0.27 mmol) and CH_3I (0.02 mL, 0.36 mmol) in acetone (10 mL) for 2 h to give, after flash chromatography (EtOAc/petroleum ether, 3:7), compound **8** (57 mg, 77%) as a colorless solid: mp 68−70 °C; $[\alpha]^{25}_D$ +40 (*c* 0.25, $CHCl_3$); IR (KBr) ν 2989, 2942, 1455, 1378, 1346, 1216, 1147, 1105, 1029 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.34−7.32 (m, 5 H, $OCH_2C_6H_5$), 5.90 (d, $J_{1,2}$= 3.7 Hz, 1 H, H-1), 5.11 (d, 1 H, H-2), 4.68 (dd, $J_{4,5a}$ = 5.6 Hz, $J_{4,5b}$ = 5.3 Hz, 1 H, H-4), 4.65 (d, $J_{A;B}$ = 11.8 Hz, 1 H, H−A, O$CH_2C_6H_5$), 4.56 (d, 1 H, H−B, O$CH_2C_6H_5$), 3.99 (dd, $J_{4,5b}$ = 5.3 Hz, $J_{5a,5b}$ = 10.5 Hz, 1 H, H-5b), 3.92 (d, $J_{4,5a}$ = 5.6 Hz, 1 H, H-5a), 2.94 (q, J = 7.4 Hz, 2 H, $SO_2CH_2CH_3$), 3.05 (s, 3 H, NCH_3), 1.57 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.30 (t, 3 H, $SO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 137.0−127.9 ($OCH_2C_6H_5$), 115.6 (CN), 113.3 [O$C(CH_3)_2$], 103.1 (C-1), 84.8 (C-2), 76.7 (C-4), 74.0 (O$CH_2C_6H_5$), 69.1 (C-5), 66.3 (C-3), 48.1 ($SO_2CH_2CH_3$), 35.5 (NCH_3), 26.9 (CH_3), 26.4 (CH_3), 7.8 ($SO_2CH_2CH_3$); MS (ES) 411 $[M + 1]^+$, 428 $[M + NH_4]^+$, 433 $[M + Na]^+$. Anal. Calcd for $C_{19}H_{26}N_2O_6S$ (410.49 g/mol): C, 55.59; H, 6.38; N, 6.82; S, 7.81. Found: C, 55.72; H, 6.21; N, 6.54; S, 7.93.

3-Amino-3-*N*-benzyl-5-*O*-benzyl-3-*C*-cyano-3-deoxy-3-*N*-ethanesulfonyl-1,2-*O*-isopropylidene-α-D-ribofuranose (9). Likewise, a mixture of compounds **2** and **4** (82 mg, ratio 0.6:1), K_2CO_3 (44 mg, 0.32 mmol), and $C_6H_5CH_2Br$ (0.05 mL, 0.42 mmol) in acetone (8 mL) for 3 h gave, after flash chromatography (EtOAc/petroleum ether, 1:4), the unreacted α-aminonitrile **2** (16 mg) and compound **9** (60 mg, 62%) as a colorless solid: mp 79−81 °C; $[\alpha]^{25}_D$ +38 (*c* 0.38, $CHCl_3$); IR (KBr) ν 3435, 2981, 2880, 1631, 1604, 1497, 1455, 1346, 1147, 1148, 1061, 1027 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.32−7.16 (m, 10 H, 2 × $CH_2C_6H_5$), 5.76 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 5.01 (d, 1 H, H-2), 4.61 (m, 1 H, H-4), 4.52 (s, 2 H, N$CH_2C_6H_5$), 4.41 (d, J = 7.5 Hz, 2 H, O$CH_2C_6H_5$), 3.76 (m, 2 H, 2 H-5), 2.89 (q, J = 7.7 Hz, 2 H, $SO_2CH_2CH_3$), 1.20 (m, 9 H, $SO_2CH_2CH_3$, 2 × CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 137.4 (1 C, Cipso, $CH_2C_6H_5$), 136.7 (1 C, Cipso, $CH_2C_6H_5$), 129.2−128.6 (10 C, 2 × $CH_2C_6H_5$), 116.5 (CN), 113.8 [O$C(CH_3)_2$], 103.4 (C-1), 84.9 (C-2), 78.1 (C-4), 74.3 (O$CH_2C_6H_5$), 70.1 (C-5), 68.0 (C-3), 52.2 (N$CH_2C_6H_5$), 49.4 ($SO_2CH_2CH_3$), 26.9 (CH_3), 26.4 (CH_3), 8.2 ($SO_2CH_2CH_3$); MS (ES) 487 $[M + 1]^+$, 504 $[M + NH_4]^+$, 509 $[M + Na]^+$. Anal. Calcd for $C_{25}H_{30}N_2O_6S$ (486.58 g/mol): C, 61.71; H, 6.21; N, 5.76; S, 6.59. Found: C, 61.54; H, 6.42; N, 5.68; S, 6.44.

3-Amino-3-*N*-benzyl-5-*O*-benzyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (2B). K_2CO_3 (41 mg, 0.30 mmol) and $PhCH_2Br$ (0.05 mL, 0.40 mmol) were added to a solution of the α-aminonitrile **2** (60 mg, 0.20 mmol) in acetone (5 mL). After 3 h at reflux, no reaction was observed. Then, the reaction mixture was refluxed for 2 days. The mixture was filtered through Celite and evaporated to dryness. The residue was then flash chromatographed (hexane/AcOEt, 9:1) to give **2B** (31 mg, 39%) as a colorless oil: $[\alpha]^{25}_D$ +34 (*c* 0.45, $CHCl_3$); IR (film) ν 3331, 3060, 3031, 2924, 2862, 1496, 1454, 1376, 1216, 1164, 1099 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.36−7.28 (m, 10 H, $OCH_2C_6H_5$, $NCH_2C_6H_5$), 5.99 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 4.77 (d, 1 H, H-2), 4.60 (s, $CH_2C_6H_5$), 4.15 (t, J = 5.9 Hz, 1 H, H-5a), 4.02 (m, 1 H, H-4), 3.90 (m, 3 H, H-5b, $NCH_2C_6H_5$), 2.21 (br t, J = 6.6 Hz, NH), 1.57 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3); ^{13}C ($CDCl_3$, 50 MHz) δ 138.9−127.9 ($OCH_2C_6H_5$, $NCH_2C_6H_5$), 117.8 (CN), 114.0 [O$C(CH_3)_2$O], 105.0 (C-1), 81.8 (C-2), 79.9 (C-4), 74.3 ($OCH_2C_6H_5$), 69.8 (C-5), 68.4 (C-3), 52.3 ($NCH_2C_6H_5$), 27.1, 26.8 [2 (CH_3)$_2$]; MS (ES) 395 $[M + 1]^+$, 417 $[M + Na]^+$. Anal. Calcd for $C_{23}H_{26}N_2O_4$ (394.46 g/mol): C, 70.03; H, 6.64; N, 7.10. Found: C, 70.11; H, 6.57; N, 6.99.

N-Methylation of 3-Amino-5-*O*-benzyl-3-*C*-cyano-3-deoxy-3-*N*-phenylmethanesulfonyl-1,2-*O*-isopropylidene-

α-D-ribofuranose (5). Likewise, **5** (0.135 g, 0.29 mmol), K_2CO_3 (0.06 g, 0.44 mmol), and CH_3I (0.04 mL, 0.59 mmol) in acetone (5 mL) for 22 h gave, after flash chromatography (EtOAc/petroleum ether, 1:4), 3-amino-5-*O*-benzyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-3-*N*-phenylmethanesulfonyl-α-D-ribofuranose (**10**) (0.039 g, 28%) and 5-*O*-benzyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′,3′-dihydro-2′-*N*-methyl-1′,1′-dioxide-5′-phenyl-isothiazolyl)-α-D-ribofuranose (**11**) (0.039 g, 28%) as colorless solids. **10**: mp 46−49 °C; $[\alpha]^{25}_D$ +72 (*c* 0.39, $CHCl_3$); IR (KBr) *ν* 3436, 1630, 1353, 1153, 1029 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 7.36−7.30 (m, 10 H, $OCH_2C_6H_5$, $SO_2CH_2C_6H_5$), 5.92 (d, $J_{1,2}$ = 3.9 Hz, 1 H, H-1), 5.14 (d, 1 H, H-2), 4.70 (d, $J_{A,B}$ = 12.1 Hz, 1 H, H−A, $OCH_2C_6H_5$), 4.59 (d, 1 H, H−B, $OCH_2C_6H_5$), 4.57 (dd, $J_{4,5a}$ = 4.4 Hz, $J_{4,5b}$ = 5.8 Hz, 1 H, H-4), 4.40 (s, 2 H, $SO_2CH_2C_6H_5$), 3.92 (dd, $J_{4,5b}$= 5.8 Hz, $J_{5a,5b}$ = 11.0 Hz, 1 H, H-5b), 3.84 (dd, 1 H, H-5a), 2.63 (s, 3 H, NCH_3), 1.56 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 137.3−127.9 ($OCH_2C_6H_5$, $SO_2CH_2C_6H_5$), 115.6 (CN), 113.4 [$OC(CH_3)_2$], 103.2 (C-1), 84.9 (C-2), 77.3 (C-4), 74.0 ($OCH_2C_6H_5$), 69.2 (C-5), 66.5 (C-3), 60.0 ($SO_2CH_2C_6H_5$), 36.0 (NCH_3), 26.4 (CH_3), 26.3 (CH_3); MS (ES) 473.2 $[M + 1]^+$, 490.3 $[M + NH_4]^+$, 495.1 $[M + Na]^+$, 967.3 $[2M + Na]^+$. Anal. Calcd for $C_{24}H_{28}N_2O_6S$ (472.56 g/mol): C, 61.00; H, 5.97; N, 5.93; S, 6.78. Found: C, 61.23; H, 5.81; N, 5.78; S, 6.99. **11**: mp 61−62 °C; $[\alpha]^{25}_D$ +52 (*c* 0.5, $CHCl_3$); IR (KBr) *ν* 3459, 3368, 2926, 1650, 1377, 1273, 1155, 1057 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 7.43−7.28 (m, 10 H, $OCH_2C_6H_5$, $CH_2C_6H_5$), 5.80 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 4.63 (d, 1 H, H-2), 4.57 (dd, $J_{4,5a}$ = 2.9 Hz, $J_{4,5b}$ = 5.9 Hz, 1 H, H-4), 4.44 (s, 2 H, $CH_2C_6H_5$), 4.32 (br s, 2 H, NH_2), 3.73 (dd, $J_{4,5a}$ = 2.9 Hz, $J_{5a,5b}$ = 11.3 Hz, 1 H, H-5a), 3.59 (dd, $J_{4,5b}$ = 5.9 Hz, $J_{5a,5b}$ = 11.3 Hz, 1 H, H-5b), 2.94 (s, 3 H, NCH_3), 1.54 (s, 3 H, CH_3), 1.25 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 146.5 (C-4′), 137.7−128.2 ($OCOC_6H_5$, $CH_2C_6H_5$), 126.8 (C-5′), 113.8 [$OC(CH_3)_2$], 104.2 (C-1), 85.0 (C-2), 75.4 (C-4), 74.3 ($CH_2C_6H_5$), 69.6 (C-3), 67.2 (C-5), 27.3 (NCH_3), 26.6, 26.3 (2 × CH_3); MS (ES) 473 $[M + 1]^+$, 967 $[2M + Na]^+$. Anal. Calcd for $C_{24}H_{28}N_2O_6S$ (472.56 g/mol): C, 61.00; H, 5.97; N, 5.93; S, 6.78. Found: C, 59.92; H, 6.06; N, 5.98; S, 6.85.

N-Benzylation of 3-Amino-5-*O*-benzyl-3-*C*-cyano-3-deoxy-3-*N*-phenylmethanesulfonyl-1,2-*O*-isopropylidene-α-D-ribofuranose (5). Likewise, **5** (0.105 g, 0.23 mmol), K_2CO_3 (50 mg, 0.35 mmol), and $C_6H_5CH_2Br$ (0.06 mL, 0.46 mmol) was refluxed in acetone (7 mL) for 4 h gave, after flash chromatography (EtOAc/petroleum ether, 1:4), 3-amino-3-*N*-benzyl-5-*O*-benzyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-3-*N*-phenylmethanesulfonyl-α-D-ribofuranose (**12**) (67 mg, 53%) and 5-*O*-benzyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′-*N*-benzyl-2′,3′-dihydro-1′,1′-dioxide-5′-phenyl-isothiazolyl)-α-D-ribofuranose (**13**) (44 mg, 35%) as colorless solids. **12**: mp 45−46 °C; $[\alpha]^{25}_D$ +70 (*c* 0.4, $CHCl_3$); IR (KBr) *ν* 3435, 2989, 2935, 1630, 1496, 1455, 1355, 1154, 1096, 1026 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 7.41−7.28 (m, 15 H, $OCH_2C_6H_5$, $SO_2CH_2C_6H_5$, $NCH_2C_6H_5$), 5.83 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 5.11 (d, 1 H, H-2), 4.70−4.35 (m, 5 H, H-4, $OCH_2C_6H_5$, $SO_2CH_2C_6H_5$), 4.21 (s, 2 H, $NCH_2C_6H_5$), 3.91 (d, 2 H, *J* = 4.5 Hz, 2 H-5), 1.27 (s, 3 H, CH_3), 1.06 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 137.0−127.9 ($OCH_2C_6H_5$, $SO_2CH_2C_6H_5$, $NCH_2C_6H_5$), 116.1 (CN), 113.4 [$OC(CH_3)_2O$], 100.8 (C-1), 84.4 (C-2), 76.7 (C-4), 73.8 ($OCH_2C_6H_5$), 69.9 (C-5), 67.5 (C-3), 59.9 ($SO_2CH_2C_6H_5$), 52.3 ($NCH_2C_6H_5$), 26.3 (CH_3), 25.5 (CH_3); EM (ES) 549 $[M + 1]^+$, 571 $[M + Na]^+$. Anal. Calcd for $C_{30}H_{32}N_2O_6S$ (548.6 g/mol): C, 65.68; H, 5.88; N, 5.11; S, 5.84. Found: C, 65.73; H, 5.94; N, 5.03; S, 5.71. **13**: mp 64−66 °C; $[\alpha]^{25}_D$ +91 (*c* 0.53, $CHCl_3$); IR (KBr) *ν* 3434, 3349, 2991, 1659, 1605, 1274, 1163, 1050 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 7.49−7.09 (m, 15 H, $NCH_2C_6H_5$, $OCH_2C_6H_5$, $CH_2C_6H_5$), 5.80 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 4.74 (br s, 3 H, H-2, $NCH_2C_6H_5$), 4.39 (br s, 3 H, H-4, NH_2), 4.22 (d, *J* = 6.9 Hz, 2 H, $OCH_2C_6H_5$), 3.39 (m, 2 H, 2 H-5), 1.60 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 146.5 (C-4′), 137.4−127.8 ($NCH_2C_6H_5$, $OCH_2C_6H_5$, $CH_2C_6H_5$), 126.5 (C-5′), 113.6 [$OC(CH_3)_2$], 103.9 (C-1), 84.8 (C-2), 75.8 (C-4), 73.6 ($CH_2C_6H_5$), 69.6 (C-3), 66.4 (C-5), 44.7 ($NCH_2C_6H_5$), 26.5, 25.9 (2 × CH_3); MS (ES) 549 $[M + 1]^+$, 571 $[M + Na]^+$, 1119 $[2M + Na]^+$. Anal. Calcd for $C_{30}H_{32}N_2O_6S$ (548.65 g/mol): C, 65.68; H, 5.88; N, 5.11; S, 5.84. Found: C, 65.59; H, 5.97; N, 5.02; S, 5.62.

N-Methylation of 3-Amino-5-*O*-benzoyl-3-*C*-cyano-3-deoxy-3-*N*-phenylmethanesulfonyl-1,2-*O*-isopropylidene-α-D-ribofuranose (5a). Likewise, **5a** (0.30 g, 0.64 mmol), K_2CO_3 (0.132 g, 0.95 mmol), and CH_3I (0.08 mL, 1.28 mmol) refluxing in acetone (10 mL) for 2 h gave, after flash chromatography (EtOAc/petroleum ether, 1:9), 3-amino-5-*O*-benzoyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-3-*N*-methyl-3-*N*-phenylmethanesulfonyl-α-D-ribofuranose **(10a)** (240 mg, 76%) and **11a** (21 mg, 7%) as colorless solids. **10a**: mp 51−53 °C; $[\alpha]^{25}_D$ +53 (*c* 0.27, $CHCl_3$); IR (KBr) *ν* 3435, 1723, 1273, 1110 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 8.12−7.41 (m, 10 H, $OCOC_6H_5$, $SO_2CH_2C_6H_5$), 5.98 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 5.19 (d, 1 H, H-2), 4.90 (dd, $J_{4,5a}$ = 1.7 Hz, $J_{5a,5b}$ = 12.1 Hz, 1 H, H-5a), 4.67 (dd, $J_{4,5b}$ = 7.9 Hz, 1 H, H-4), 4.50 (m, 3 H, H-5b, $SO_2CH_2C_6H_5$), 2.79 (s, 3 H, NCH_3),1.56 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 166.3 (CO), 133.5−128.2 ($OCOC_6H_5$, $SO_2CH_2C_6H_5$), 115.3 (CN), 113.6 [$OC(CH_3)_2$], 103.4 (C-1), 84.7 (C-2), 76.3 (C-4), 65.8 (C-3), 63.4 (C-5), 60.1 ($SO_2CH_2C_6H_5$), 35.9 (NCH_3), 26.4 (CH_3), 26.2 (CH_3); MS (ES) 504 $[M + NH_4]^+$, 509 $[M + Na]^+$, 995 $[2M + Na]^+$. Anal. Calcd for $C_{24}H_{26}N_2O_7S$ (486.54 g/mol): C, 59.25; H, 5.39; N, 5.76; S, 6.59. Found: C, 59.11; H, 5.60; N, 5.49; S, 6.35. **11a**: mp 200−202 °C; $[\alpha]^{26}_D$ +24 (*c* 0.34, $CHCl_3$); IR (KBr) *ν* 3457, 2930, 1711, 1660, 1272, 1058, 719 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 8.07−7.43 (m, 10 H, $OCOC_6H_5$, $CH_2C_6H_5$), 5.95 (d, $J_{1,2}$= 3.8 Hz, 1 H, H-1), 4.88 (dd, $J_{4,5a}$ = 3.3 Hz, $J_{4,5b}$ = 7.5 Hz, 1 H, H-4), 4.83 (d, 1 H, H-2), 4.62 (m, 4 H, H-5a, H-5b, NH_2), 3.17 (s, 3 H, NCH_3), 1.68 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 166.5 (CO), 144.5 (C-4′), 133.3−128.4 ($OCOC_6H_5$, $CH_2C_6H_5$), 126.5 (C-5′), 113.6 [$OC(CH_3)_2$], 103.9 (C-1), 84.7 (C-2), 73.7 (C-4), 69.4 (C-3), 61.6 (C-5), 27.1 (NCH_3), 26.2, 25.9 (2 × CH_3); MS (ES) 487 $[M + 1]^+$, 995 $[2M + Na]^+$. Anal. Calcd for $C_{24}H_{26}N_2O_7S$ (486.54 g/mol): C, 59.25; H, 5.39; N, 5.76; S, 6.59. Found: C, 58.19; H, 5.42; N, 5.58; S, 6.88.

N-Benzylation of 3-Amino-5-*O*-benzoyl-3-*C*-cyano-3-deoxy-3-*N*-phenylmethanesulfonyl-1,2-*O*-isopropylidene-α-D-ribofuranose (5a). Likewise, **5a** (0.29 g, 0.61 mmol), K_2CO_3 (0.130 g, 0.92 mmol), and $C_6H_5CH_2Br$ (0.15 mL, 1.22 mmol) refluxing in acetone (15 mL) for 6 h gave, after flash chromatography (EtOAc/petroleum ether, 1:4), 3-amino-3-*N*-benzyl-5-*O*-benzoyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-3-*N*-phenylmethanesulfonyl-α-D-ribofuranose (**12a**) (162 mg, 47%) and 5-*O*-benzoyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′-*N*-benzyl-2′,3′-dihydro-l′,1′-dioxide-5′-phenyl-isothiazolyl)-α-D-ribofuranose (**13a**) (10 mg, 3%) as colorless solids. **12a**: mp 63−65 °C; $[\alpha]^{25}_D$ +79 (*c* 0.26, $CHCl_3$); IR (KBr) *ν* 3436, 2927, 1721, 1627, 1272, 1096, 1024 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 8.11−7.28 (m, 15 H, $OCOC_6H_5$, $SO_2CH_2C_6H_5$, $CH_2C_6H_5$), 5.93 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 5.17 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-2), 4.82 (m, 2 H, H-4, H-5a), 4.46 (m, 5 H, H-5b, $CH_2C_6H_5$, $SO_2CH_2C_6H_5$), 1.33 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 166.3 (CO), 136.0−128.0 ($OCOC_6H_5$, $SO_2CH_2C_6H_5$, $CH_2C_6H_5$), 115.9 (CN), 113.8 [$OC(CH_3)_2$], 103.2 (C-1), 84.4 (C-2), 77.3 (C-4), 66.9 (C-3), 64.2 (C-5), 60.5 ($SO_2CH_2C_6H_5$), 52.6 ($CH_2C_6H_5$), 26.5 (CH_3), 25.9 (CH_3); MS (ES) 580.3 $[M + NH_4]^+$, 585.2 $[M + Na]^+$, 1148.3 $[2M + Na]^+$. Anal. Calcd for $C_{30}H_{30}N_2O_7S$ (562.64 g/mol): C, 64.04; H, 5.37; N, 4.98; S, 5.70. Found: C, 63.95; H, 5.17; N, 4.84; S, 5.98. **13a**: mp 210−212 °C; $[\alpha]^{25}_D$ +47 (*c* 0.38, $CHCl_3$); IR (KBr) *ν* 3336, 1722, 1644, 1455, 1376, 1271, 1062 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 7.92−7.28 (m, 15 H, $NCH_2C_6H_5$, $OCOC_6H_5$, C_6H_5), 5.94 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 4.95 (s, 2 H, $CH_2C_6H_5$), 4.94 (d, 1 H, H-2), 4.64 (br s, 2 H, NH_2), 4.62 (m, 1 H, H-4), 4.41(dd, $J_{4,5a}$ = 7.7 Hz, $J_{5a,5b}$ = 12.4 Hz, 1 H, H-5a), 4.23 (dd, $J_{4,5b}$ = 1.8 Hz, $J_{5a,5b}$ = 12.4 Hz, 1 H, H-5b), 1.77 (s, 3 H, CH_3), 1.44 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 166.0 (CO), 144.9 (C-4′), 137.3−128.1 ($OCOC_6H_5$, $CH_2C_6H_5$, C_6H_5), 126.2

(C-5′), 113.9 [O*C*(CH$_3$)$_2$], 104.1 (C-1), 84.7 (C-2), 75.0 (C-4), 69.8 (C-3), 61.8 (C-5), 44.8 (N*C*H$_2$C$_6$H$_5$), 26.6, 26.0 (2 × CH$_3$); MS (ES) 563 [M + 1]$^+$, 580 [M + NH$_4$]$^+$, 1147 [2M + Na]$^+$. Anal. Calcd for $C_{30}H_{30}N_2O_7S$ (562.60 g/mol): C, 64.04; H, 5.37; N, 4.98; S, 5.70. Found: C, 63.90; H, 5.43; N, 4.72; S, 5.89.

Likewise, **5a** (106 mg, 0.22 mmol), K_2CO_3 (50 mg, 0.34 mmol), and $C_6H_5CH_2Br$ (0.05 mL, 0.44 mmol) in acetone (8 mL) for 24 h gave, after flash chromatography (EtOAc/petroleum ether, 1:4), compound **13b** (20 mg, 14%) and **13a** (82 mg, 66%) as colorless solids. **13b**: mp 208−210 °C; [α]$^{25}_D$ +33 (*c* 0.21, $CHCl_3$); IR (KBr) *ν* 3430, 3379, 2934, 1723, 1637, 1273, 1143 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) *δ* 7.80−6.87 (m, 20 H, NCH$_2$C$_6$*H*$_5$, NHCH$_2$C$_6$*H*$_5$, COC$_6$*H*$_5$, C$_6$*H*$_5$), 5.55 (d, $J_{1,2}$ = 3.9 Hz, 1 H, H-1), 4.86 (br s, 3 H, NH, NHC*H*$_2$C$_6$H$_5$), 4.77 (d, 1 H, H-2), 4.51 (dd, $J_{4,5a}$ = 7.8 Hz, $J_{4,5b}$ = 1.3 Hz, 1 H, H-4), 4.32 (dd, $J_{4,5a}$ = 7.9 Hz, $J_{5a,5b}$ = 12.4 Hz, 1 H, H-5a), 4.09 (dd, $J_{4,5b}$ = 1.3 Hz, 1 H, H-5b), 3.71 (m, 2 H, NHC*H*$_2$C$_6$H$_5$), 1.65 (s, 3 H, CH$_3$), 1.28 (s, 3 H, CH$_3$); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 166.3 (CO), 144.9 (C-4′), 137.7−127.6 (NCH$_2$*C*$_6$H$_5$, NHCH$_2$*C*$_6$H$_5$, CO*C*$_6$H$_5$, *C*$_6$H$_5$), 114.1 [O*C*(CH$_3$)$_2$], 107.0 (C-5′), 104.5 (C-1), 85.3 (C-2), 75.7 (C-4), 70.3 (C-3), 62.2 (C-5), 50.4 (NH*C*H$_2$C$_6$H$_5$), 45.2 (N*C*H$_2$C$_6$H$_5$), 26.9 (CH$_3$), 26.2 (CH$_3$); MS (ES) 653 [M + 1]$^+$, 675 [M + Na]$^+$, 1328 [2M + Na]$^+$. Anal. Calcd for $C_{37}H_{36}N_2O_7S$ (652.76 g/mol): C, 68.08; H, 5.56; N, 4.29; S, 4.91. Found: C, 68.24; H, 5.39; N, 3.99; S, 5.07.

General Method for the Synthesis of Compounds 11, 13−17, 11a, and 13a−15a via CSIC Reaction Using Cs_2CO_3. Cs_2CO_3 (1 equiv) was added to a solution of compounds **6**−**10**, **12**, **6a**, **7a**, **10a**, and **12a**, in CH_3CN. The mixture was refluxed until complete reaction and then filtered through Celite and evaporated to dryness. The residue was purified by flash chromatography to give compounds **11**, **13**−**17**, **11a**, and **13a**−**15a** as indicated.

5-*O*-Benzyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′,3′-dihydro-2′-*N*-methyl-1′,1′-dioxide-5′-phenylisothiazolyl)-α-D-ribofuranose (11). Following the general method, Cs_2CO_3 (25 mg, 0.8 mmol) was added to a solution of **10** (30 mg, 0.06 mmol) in CH_3CN (3 mL). The reaction mixture was refluxed for 1 h and then evaporated to dryness. The residue was purified by flash chromatography (EtOAc/petroleum ether, 3:7) to give **11** (29 mg, 99%).

5-*O*-Benzyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′-*N*-benzyl-2′,3′-dihydro-1′,1′-dioxide-5′-phenylisothiazolyl)-α-D-ribofuranose (13). Following the general method, Cs_2CO_3 (25 mg, 0.8 mmol) was added to a solution of **12** (34 mg, 0.06 mmol) in CH_3CN (3 mL). The reaction mixture was refluxed for 2 h and then evaporated to dryness. The residue was purified by flash chromatography (EtOAc/petroleum ether, 1:4) to give **13** (27 mg, 77%).

5-*O*-Benzoyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′,3′-dihydro-2′-*N*-methyl-l′,1′-dioxide-5′-phenylisothiazolyl)-α-D-ribofuranose (11a). Following the general method, Cs_2CO_3 (0.12 g, 0.35 mmol) was added to a solution of **10a** (142 g, 0.29 mmol) in CH_3CN (5 mL). The reaction mixture was refluxed for 1 h and then evaporated to dryness. The residue was purified by flash chromatography (EtOAc/petroleum ether, 1:4) to give **11a** (140 g, 98%).

5-*O*-Benzoyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′-*N*-benzyl-2′,3′-dihydro-l′,1′-dioxide-5′-phenylisothiazolyl)-α-D-ribofuranose (13a). Following the general method, Cs_2CO_3 (37 mg, 0.11 mmol) was added to a solution of **12a** (53 g, 0.09 mmol) in CH_3CN (4 mL). The reaction mixture was refluxed for 1.2 h and then evaporated to dryness. The residue was purified by flash chromatography (EtOAc/petroleum ether, 1:1) to give **13a** (53 g, 99%).

5-*O*-Benzyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′,3′-dihydro-2′-*N*-methyl-1′,1′-dioxide-isothiazolyl)-α-D-ribofuranose (14). Following the general method, Cs_2CO_3 (0.63 g, 1.94 mmol) was added to a solution of **6** (0.77 g, 1.94 mmol) in CH_3CN (5 mL). The reaction mixture was refluxed for 19 h and then evaporated to dryness. The residue was purified by flash chromatography (EtOAc/petroleum ether, 7:3) to give **14** (0.45 g, 59%) as a colorless solid: mp 214−217 °C; [α]$^{25}_D$ +27 (*c* 0.69, acetone); IR (ATR) *ν* 3430, 1658, 1276, 1134, 1056 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz) *δ* 7.31 (m, 5 H, CH$_2$C$_6$*H*$_5$), 6.05 (s, 2 H, NH$_2$), 6.03 (d, $J_{1,2}$ = 4.0 Hz, 1 H, H-1), 5.45 (s, 1 H, H-5′), 4.57 (d, 1 H, H-2), 4.54 (dd, $J_{4,5a}$ = 4.3 Hz, $J_{4,5b}$ = 5.8 Hz, 1 H, H-4), 4.50 (s, 1 H, C*H*$_2$C$_6$H$_5$), 3.52 (m, 2 H, H-5), 2.75 (s, 3 H, NCH$_3$), 1.54 (s, 3 H, CH$_3$), 1.28 (s, 3 H, CH$_3$); ^{13}C NMR (DMSO d$_6$, 75 MHz) *δ* 153.4 (C-4′), 138.7−128.4 (6C, CH$_2$*C*$_6$H$_5$), 113.0 [O*C*(CH$_3$)$_2$], 104.2 (C-1), 90.3 (C-5′), 84.3 (C-2), 75.2 (C-4), 73.4 (O*C*H$_2$C$_6$H$_5$), 71.1 (C-3), 68.4 (C-5), 27.5 (NCH$_3$), 26.6 (2 × CH$_3$); MS (ES): 397.13 [M + 1]$^+$, 419.06 [M + Na]$^+$, 435.16 [M + K]$^+$, 815.29 [2M + Na]$^+$. Anal. Calcd. for $C_{18}H_{24}N_2O_6S$ (396.14 g/mol): C, 54.53; H, 6.10; N, 7.07; S, 8.09. Found: C, 54.47; H, 6.21; N, 6.84; S, 8.29.

N-Methylation of 3-Amino-5-*O*-benzoyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-3-*N*-methanesulfonyl-3-*N*-methyl-α-D-ribofuranose (6a). Following the general method, Cs_2CO_3 (0.33 g, 1.0 mmol) was added to a solution of **6a** (0.41 g, 1.0 mmol) in CH_3CN (10 mL). The reaction mixture was refluxed for 2 h and then evaporated to dryness. The residue was purified by flash chromatography to give successively **14c** (93 mg, 18%) (EtOAc/petroleum ether, 55:45), **14b** (51 mg, 17%) (EtOAc/petroleum ether, 3:2), and 5-*O*-benzoyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′,3′-dihydro-2′-*N*-methyl-1′,1′-dioxide-isothiazolyl)-α-D-ribofuranose (**14a**) (142 mg, 34%) (EtOAc/petroleum ether, 4:1). **14c**: mp 90−92 °C; [α]$^{25}_D$ +25 (*c* 0.42, $CHCl_3$); IR (ATR) *ν* 3364, 2921, 1721, 1511, 1488, 1269, 1121, 1057, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ* 8.74 (s, 1 H, NH), 7.98 (m, 2 H, COC$_6$*H*$_5$), 7.76 (m, 2 H, COC$_6$*H*$_5$), 7.62 (m, 2 H, COC$_6$*H*$_5$), 7.52 (m, 3 H, H-5′, COC$_6$*H*$_5$), 7.38 (m, 2 H, COC$_6$*H*$_5$), 6.01 (d, $J_{1,2}$ = 3.9 Hz, 1 H, H-1), 4.87 (dd, $J_{4,5a}$ = 3.1 Hz, $J_{4,5b}$ = 7.3 Hz, 1 H, H-4), 4.77 (d, 1 H, H-2), 4.63 (dd, $J_{5a,5b}$ = 12.8 Hz, 1 H, H-5a), 4.53 (dd, 1 H, H-5b), 3.10 (s, 3 H, NCH$_3$), 1.67 (s, 3 H, CH$_3$), 1.35 (s, 3 H, CH$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ* 166.4, 165.4 (2 C, CO), 141.3 (C-4′), 133.8−127.4 (12 C, 2 × COC$_6$H$_5$), 114.5 [O*C*(CH$_3$)$_2$], 108.8 (C-5′), 103.9 (C-1), 84.5 (C-2), 74.1 (C-4), 70.9 (C-3), 6 1.1 (C-5), 27.1 (NCH$_3$), 26.3 (CH$_3$), 26.2 (CH$_3$); MS (ES) 515.3 [M + H]$^+$, 537.2 [M + Na]$^+$, 553.2 [M + K]$^+$. Anal. Calcd for $C_{25}H_{26}N_2O_8S$ (514.14 g/mol): C, 58.36; H, 5.09; N, 5.44; S, 6.23. Found: C, 58.47; H, 5.18; N, 5.65; S, 6.03. **14b**: mp 139−141 °C; [α]$^{25}_D$ +117 (*c* 0.59, $CHCl_3$); IR (ATR) *ν* 3364, 2915, 1370, 1293, 1235, 1121, 1060 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ* 5.77 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 4.97 (d, 1 H, H-2), 4.80 (d, $J_{4,5}$ = 3.1 Hz, 1 H, H-4), 4.18 (dd, $J_{5a,5b}$ = 10.7 Hz, 1 H, H-5a), 3.99 (dd, 1 H, H-5b), 3.58 (d, $J_{5'a,5'b}$ = 13.2 Hz, 1 H, H-5′b), 3.36 (d, 1 H, H-5′a), 3.01 (s, 3 H, NCH$_3$), 2.14 (s, 2 H, NH$_2$), 1.60 (s, 3 H, CH$_3$), 1.36 (s, 3 H, CH$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ* 113.0 [O*C*(CH$_3$)$_2$], 106.4 (C-1), 95.5 (C-4′), 82.4 (C-2), 79.7 (C-4), 79.4 (C-3), 70.3 (C-5), 57.1 (C-5′), 28.3 (NCH$_3$), 27.1 (CH$_3$), 26.4 (CH$_3$); MS (ES) 329.2 [M + Na]$^+$. Anal. Calcd for $C_{11}H_{18}N_2O_6S$ (306.09 g/mol): C, 43.13; H, 5.92; N, 9.14; S, 10.47. Found: C, 43.35; H, 5.73; N, 9.07; S, 10.66**. 14a**: mp 130−132 °C; [α]$^{27}_D$ −4 (*c* 1.29, $CHCl_3$); IR (ATR) *ν* 1721, 1646, 1270, 1065, 1019 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ* 7.99−7.54 (m, 5 H, COC$_6$*H*$_5$), 6.19 (s, 2 H, NH$_2$), 6.10 (d, $J_{1,2}$= 3.8 Hz, 1 H, H-1), 5.56 (s, 1 H, H-5′), 4.75 (dd, $J_{4,5a}$ = 8,3 Hz, $J_{4,5b}$ = 2.1 Hz, 1 H, H-4), 4.66 (d, 1 H, H-2), 4.42 (dd, $J_{5a,5b}$ = 12.0 Hz, 1 H, H-5b), 4.26 (dd, 1 H, H-5a), 2.84 (s, 3 H, NCH$_3$), 1.56 (s, 3 H, CH$_3$), 1.30 (s, 3 H, CH$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ* 166.4 (CO), 153.1 (C-4′), 134.5−129.9 (COC$_6$*H*$_5$), 113.2 [O*C*(CH$_3$)$_2$], 104.3 (C-1), 90.6 (C-5′), 84.5 (C-2), 73.5 (C-4), 71.3 (C-3), 63.1 (C-5), 27.5 (NCH$_3$), 26.7 (CH$_3$), 26.6 (CH$_3$); MS (ES) 433.18 [M + Na]$^+$, 449.17 [M + K]$^+$, 843.25 [2M + Na]$^+$. Anal. Calcd for $C_{18}H_{22}N_2O_7S$ (410.11 g/mol): C, 52.67; H, 5.40; N, 6.83; S, 7.81. Found: C, 52.54; H, 5.52; N, 6.68; S, 7.61.

5-*O*-Benzyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′-*N*-benzyl-2′,3′-dihydro-1′,1′-dioxide-2′,3′-isothiazolyl)-α-D-ribofuranose (15). Following the general method, Cs_2CO_3 (0.207 g, 0.63 mmol) was added to a solution of **7** (0.30 g, 0.63 mmol) in CH_3CN (10 mL). The reaction mixture was refluxed for 2 h and then evaporated to dryness. The residue was

purified by flash chromatography (EtOAc/petroleum ether, 7:3) to give **15** (0.20 g, 65%) as a colorless solid: mp 192−194 °C; $[\alpha]^{25}_D$ +27 (*c* 0.21, $CHCl_3$); IR (ATR) ν 3430, 3107, 2351, 1649, 1280, 1141, 1064 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.38 (m, 10 H, 2 × $CH_2C_6H_5$), 5.84 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 5.49 (s, 1 H, H-5′), 4.71 (m, 3 H, H-2, $OCH_2C_6H_5$), 4.61 (s, 2 H, NH_2), 4.46 (dd, $J_{4,5a}$ = 3.8 Hz, $J_{4,5b}$ = 5.5 Hz, 1 H, H-4), 4.33 (d, $J_{A,B}$ = 11.8 Hz, 1 H, H−A, $NCH_2C_6H_5$), 4.28 (d, 1 H, H−B, $NCH_2C_6H_5$), 3.47 (m, 2 H, H-5), 1.66 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.7 (C-4′), 137.9−128.2 (12 C, 2 × $CH_2C_6H_5$), 113.9 [$OC(CH_3)_2$], 104.3 (C-1), 93.9 (C-5′), 84.8 (C-2), 76.1 (C-4), 73.9 ($OCH_2C_6H_5$), 71.4 (C-3), 67.4 (C-5), 45.1 ($NCH_2C_6H_5$), 26.8, 26.3 (2 × CH_3); MS (ES) 495.14 $[M + Na]^+$, 511.06 $[M + K]^+$, 967.09 $[2M + Na]^+$. Anal. Calcd for $C_{24}H_{28}N_2O_6S$ (472.17 g/mol): C, 61.00; H, 5.97; N, 5.93; S, 6.79. Found: C, 61.15; H, 5.69; N, 5.89; S, 6.58.

N-Benzylation of 3-Amino-5-*O*-benzoyl-3-*N*-benzyl-3-*C*-cyano-3-deoxy-1,2-*O*-isopropylidene-3-*N*-methanesulfonyl-α-D-ribofuranose (7a). Following the general method, Cs_2CO_3 (86 mg, 0.26 mmol) was added to a solution of **7a** (107 mg, 0.22 mmol) in CH_3CN (6 mL). The reaction mixture was refluxed for 1 h and then evaporated to dryness. The residue was purified by flash chromatography with (EtOAc/petroleum ether, 1:4) to give successively **15c** (36 mg, 34%), **15b** (51 mg, 28%), and 5-*O*-benzoyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′-*N*-benzyl-2′,3′-dihydro-1′,1′-dioxide-isothiazolyl)-α-D-ribofuranose (**15a**) (42 mg, 38%). **15c**: mp 172−174 °C; $[\alpha]^{25}_D$ +5 (*c* 0.32, $CHCl_3$); IR (KBr) ν 3378, 1724, 1700, 1517, 1488, 1271, 1123 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.81 (s, 1 H, NH), 7.72−7.00 (m, 16 H, H-5′, 3 × $CH_2C_6H_5$), 5.84 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 4.84 (s, 2 H, $NCH_2C_6H_5$), 4.77 (d, 1 H, H-2), 4.51 (dd, 1 H, H-4), 4.09 (m, 2 H, 2 H-5), 1.69 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 166.1 (CO), 165.2 (CO), 141.6 (C-4′), 137.2−127.4 (3 × $CH_2C_6H_5$), 114.8 [$OC(CH_3)_2$], 108.8 (C-5′), 103.9 (C-1), 84.8 (C-2), 75.5 (C-4), 71.2 (C-3), 60.9 (C-5), 44.5 ($NCH_2C_6H_5$), 26.8 (CH_3), 26.2 (CH_3). Anal. Calcd for $C_{31}H_{30}N_2O_8S$ (590.17 g/mol): C, 63.04; H, 5.12; N, 4.74; S, 5.43. Found: C, 62.86; H, 5.62; N, 4.71; S, 6.00. **15b**: mp 92−94 °C; $[\alpha]^{25}_D$ +22 (*c* 0.9, $CHCl_3$); IR (KBr) ν 3486, 2928, 1629, 1496, 1457, 1384, 1295, 1211, 1154, 1072, 1021 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.31−7.25 (m, 5 H, C_6H_5), 5.65 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H−l), 4.99 (d, 1 H, H-2), 4.78 (s, 2 H, $NCH_2C_6H_5$), 4.37 (d, $J_{4,5b}$ = 3.5 Hz, 1H, H-4), 3.71 (d, $J_{5a,5b}$ =10 Hz, 1 H, H-5a), 3.61 (d, $J_{5'a,5'b}$ = 13 Hz, 1 H, H-5′a), 3.29 (dd, 1 H, H-5b), 3.27 (d, 1 H, H-5′b), 2.00 (br s, 2 H, NH_2), 1.61 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 137.6−128.0 (C_6H_5), 112.6 [$OC(CH_3)_2$], 106.1 (C-1), 95.6 (C-4′), 81.6 (C-2), 80.3 (C-4), 78.5 (C-3), 70.0 (C-5), 58.5 (C-5′), 44.8 ($NCH_2C_6H_5$), 26.9 (CH_3), 25.9 (CH_3); MS (ES) 383 $[M + 1]^+$, 405 $[M + Na]^+$, 765 $[2M + 1]^+$, 787 $[2M + Na]^+$. Anal. Calcd for $C_{17}H_{22}N_2O_6S$ (382.46 g/mol): C, 53.39; H, 5.80; N, 7.33; S, 8.38. Found: C, 53.12; H, 5.97; N, 7.12; S, 8.42. **15a**: mp 96−97 °C; $[\alpha]^{25}_D$ −10 (*c* 0.34, $CHCl_3$); IR (KBr) ν 3455, 2928, 1722, 1646, 1273, 1130, 1069, 1025 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.81−6.98 (m, 10 H, $NCH_2C_6H_5$, $OCOC_6H_5$), 5.79 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 5.54 (s, 1 H, H-5′), 4.73 (br s, 5 H, H-2, $NCH_2C_6H_5$, NH_2), 4.43 (d, J = 6.6 Hz, 1 H, H-4), 4.29−4.02 (m, 2 H, 2 H-5), 1.61 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) 166.1 (CO), 151.2 (C-4′), 137.1−128.0 ($NCH_2C_6H_5$, $OCOC_6H_5$), 113.8 [$OC(CH_3)_2$], 104.0 (C-1), 93.9 (C-5′), 84.2 (C-2), 74.7 (C-4), 71.0 (C-3), 62.0 (C-5), 44.6 ($NCH_2C_6H_5$), 26.5 (CH_3), 25.8 (CH_3); MS (ES) 487 $[M + 1]^+$, 504 $[M + NH_4]^+$, 509 $[M + Na]^+$, 973 $[2M + 1]^+$, 995 $[2M + Na]^+$. Anal. Calcd for $C_{24}H_{26}N_2O_7S$ (486.54 g/mol): C, 59.25; H, 5.39; N, 5.76; S, 6.59. Found: C, 58.99; H, 5.48; N, 5.61; S, 6.42.

5-*O*-Benzyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′,3′-dihydro-2′-*N*-methyl-5′-methyl-1′,1′-dioxide-isothiazolyl)-α-D-ribofuranose (16). Following the general method, Cs_2CO_3 (33 mg, 0.10 mmol) was added to a solution of **8** (35 mg, 0.08 mmol) in CH_3CN (6 mL). The reaction mixture was refluxed for 2 h and then evaporated to dryness. The residue was purified by flash chromatography (EtOAc/petroleum ether, 1:1) to give **16** (30 mg, 86%) as a colorless solid: mp 189−191 °C; $[\alpha]^{25}_D$ +35 (*c* 0.27, $CHCl_3$); IR (KBr) ν 3418, 2930, 1675, 1382, 1271, 1197, 1116, 1060, 1032 cm^{-1}; ^1H NMR, ($CDCl_3$, 200 MHz) δ 7.25−7.16 (m, 5 H, $OCH_2C_6H_5$), 5.76 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H−1), 4.50 (dd, $J_{4,5a}$ = 2.7 Hz, $J_{4,5b}$ = 6.4 Hz, 1 H, H-4), 4.46 (d, 1 H, H-2), 4.41 (s, 2 H, $CH_2C_6H_5$), 3.92 (br s, 2 H, NH_2), 3.58 (dd, $J_{4,5a}$ = 2.7 Hz, $J_{5a,5b}$ = l1.3 Hz, 1 H, H-5a), 3.46 (dd, $J_{4,5b}$ = 6.4 Hz, 1 H, H-5b), 2.86 (s, 3 H, NCH_3), 1.74 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 1.21 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 145.0 (C-4′), 137.6−127.9 ($OCH_2C_6H_5$), 113.4 [$OC(CH_3)_2$], 103.9 (C-1), 102.4 (C-5′), 84.5 (C-2), 75.0 (C-4), 73.9 ($CH_2C_6H_5$), 69.8 (C-3), 67.2 (C-5), 27.2 (CH_3), 26.3 (CH_3), 26.1 (CH_3), 5.6 (CH_3); MS (ES) 411 $[M + l]^+$, 843 $[2M + Na]^+$. Anal. Calcd for $C_{19}H_{26}N_2O_6S$ (410.49 g/mol): C, 55.59; H, 6.38; N, 6.82; S, 7.81. Found: C, 55.82; H, 6.70; N, 6.86; S, 7.60.

5-*O*-Benzyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-2′-*N*-benzyl-2′,3′-dihydro-5′-methyl-1′,1′-dioxide-isothiazolyl)-α-D-ribofuranose (17). Following the general method, Cs_2CO_3 (76 mg, 0.23 mmol) was added to a solution of **9** (95 mg, 0.19 mmol) in CH_3CN (4 mL). The reaction mixture was refluxed for 2 h and then evaporated to dryness. The residue was purified by flash chromatography (EtOAc/petroleum ether, 1:1) to give **17** (82 mg, 87%) as a colorless solid: mp 87−89 °C; $[\alpha]^{25}_D$ +12 (*c* 0.21, $CHCl_3$); IR (KBr) ν 3436, 2923, 1673, 1630, 1270, 1213, 1116 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.52−7.21 (m, 10 H, $NCH_2C_6H_5$, $OCH_2C_6H_5$), 5.86 (d, $J_{1,2}$ = 3.9 Hz, 1 H, H-1), 4.77 (br s, 2 H, $NCH_2C_6H_5$), 4.67 (d, 1 H, H-2), 4.43 (dd, 1 H, H-4), 4.31 (d, $J_{A,B}$ = 11.9 Hz, 1 H, H−A, $OCH_2C_6H_5$), 4.22 (d, 1 H, H−B, $OCH_2C_6H_5$), 4.08 (br s, 2 H, NH_2), 3.39 (m, 2 H, 2 H-5), 1.84 (s, 3 H, CH_3), 1.66 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 145.4 (C-4′), 137.7−127.9 ($NCH_2C_6H_5$, $OCH_2C_6H_5$), 113.7 [$OC(CH_3)_2$], 104.2 (C-1), 102.2 (C-5′), 84.8 (C-2), 75.9 (C-4), 73.7 ($CH_2C_6H_5$), 70.3 (C-3), 67.0 (C-5), 44.9 ($NCH_2C_6H_5$), 26.7 (CH_3), 26.1 (CH_3), 5.6 (CH_3); MS (ES) 487 $[M + 1]^+$, 504 $[M + NH_4]^+$, 509 $[M + Na]^+$, 973 $[2M + 1]^+$, 995 $[2M + Na]^+$. Anal. Calcd for $C_{25}H_{30}N_2O_6S$ (486.58 g/mol): C, 61.71; H, 6.21; N, 5.76; S, 6.59. Found: C, 61.46; H, 6.04; N, 5.47; S, 6.68.

General Method for the Synthesis of Compounds 18−20. To a solution of compounds **3** and **4** in dry THF was added *n*-BuLi (3 equiv, 1.6 M in hexane). The reaction mixture was stirred for from 10 min to 6 h at −10 °C. Water and 1 M HCl were added until pH 6 was achieved. Then, ethyl acetate was added. The organic layer was separated and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by flash chromatography (EtOAc/petroleum ether) to give products **18−20** as indicated.

5-*O*-Benzyl-1,2-*O*-isopropylidene-3-spiro-(2′-*H*-4′-amino-2′,3′-dihydro-1′,1′-dioxo-isothiazolyl)-α-D-ribofuranose (18). Following the general method, *n*-BuLi (3.33 mL, 5.34 mmol) was added to a solution of **3** (680 mg, 1.78 mmol) in THF (15 mL). The reaction mixture was stirred for 10 min at −10 °C. The crude was flash chromatographed (EtOAc/petroleum ether, 1:1) to give **18** (680 mg, 99%) as a colorless oil: $[\alpha]^{25}_D$ +11 (*c* 1.68, $CHCl_3$); IR (ATR) ν 1643, 1268, 1216, 1124, 1068, 1036 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.21 (m, 5 H, $CH_2C_6H_5$), 5.86 (d, $J_{1,2}$ = 3.6 Hz, 1 H, H-1), 5.34 (s, 1 H, $CHSO_2$), 5.28 (s, 1 H, NH), 4.89 (s, 2 H, NH_2), 4.49 (d, 1 H, H-2), 4.45 (s, 2 H, $CH_2C_6H_5$), 4.15 (m, 1 H, H-4), 3.70 (m, 2 H, 2 H-5), 1.47 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.6 (C-4′), 137.5−127.8 ($CH_2C_6H_5$), 113.5 [$OC(CH_3)_2$], 104.5 (C-1), 92.3 (C-5′), 81.6 (C-2), 79.5 (C-4), 73.5 ($OCH_2C_6H_5$), 69.4 (C-5), 66.8 (C-3), 26.4 (CH_3), 26.0 (CH_3); MS (ES) 405.17 $[M + Na]^+$, 421.20 $[M + K]^+$, 787.39 $[2M + Na]^+$. Anal. Calcd for $C_{17}H_{22}N_2O_6S$ (382.12 g/mol): C, 53.39; H, 5.80; N, 7.33; S, 8.38. Found: C, 53.25; H, 5.90; N, 7.12; S, 8.45.

5-*O*-Benzyl-1,2-*O*-isopropylidene-3-spiro-(2′-*H*-4′-amino-2′,3′-dihydro-5′-methyl-1′,1′-dioxo-isothiazolyl)-α-D-ribofuranose (19). Following the general method, *n*-BuLi (0.18 mL, 0.3 mmol) was added to a solution of **4** (40 mg, 0.1 mmol) in THF (3 mL). The reaction mixture was stirred for 2 h at

−10 °C. The crude was purified by flash chromatography (EtOAc/petroleum ether, 2:3) to give **2** (5 mg, 41%) and **19** (8 mg, 20%) as a colorless solid. **19**: mp 175−177 °C; $[\alpha]^{25}_D$ +32 (*c* 0.3, $CHCl_3$); IR (KBr) *ν* 3454, 3359, 3210, 2928, 1676, 1620, 1270, 1123, 1105 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 7.26−7.16 (m, 5 H, $OCH_2C_6H_5$), 5.86 (d, $J_{1,2}$ = 4.0 Hz, 1 H, H-1), 4.93 (br s, 1 H, NH), 4.45 (d, 1 H, H-2), 4.44 (d, *J* = 3.1 Hz, 2 H, $CH_2C_6H_5$), 4.10 (dd, $J_{4,5a}$ = 2.9 Hz, $J_{4,5b}$ = 5.9 Hz, 1 H, H-4), 3.91 (br s, 2 H, NH_2), 3.71 (dd, $J_{5a,5b}$ = 11.2 Hz, 1 H, H-5a), 3.62 (dd, $J_{4,5b}$ = 5.9 Hz, 1 H, H-5b), 1.71 (s, 3 H, CH_3), 1.46 (s, 3H, CH_3), 1.25 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 145.4 (C-4′), 137.6−127.9 ($OCH_2C_6H_5$), 113.8 [$OC(CH_3)_2$], 104.2 (C-1), 103.0 (C-5′), 82.1 (C-2), 79.8 (C-4), 74.0 ($CH_2C_6H_5$), 68.4 (C-3), 66.4 (C-5), 26.6 (CH_3), 26.3 (CH_3), 5.6 (CH_3); MS (ES) 397 $[M + l]^+$, 419 $[M + Na]^+$, 793 $[2M + 1]^+$, 815 $[2M + Na]^+$. Anal. Calcd for $C_{l8}H_{24}N_2O_6S$ (396.46 g/mol): C, 54.53; H, 6.10; N, 7.07; S, 8.09. Found: C, 54.79; H, 5.82; N, 7.21; S, 8.14.

5-*O*-Benzyl-1,2-*O*-isopropylidene-3-spiro-(2′-*H*-4′-amino-2′,3′-dihydro-1′,1′-dioxo-5′-phenyl-isothiazolyl)-α-D-ribofuranose (20). Following the general method, *n*-BuLi (1 mL, 1.64 mmol) was added to a solution of **5** (251 mg, 0.54 mmol) in THF (5 mL). The reaction mixture was stirred for 6 h at −10 °C. The crude was purified by flash chromatography (EtOAc/petroleum ether, 1:4) to give **20** (171 mg, 73%) as a colorless solid: mp 68−69 °C; $[\alpha]^{25}_D$ +57 (*c* 0.26, $CHCl_3$); IR (KBr) *ν* 3459, 1646, 1274, 1111 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 7.53−7.28 (m, 10 H, $OCOC_6H_5$, C_6H_5), 6.03 (d, $J_{1,2}$ = 4.0 Hz, 1 H, H-1), 5.22 (br s, 1 H, NH), 4.73 (d, 1 H, H-2), 4.57 (s, 2 H, CH_2), 4.46 (br s, 2 H, NH_2), 4.29 (dd, $J_{4,5a}$ = 3.1 Hz, $J_{4,5b}$ = 5.3 Hz, 1 H, H-4), 3.96 (dd, $J_{5a,5b}$ = 11.2 Hz, 1 H, H-5a), 3.86 (dd, 1 H, H-5b), 1.61 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 146.6 (C-4′), 137.4−127.9 ($OCOC_6H_5$, C_6H_5), 126.7 (C-5′), 113.9 [$OC(CH_3)_2$], 104.2 (C-1), 82.3 (C-2), 80.0 (C-4), 73.9 ($CH_2C_6H_5$), 67.8 (C-3), 66.2 (C-5), 26.6 (CH_3), 26.2 (CH_3); MS (ES) 476.1 $[M + NH_4]^+$, 481.1 $[M + Na]^+$, 939.3 $[2M + Na]^+$. Anal. Calcd for $C_{23}H_{26}N_2O_6S$ (458.53 g/mol): C, 60.25; H, 5.72; N, 6.11; S, 6.99. Found: C, 60.37; H, 5.57; N, 6.19; S, 6.82.

1,2-*O*-Isopropylidene-α-D-erythro-[3,4-*c*]-tetrahydrofuro-[4,5-*d*]-(2*H*,5*H*-4′-amino-1′,1′-dioxide-1′,2′-thiazole) (21). Following the general method, *n*-BuLi (3.88 mL, 6.21 mmol) was added to a solution of **3a** (820 mg, 2.07 mmol) in THF (10 mL). The reaction mixture was stirred for 10 min at −10 °C. The crude was purified by flash chromatography (EtOAc/petroleum ether, 3:2) to give **21** (260 mg, 42%) as an amorphous solid: IR (ATR) *ν* 1479, 1441, 1370, 1205, 1079, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) *δ* 5.88 (d, $J_{1,2}$ = 3.9 Hz, 1 H, H-1), 5.50 (s, 1 H, NH), 4.93 (d, 1 H, H-2), 4.48 (d, $J_{4,5a}$ = 2.9 Hz, 1 H, H-4), 4.18 (d, $J_{5a,5b}$ = 10.8 Hz, 1 H, H-5b), 4.10 (dd, 1 H, H-5a), 3.62 (d, $J_{5a',5b'}$ = 13.2 Hz, 1 H, H-5b′), 3.37 (dd, $J_{5a',NH}$ = 1.6 Hz, 1 H, H-5a′), 2.15 (s, 2 H, NH_2), 1.57 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ* 112.9 [$OC(CH_3)_2$], 106.0 (C-1), 96.1 (C-4′), 83.7 (C-4), 79.3 (C-2), 77.3 (C-3), 69.2 (C-5), 58.6 (C-5′), 26.8 (CH_3), 26.6 (CH_3); MS (ES) 314.99 $[M + Na]^+$. Anal. Calcd for $C_{10}H_{16}N_2O_6S$ (292.07 g/mol): C, 41.09; H, 5.52; N, 9.58; S, 10.97. Found: C, 41.11; H, 5.57; N, 9.54.

1,2-*O*-Isopropylidene-3-spiro-(2′-*H*-4′-amino-2′,3′-dihydro-1′,1′-dioxo-5′-phenyl-isothiazolyl)-α-D-ribofuranose (22). Following the general method, *n*-BuLi (0.28 mL, 0.45 mmol) was added to a solution of **5a** (70 mg, 0.15 mmol) in THF (2 mL). The reaction mixture was stirred for 2 h at −10 °C. The crude was purified by flash chromatography (EtOAc/petroleum ether, 3:7) to give **22** (30 mg, 54%) as a colorless solid: mp 200−202 °C; $[\alpha]^{25}_D$ +4 (*c* 0.4, $CHCl_3$); IR (KBr) *ν* 3493, 1650, 1272, 1065 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 7.72−7.52 (m, 5 H, C_6H_5), 6.28 (d, $J_{1,2}$ = 3.9 Hz, 1 H, H-1), 4.88 (d, 1 H, H-2), 4.42 (dd, $J_{4,5a}$ = 2.3 Hz, $J_{4,5b}$ = 7.8 Hz, 1 H, H-4), 4.10 (dd, $J_{5a,5b}$ = 12.3 Hz, 1 H, H-5a), 4.01 (dd, 1 H, H-5b), 1.79 (s, 3 H, CH_3), 1.75 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 147.4 (C-4′), 137.5−128.2 (C_6H_5), 127.6 (C-5′), 113.2 [$OC(CH_3)_2$], 104.5 (C-1), 82.7 (C-2), 81.7 (C-4), 68.2 (C-3), 59.2 (C-5), 25.4, 25.3 (2 × CH_3); MS (ES): 369 $[M + l]^+$, 391 $[M + Na]^+$, 759 $[2M + Na]^+$. Anal. Calcd for $C_{16}H_{20}N_2O_6S$ (368.40 g/mol): C, 52.16; H, 5.47; N, 7.60; S, 8.7 Found: C, 52.45; H, 5.18; N, 7.34; S, 8.52.

1,2-*O*-Isopropylidene-3-spiro-(2′-*H*-4′-amino-2′,3′-dihydro-1′,1′-dioxo-*N*-methyl-5′-phenyl-isothiazolyl)-α-D-ribofuranose (23). Following the general method, *n*-BuLi in 1.6 M hexane (0.29 mL, 0.47 mmol) was added to a solution of **10a** (76 mg, 0.16 mmol) in THF (5 mL). The reaction mixture was stirred for 8 h at −10 °C. A few drops of water and 1.2 M HCl were added until pH 5 was achieved. Then, diethyl ether was added. The organic layer was separated and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by flash chromatography (hexane/AcOEt, 3:2) to give **23** (42 mg, 68%) as a colorless solid: mp 211−213 °C; $[\alpha]_D^{25}$ +51 (*c* 0.25, $CHCl_3$); IR (KBr) *ν* 3436, 2927, 2598, 2442, 1629, 1252, 1137 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 7.58−7.41 (m, 5 H, C_6H_5), 5.89 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1), 4.80 (d, 1 H, H-2), 4.65 (t, *J* = 5.6 Hz, 1H, H-4), 4.48 (br s, 2H, NH_2), 3.85 (m, 2 H, 2 H-5), 3.10 (s, 3 H, NCH_3), 1.67 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 145.7 (C-4′), 129.7−128.7 (C_6H_5), 126.1 (C-5′), 113.6 [$OC(CH_3)_2O$], 103.6 (C-1), 85.0 (C-2), 75.4 (C-4), 69.7 (C-3), 59.9 (C-5), 27.3 (NCH_3), 26.1, 25.9 [$OC(CH_3)_2O$]; EM (ES) $[M + 1]^+$ 383, $[M + Na]^+$ 405, $[2M + Na]^+$ 787. Anal. Calcd for $C_{17}H_{22}N_2O_6S$ (383.43 g/mol): C, 53.39; H, 5.80; N, 7.33; S, 8.38. Found: C, 53.67; H, 5.46; N, 7.13; S, 8.39.

5-*O*-*tert*-Butyldimethylsilyl-1,2-*O*-isopropylidene-3-spiro-(2′-*H*-4′-amino-2′,3′-dihydro-1′,1′-dioxo-5′-phenyl-isothiazolyl)-α-D-ribofuranose (24). To a solution of **21** (110 mg, 0.38 mmol) in DMF (5 mL) were added TBDMSCl (140 mg, 0.95 mmol) and imidazole (77 mg, 1.14 mmol). The reaction mixture was stirred for 3 h at room temperature. Then, the solvent was removed under vacuo and the residue flash chromatographed (EtOAc/petroleum ether, 4:6) to give **24** (80 mg, 53%) as a colorless solid: mp 118−120 °C; $[\alpha]_D^{28}$ −0.05 (*c* 0.8, $CHCl_3$); IR (ATR) 3332, 2921, 2844, 1639, 1255, 1217, 1115, 1040, 877, 837, 779 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) *δ* 5.94 (d, $J_{1,2}$ = 3.9 Hz, 1 H, H-1), 5.44 (s, 1 H, $CHSO_2$), 5.12 (s, 1 H, NH), 4.84 (s, 2 H, NH_2), 4.59 (d, 1 H, H-2), 4.06 (dd, $J_{4,5a}$ = 6.1 Hz, $J_{4,5b}$ = 3.0 Hz, 1 H, H-4), 3.97 (dd, $J_{5a,5b}$ = 11.9 Hz, 1 H, H-5b), 3.90 (dd, 1 H, H-5a), 1.56 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 0.87 (s, 9 H, $SiC(CH_3)_3$), 0.05 (s, 6 H, $Si(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ* 152.9 (C-4′), 113.5 (1C, $OC(CH_3)_2$), 103.8 (C-1), 94.1 (C-5′), 82.0, 80.8 (2C, C-2, C-4), 69.3 (C-3), 59.8 (C-5), 26.4 (CH_3), 26.0 (CH_3), 25.8 (3C, $SiC(CH_3)_3$), 18.2 (1C, $SiC(CH_3)_3$), −5.4 (1C, $Si(CH_3)_2$), −5.5 (1C, $Si(CH_3)_2$); EM (ES) 407.14 $[M + Na]^+$, 429.14 $[M + Na]^+$, 445.23 $[M + K]^+$, 835.32 $[2M + Na]^+$. Anal. Calcd for $C_{16}H_{30}N_20_6SSi$ (406.16 g/mol): C, 47.27; H, 7.44; N, 6.89; S, 7.89. Found: C, 47.38; H, 7.55; N, 6.91; S, 8.02

General Method for Acetylation. Pyridine and Ac_2O (1:1, v/v) were added to the compound. The reaction mixture was stirred at room temperature. After complete reaction, the solvent was evaporated to dryness, and the residue was purified by flash chromatography eluting with mixtures of hexane/AcOEt.

5-*O*-Benzyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-1′,1′-dioxo-2′-*N*-acetyl-5′-phenyl-2′,3′-dihydroisothiazolyl)-α-D-ribofuranose (25). Following the general method for acetylation, pyridine (1.3 mL) and Ac_2O (1.3 mL) were added to the compound **20** (160 mg, 0.34 mmol). After 2 days and flash chromatography (hexane/EtOAc, 4:1), product **25** [31 mg, 39% (69% taking into account the recovered starting material)] and unreacted **20** (34 mg) were isolated. **25**: mp 50−52 °C; $[\alpha]_D^{25}$ +69 (*c* 0.38, $CHCl_3$); IR (KBr) *ν* 3347, 3352, 2928, 1712, 1654, 1385, 1313, 1273, 1097 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) *δ* 7.44 (br s, 5 H, $OCH_2C_6H_5$), 7.29 (br s, 5 H, C_6H_5), 6.30 (dd, $J_{4,5a}$ = 3.1 Hz, $J_{4,5b}$ = 4.6 Hz, 1 H, H-4), 5.96 (d, $J_{1,2}$ = 4.2 Hz, 1 H, H-1), 4.77 (br s, 2 H, NH_2), 4.68 (d, 1H, H-2), 4.60 (d, $J_{A,B}$ = 11.7 Hz, 1 H, H−A), 4.53 (d, 1 H, H−B), 3.95 (dd, $J_{5a,5b}$ = 11.7 Hz, 1 H, H-5a), 3.85 (dd, 1 H, H-5b), 2.67 (s, 3 H, NCH_3),

1.62 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 169.0 (CO), 147.5 (C-4′), 137.6 (Cipso), 129.8−127.8 ($OCH_2C_6H_5$, C_6H_5), 125.4 (C-5′), 114.1 [$OC(CH_3)_2$], 103.8 (C-1), 84.4 (C-2), 74.8 (C-4), 73.7 ($OCH_2C_6H_5$), 71.7 (C-3), 66.3 (C-5), 26.7 (CH_3), 25.7 ($COCH_3$), 25.4 (CH_3); MS (ES) 523 [M + Na]$^+$, 1023 [2M + Na]$^+$. Anal. Calcd for $C_{25}H_{28}N_2O_7S$ (500.57 g/mol): C, 59.99; H, 5.64; N, 5.60; S, 6.40. Found: C, 59.75; H, 5.91; N, 5.56; S, 6.44.

5-*O*-Acetyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-1′,1′-dioxo-2′-*N*-acetyl-5-acetyl-5′-phenyl-2′,3′-dihydroisothiazolyl)-α-D-ribofuranose (26). Following the general method for acetylation, pyridine (1 mL) and Ac_2O (1 mL) were added to the compound **22** (15 mg, 0.04 mmol). After 3 days and flash chromatography (hexane/EtOAc, 4:1) product **26** (9.7 mg, 53%) was isolated as a colorless solid: mp 74−76 °C; $[\alpha]^{25}_D$ + 63 (*c* 0.74, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.54−7.47 (m, 5 H, H arom.), 6.41 (dd, $J_{4,5a}$ = 4.7 Hz, $J_{4,5b}$ = 7.5 Hz, 1 H, H-4), 5.98 (d, $J_{1,2}$ = 4.2 Hz, 1 H, H-1), 4.87 (br s, 2 H, NH_2), 4.75 (d, 1 H, H-2), 4.50 (dd, $J_{5a,5b}$ = 12.2 Hz, 1 H, H-5b), 4.34 (dd, 1 H, H-5a), 2.67 (s, 3 H, CH_3CO), 2.10 (s, 3 H, CH_3CO), 1.64 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 170.6 (CO), 168.8 (CO), 145.0 (C4′), 129.8−129.6 (C_6H_5), 124.8 (C5′), 114.3 [$OC(CH_3)_2$], 103.7 (C-1), 84.1 (C-2), 73.2 (C-4), 71.6 (C-3), 60.5 (C-5), 26.6, 26.3 [2 × $OC(CH_3)_2$], 25.2 (CH_3CO), 20.7 (CH_3CO); MS (ES) 453 [M + 1]$^+$, 470 [M + NH_4]$^+$, 475 [M + Na]$^+$, 927 [2M + Na]$^+$. Anal. Calcd for $C_{20}H_{24}N_2O_8S$ (452.57 g/mol): C, 53.09; H, 5.35; N, 6.19; S, 7.09. Found: C, 53.22; H, 5.68; N, 5.84; S, 6.86.

5-*O*-Acetyl-1,2-*O*-isopropylidene-3-spiro-(4′-amino-1′,1′-dioxo-2′-*N*-methyl-5′-phenyl-2′,3′- dihydroisothiazolyl)-α-D-ribofuranose (27). Following the general method for acetylation, pyridine (1 mL) and Ac_2O (1 mL) were added to compound **23** (27 mg, 0.07 mmol). After 18 days and flash chromatography (hexane/EtOAc, 3:2) compound **27** (30 mg, 99%) was isolated as a colorless solid. **26**: mp 207−209 °C; $[\alpha]_D^{25}$ +50 (*c* 0.2, $CHCl_3$); IR (KBr) ν 3455, 2924, 1755, 1651, 1270, 1146, 1064 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.57−7.40 (m, 5 H, C_6H_5), 5.92 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 4.80 (d, 1 H, H-2), 4.76 (dd, $J_{4,5a}$ = 4.0 Hz, $J_{4,5b}$ = 4.4 Hz, 1 H, H-4), 4.51 (br s, 2 H, NH_2), 4.33 (m, 2 H, 2 H-5), 3.10 (s, 3 H, NCH_3), 1.62 (s, 3 H, NCH_3), 2.11 (s, 3 H, $COCH_3$), 1.67 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 170.6 (CO), 144.5 (C-4′), 129.7−129.0 (C_6H_5), 126.2 (C-5′), 113.7 [$OC(CH_3)_2$], 103.9 (C-1), 84.8 (C-2), 73.2 (C-4), 69.5 (C-3), 61.2 (C-5), 27.4 (NCH_3), 26.3 (CH_3), 26.0 (CH_3), 20.9 ($COCH_3$); MS (ES) 425 [M + 1]$^+$, 442 [M + NH_4]$^+$, 871 [2M + Na]$^+$. Anal. Calcd for $C_{19}H_{24}N_2O_7S$ (424.47 g/mol): C, 53.76; H, 5.7; N, 6.6; S, 7.55. Found: C, 53.58; H, 5.57; N, 6.53; S, 7.24.

3-Amino-3-*C*-3,5-carbolactono-3-deoxy-3-*N*-ethanesulfonyl-1,2-*O*-isopropylidene-α-D-ribofuranose (28). The general method was followed using **4a** (163 mg, 0.39 mmol) and *n*-BuLi (0.74 mL, 1.18 mmol) in THF (4 mL). The reaction mixture was stirred for 2 h at −10 °C. The crude was purified by flash chromatography (EtOAc/petroleum ether, 1:1), and compound **28** (35 mg, 29%) was isolated as colorless solid: mp 178−180 °C; $[\alpha]^{25}_D$ +3 (*c* 0.2, $CHCl_3$); IR (KBr) ν 3434, 1781, 1316, 1152, 1100 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.95 (d, $J_{1,2}$= 4 Hz, 1 H, H-1), 5.34 (br s, 1 H, NH), 4.81 (m, 2 H, H-4, H-5a), 4.75 (d, 1 H, H-2), 4.39 (m, 1 H, H-5b), 3.19 (q, J = 7.3 Hz, 2 H, $CH_3CH_2SO_2$), 1.61 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.40 (t, 3 H, $CH_3CH_2SO_2$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 173.2 (CO), 114.2 [$OC(CH_3)_2$], 104.9 (C-1), 83.7 (C2), 82.9 (C-4), 72.4 (C-5), 68.1 (C-3), 49.7 ($CH_3CH_2SO_2$), 27.3, 27.1 (2 × CH_3), 8.0 ($CH_3CH_2SO_2$); MS (ES) 330 [M + Na]$^+$, 637 [2M + Na]$^+$. Anal. Calcd for $C_{11}H_{17}NO_7S$ (307.32 g/mol): C, 42.99; H, 5.58; N, 4.56; S, 10.43. Found: C, 42.84; H, 5.70; N, 4.61; S, 10.26.

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