134. Syntheses and Reactions of 1′,2′-Unsaturated 2′,3′-Seconucleoside Analogues

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(9.V.95)

The 1′,2′-unsaturated 2′,3′-secoadenosine and 2′,3′-secouridine analogues were synthesized by the regioselective elimination of the corresponding 2′,3′-ditosylates, **2** and **18**, respectively, under basic conditions. The observed regioselectivity may be explained by the higher acidity and, hence, preferential elimination of the anomeric H–C(1′) in comparison to H–C(4′). The retained (tol-4-yl)sulfonyloxy group at C(3′) of **3** allowed the preparation of the 3′-azido, 3′-chloro, and 3′-hydroxy derivatives **5**–**7** by nucleophilic substitution. $ZnBr_2$ in dry CH_2Cl_2 was found to be successful in the removal (85%) of the trityl group without any cleavage of the acid-sensitive, ketene-derived N,O-ketal function. In the uridine series, base-promoted regioselective elimination (→ **19**), nucleophilic displacement of the tosyl group by azide (→ **20**), and debenzylation of the protected N(3)-imide function gave 1′,2′-unsaturated 5′-*O*-trityl-3′-azido-secouridine derivative **21**. The same compound was also obtained by the elimination performed on 2,2′-anhydro-3′-azido-3′-deoxy-5′-*O*-trityl-2′,3′-secouridine (**22**) that reacted with KO(*t*-Bu) under opening of the oxazole ring and double-bond formation at C(1′).

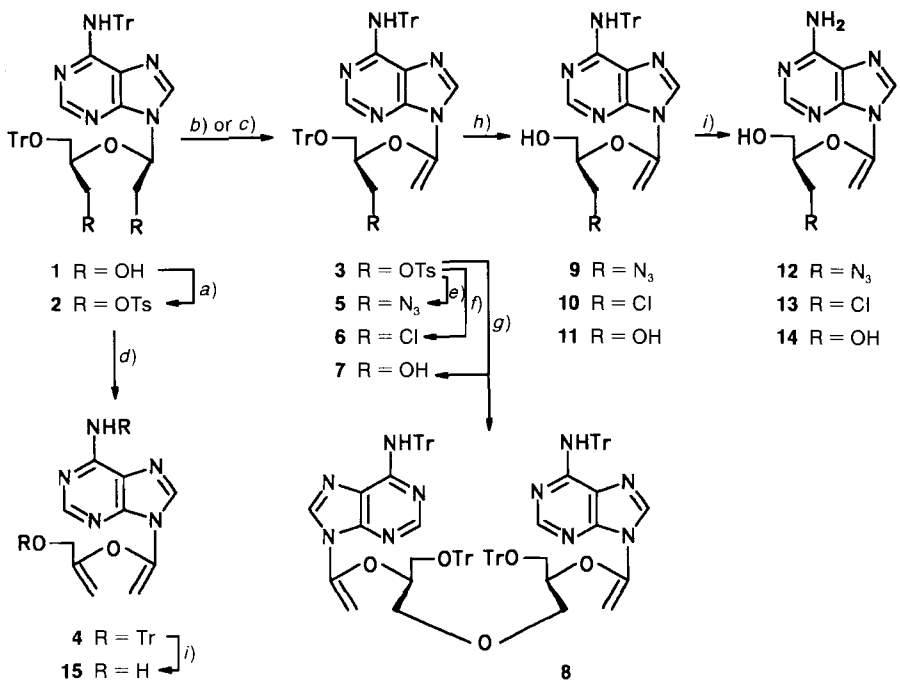
Introduction. – Synthesis and biological testing of various nucleoside analogues modified in the sugar part of the molecule has led to the development of several nucleoside analogues with antiviral properties. One important class among them are acyclonucleosides. The potent antiviral activities of some acyclonucleosides such as acyclovir [1] has generated much interest and prompted intensive search for other nucleosides with potential antiviral activity [2] [3]. Furthermore, some nucleoside analogues of the 2′,3′-dideoxy series, such as 3′-azido-3′-deoxythymidine (AZT) or unsaturated nucleoside analogues possessing a double bond in the sugar moiety, like 2′,3′-dideoxy-2′,3′-didehydrocytidine and 3′-deoxy-2′,3′-didehydrothymidine, were found to be inhibitors of HIV-1 reverse transcriptase [4] [5]. Many dideoxy-didehydro nucleosides (D4N) are more active than their saturated D2N analogues [6]. Therefore, acyclonucleosides related to AZT and D4N are attractive synthetic targets for the development of new anti-HIV gents. In this field, we investigate a series of 1′,2′-unsaturated 2′,3′-seconucleoside analogues[1]) incorporating the two above-mentioned structural features of the nucleosidic sugar moiety, continuing our earlier work on 2′,3′-seconucleosides [7–9].

The 1′,2′-unsaturated nucleoside analogues are very scarce, and only few of them have been described so far [10–12]; the first were reported by *Robins* and coworkers [13–15]. They can be seen as ketene-derived N,O-ketal structures, and herewith is presented this novel type of unsaturated seconucleoside analogues both in the purine and pyrimidine series.

[1]) Nucleoside numbering is used for 2′,3′-seconucleosides, systematic names are given in the *Exper. Part.*

Results and Discussion. – *Syntheses.* Unsaturated seconucleoside analogues investigated so far were obtained from properly protected and activated corresponding seconucleosides. Thus, ditritylated adenosine was cleaved to the secoadenosine derivative **1** [7] and activated by tosylation (*Scheme 1*) yielding **2** (78%; *Scheme 1*). Regioselective elimination under basic conditions (KO(*t*-Bu) or NaH in tetrahydrofuran (THF)) gave as the main product the 1′,2′-mono-unsaturated compound **3**. The observed regioselectivity may be explained by the higher acidity and, hence, preferential elimination of the anomeric H–C(1′) in comparison to H–C(4′), due to the electron-withdrawing effects of N- and O-substituents at the anomeric C(1′). Better results were obtained with KO(*t*-Bu) in THF at 40° for 75 h (84%) than with NaH in THF at the same temperature; in the latter case, the mono-elimination product **3** was isolated in 48% yield after 18 h, together with some of the starting material. The prolongation of the reaction time, temperature raising, or adding more equivalents of base led to the 1′,3′-diene analogue **4**, similar to that described by *Prisbe* [16]. The elimination reaction with NaH appeared to be faster than with KO(*t*-Bu), resulting in a lesser extent of regioselectivity; this could be due to smaller steric hindrance of NaH or to its higher basicity. An attempt to use 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to provoke elimination from the ditosylate **2** failed com-

Scheme 1



a) TsCl, py, r.t. *b*) KO(*t*-Bu), THF, 40° 75 h. *c*) NaH, THF, 40°, 18 h. *d*) 3 equiv. of KO(*t*-Bu), THF, 40°, 100 h. *e*) NaN_3, DMF, 80°. *f*) LiCl, DMF, 80°. *g*) H_2O/DMF, $NaHCO_3$, 100°. *h*) $ZnBr_2$, CH_2Cl_2, 1–6 h. *i*) $ZnBr_2$, CH_2Cl_2, 18 h.

pletely, presumably because of its weaker basicity (compared to KO(*t*-Bu) and NaH), in agreement with similar results observed by *Walker* and coworkers [17].

The retained (tol-4-yl)sulfonyloxy group at C(3′) enabled nucleophilic substitution and introduction of a N_3 (→**5**) or Cl substituent (→**6**; *Scheme 1*). Both reactions were performed in DMF at 80° (80–85% yield). Hydrolysis of tosylate **3** was performed in 20% aqueous DMF at 100° for 18 h in the presence of $NaHCO_3$ [18]. Besides the hydroxy product **7** (54% yield), the 'dimeric' structure **8** was also obtained (32%), presumably as a result of formation of a C(3′)–O^- anion, after hydrolysis of the 3′-TsO group, and reaction with the starting tosylate **3**. The ratio of 'monomer' to 'dimer', **7**/**8**, depended on the reaction conditions; at lower temperature and shorter reaction time, more hydroxy compound *7* was formed. We already reported in the secouridine series the formation of such dinucleoside compounds with two nucleoside units connected directly *via* an ether linkage [8].

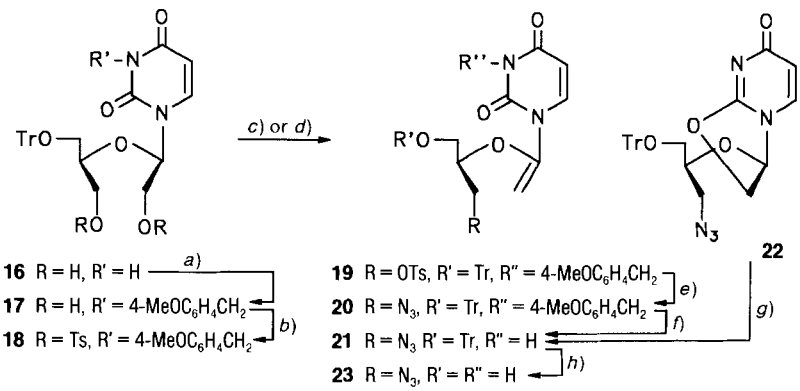
The glycosydic bond in 1′,2′-unsaturated compounds **3**–**8**, possessing a ketene-derived N,O-ketal structure, is very unstable under acidic conditions, so that trityl deprotection could not be achieved using strong or even mild acids [13] [16]. However, after unsuccessful attempts with 80% acetic acid, HBr, toluene-4-sulfonic acid in MeOH, CF_3COOH in BuOH, and ion-exchanger *Amberlite 15H*, we found that the *Lewis* acid $ZnBr_2$ in dry CH_2Cl_2 could be used for a successful removal (85%) of the Tr protecting group without any cleavage of the N,O-ketal function. Moreover, as in the secoadenosine series, the O–Tr bond was cleaved much faster than the N–Tr bond, the method thus allowing to isolate independently the *N*-protected 5′-hydroxy derivatives **9**–**11** (70–80%) as well as the fully deprotected secoadenosine derivatives **12**–**15** (80–85%, *Scheme 1*). This method was applied in our laboratory to adenosine derivatives protected with other groups, such as isopropylidene, alkylsilyl, and tolyl-4-sulfonyl, none of which was affected under the applied conditions ($ZnBr_2$, anh. CH_2Cl_2, 1–24 h, room temperature), retaining the observed O,N-selectivity.

In the uridine series, it was necessary to protect the N(3)-imide function to avoid an intramolecular cyclization under basic conditions. The 4-methoxybenzyl group [19], which was introduced for this purpose, proved to be stable under all applied conditions (periodate oxidation of starting uridine, $NaBH_4$ reduction, base-catalyzed elimination, nucleophilic displacement, detritylation). Thus, 5′-*O*-trityl-2′,3′-secouridine (**16**) [7] afforded, with 4-methoxybenzyl chloride and DBU, the N(3)-protected compound **17** (80%) that, by tosylation, gave the 2′,3′-ditosylate **18** (84%; *Scheme 2*). The sequence of introduction of protecting groups can be also reversed, DBU being not sufficiently basic for deprotonation of OH groups and, therefore, leaving 5′-OH untouched. The ditosylate **18** treated in an identical manner as the corresponding secoadenosine derivative **2** (either with KO(*t*-Bu) or NaH in THF), afforded the monounsaturated secouridine **19** in significantly lower yields (33%) in both cases. The change of the solvent (to dimethylformamide (DMF) or acetonitrile (MeCN)) did not give better results. Seconucleosides with various nucleobase moieties exhibited difference in reactivity under the elimination conditions. Apparently, the adenosine analoge **2** had a greater tendency to lose its anomeric H–C(1′) than the uridine analogue **18**, probably due to its higher acidity. The by-products with diene or dimeric structures, analogous to **4** and **8**, could be identified only in traces.

Both adenosine and uridine derivatives **2** and **18** were resistant to the treatment with DBU, and no unsaturated seconucleosides were formed, perhaps because of the weaker basicity of DBU relative to KO(*t*-Bu) or NaH, consistent with the results obtained by *Walker* and coworkers [17].

Nucleophilic displacement of the tosyl group in **19** by azide offered the protected azido compound **20** (70%), which was debenzylated by $AlCl_3$ in anisole [19] to 3′-azido-5′-*O*-trityl compound **21** (77%). The same compound was also obtained by elimination performed on 2,2′-anhydro-3′-azido-3′-deoxy-5′-*O*-trityl-2′,3′-secouridine (**22**) that was prepared starting from 2,2′-anhydro-3′-(tolyl-4-sulfonyl)-5′-*O*-trityl-2′,3′-secouridine [20] by an improved procedure with NaN_3 in DMF (2 days at 40°, 70% yield). The

Scheme 2



a) 4-$MeOC_6H_4CH_2Cl$, DBU, MeCN. *b*) TsCl, py, r.t. *c*) KO(*t*-Bu), THF, 40°, 75 h. *d*) NaH, THF, 40°, 18 h. *e*) NaN_3, DMF, 80°. *f*) $AlCl_3$ anisole. *g*) KO(*t*-Bu), THF, 5 min, r.t. *h*) $ZnBr_2$, CH_2Cl_2, 1 h.

anhydro-azido derivative **22** reacted with KO(*t*-Bu) under opening of the oxazole ring and C=C bond formation at C(1′) in **21** (44%), presumably in the same way as in the nucleoside series, where 2,2′-anhydro- and 2,3′-anhydronucleosides gave, with KO(*t*-Bu), 1′,2′-[13] and 2′,3′-unsaturated products [21], respectively. Detritylation by $ZnBr_2$ in CH_2Cl_2 gave the fully deprotected secouridine **23** (88%; *Scheme 2*). The deprotected azido derivatives **12** and **23** can be looked upon as acyclic analogues related to 3′-azido-3′-deoxythymidine (AZT).

Spectra. Introduction of a 1′,2′-double bond into seconucleosides results in UV spectra with a bathochromic shift of 4–7 nm (**1**: λ_{max} 265.6 nm; **7**: λ_{max} 272.5 nm, **16**: λ_{max} 259.2 nm; **23**: λ_{max} 263.7 nm); this can be explained by the extended conjugation of the nucleobase ring, as observed also at 1′,2′-unsaturated *C*-nucleoside analogues [12].

In the ^{1}H-NMR spectra of unsaturated compounds, the H–C(1′) signals disappear, while the diastereotopic H–C(2′)'s exhibit two sharp *d*'s (J = 3.5–4.1 Hz) at *ca.* 4.5 and 5.5–4.9 ppm (*Tables 1* and *2*). NOESY Spectra of the azido derivative **5** allowed the assignment of the downfield signal (at 5.49 ppm) to H–C(2′) *cis* to the purine moiety, while the upfield signal (at 4.44 ppm) was assigned to H–C(2′) *trans* of the purine.

Introduction of a 1′,2′-double bond in adenosine derivatives shifts the signals of the corresponding atoms in the ^{13}C-NMR spectra strongly downfield: signals of C(1′) for *ca.* 64 ppm (*Table 2*) and those of C(2′) for 2–6 ppm in unsaturated secoadenosine compounds **3**–**15**. In the unsaturated secouridine compounds **19**–**21**, **23** the difference is even larger (forC(1′), 70 ppm).

Table 1. *^{1}H-NMR* ($(CD_3)_2CO$)[a-g]). δ in ppm rel. to internal standard Me_4Si, J in Hz.

	H–C(1′) (*t*)	H_a–C(2′)	H_b–C(2′)	H–C(4′)	H–C(3′)	H–C(5′)	OH
2	6.05 (J = 5.2)	4.68 (*dd*, J = 6.1, 10.6)	4.53 (*dd*, J = 5.1, 10.6)	3.88 (*q*, J = 5.1)	4.24 (*dd*, J = 3.6, 10.9); 4.10 (*dd*, J = 5.4, 10.7)	2.88 (*m*, J = 5.10)	–
3	–	5.39 (*d*, J = 3.8)	4.31 (*d*, J = 3.8)	4.72 (*dd*, J = 3.8)	4.51 (*d*, J = 4.1)	3.49 (*d*, J = 4.7)	–
4	–	5.69 (*d*, J = 3.0)	4.75 (*d*, J = 3.0)	–	4.87 (*d*, J = 2.5); 4.73 (*d*, J = 2.5)	3.81 (*s*)	–
5	–	5.49 (*d*, J = 4.1)	4.44 (*d*, J = 4.1)	4.69 (*d*, J = 4.7)	3.84 (*d*, J = 5.6)	3.51 (*dd*, J = 4.7)	–
6	–	5.49 (*d*, J = 3.9)	4.46 (*d*, J = 3.9)	4.78 (*t*, J = 4.7)	4.07 (*dq*, J = 12.0, 16)	3.56 (*dq*, J = 10, 19)	–
7	–	5.07 (*d*, J = 3.7)	4.51 (*d*, J = 3.7)	4.61–4.57 (*m*)	3.86–3.70 (*m*)	3.44 (*t*, J = 5.9)	3.8 (*m*)
8	–	5.49 (*d*, J = 4.0)	4.46 (*d*, J = 4.0)	4.79 (*q*, J = 4.6)	4.08 (*t*, J = 4.6)	3.56 (*dd*, J = 4.5, 8.8)	–
9	–	5.17 (*d*, J = 4.0)	4.61 (*d*, J = 4.0)	4.62 (*dd*, J = 4.0)	3.72 (*d*, J = 5.4)	3.97–3.74 (*m*)	5.14 (*m*)
10		5.18 (*d*, J = 3.8)	4.61 (*d*, J = 3.8)	4.66 (*q*, J = 4.8)	3.82 (*d*, J = 5.4)	3.99 (*dd*, J = 4.8, 11.8)	5.24 (*t*, J = 6.2)
11	–	4.92 (*d*, J = 3.6)	4.56 (*d*, J = 3.6)	4.65 (*dd*, J = 5.3)	3.86–3.71 (*m*)	3.86–3.71 (*m*)	4.81 (*t*, J = 5.8)
12	–	5.17 (*d*, J = 3.8)	4.63 (*d*, J = 3.8)	4.65 (*dd*, J = 5.3)	3.74 (*d*, J = 5.4)	3.96 (*dd*, J = 3.4, 12.2) 3.76 (*dd*, J = 5.0, 11.9)	5.44 (*m*)
13	–	5.29 (*d*, J = 3.9)	4.60 (*d*, J = 3.9)	4.56 (*t*, J = 4.7)	3.74 (*dq*, J = 11.6, 16.2)	3.95 (*dq*, J = 10, 19)	5.42 (*m*)
14	–	4.82 (*d*, J = 3.7)	4.58 (*d*, J = 3.7)	4.49–4.44 (*m*)	3.86 (*dd*, J = 3.7, 12.7)	3.75 (*dd*, J = 6.3, 12)	4.35 (*m*)
17	6.00 (J = 5.4)	3.78 (*m*)	3.78 (*m*)	3.78 (*m*)	3.78 (*m*)	3.60 (*m*)	4.44 (*t*, J = 6.0); 4.02 (*t*, J = 5.6)
18	5.99 (J = 5.0)	4.22 (*d*, J = 5.0)	4.22 (*d*, J = 5.0)	3.72 (*m*)	4.22 (*d*, J = 5.0)	3.11 (*d*, J = 5.3)	–
19	–	4.51–4.32 (*m*)		4.18 (*m*)	4.35 (*m*)	3.37 (*d*, J = 5.1)	–
20	–	4.62 (*d*, J = 3.6)	4.56 (*d*, J = 3.6)	4.50 (*q*, J = 3.6)	3.72 (*d*, J = 6.0)	3.42 (*d*, J = 5.0	–
21	–	4.91 (*d*, J = 3.7)	4.87 (*d*, J = 3.7)	4.57 (*t*, J = 3.6)	3.73 (*d*, J = 4.2)	3.42 (*d*, J = 4.99)	–
23	–	4.70 (*d*, J = 3.6)	4.63 (*d*, J = 3.6)	4.45 (*q*, J = 4.9)	3.89 (*m*) 3.68 (*m*)	3.64 (*t*, J = 5.3)	4.19 (*t*, J = 6.3)

[a]) Purine: 8.31–8.11 (*s*, H–C(2)) and 8.25–7.92 (*s*, H–C(8)) for **2–14**. [b]) Pyrimidine: 7.78–7.58 (*d*, J = 8.0, H–C(6)) and 5.78–5.42 (*d*, J = 8.0, H–C(5)) for **17–23**. [c]) Aryl: 7.63–7.10 (*m*) for **2–11** and **17–20**. [d]) Me: 2.45–2.29 (*s*) for **2**, **3**, **18**, and **19**. [e]) NH: 7.6–7.2 for **3–11**. [f]) NH_2: 6.86–6.18 (br. *s*) for **12–14**. [g]) 4-Methoxybenzyl: 7.44–7.37 (*d*, J = 8.8), 5.03–4.87 (*s*, CH_2), and 3.81–3.73 (*s*, MeO) for **17–20**.

Table 2. *^{13}C-NMR Data* ($(CD_3)_2CO$[a–e]). δ in ppm rel. to internal standard Me_4Si.

	C(1′)	C(2′) (*t*)	C(4′)	C(3′) (*t*)	C(5′) (*t*)
2	81.28 (*d*)	76.30	67.68 (*d*)	68.91	62.70
3	147.55 (*s*)	78.13	75.94 (*d*)	68.49	61.45
4	148.16 (*s*)	78.89	145.86 (*s*)	94.91	62.51
5	148.31 (*s*)	78.90	78.90 (*d*)	51.92	62.81
6	147.95 (*s*)	78.66	78.33 (*d*)	43.32	62.30
7	148.56 (*s*)	82.08	79.65 (*d*)	61.24	63.06
8	147.94 (*s*)	78.69	78.33 (*d*)	43.32	62.32
9	148.81 (*s*)	81.37	80.75 (*d*)	51.61	60.98
10	148.39 (*s*)	81.36	80.37 (*d*)	42.81	60.42
11	148.78 (*s*)	84.73	80.57 (*d*)	61.45	61.45
12	149.14 (*s*)	80.94	80.21 (*d*)	51.07	60.45
13[f])	148.66 (*s*)	79.75	79.50 (*d*)	43.25	59.75
14[g])	148.59 (*s*)	82.63	78.89 (*d*)	59,85	59.85
17	85.55 (*d*)	64.23	80.30 (*d*)	62.87	61.23
18	88.07 (*d*)	68.95	82.69 (*d*)	63.49	55.50
19	155.97 (*s*)	87.75	76.57 (*d*)	68.38	61.54
20	150.33 (*s*)	87.28	78.17 (*d*)	51.13	62.50
21	151.24 (*s*)	86.72	77.73 (*d*)	66.75	62.47
23	148.59 (*s*)	82.63	78.89 (*d*)	59.85	59.85

[a]) Purine: 157.17–154.09 (*s*, C(6)), 153.64–151.87 (*d*, C(2)), 150.46–148.42 (*s*, C(4)), 140.27–138.25 (*d*, C(8)), and 122.35–119.51 (*s*, C(5)) for **2–14**. [b]) Pyrimidine: 162.64–162.24 (*s*, C(4)), 152.25–151.75 (*s*, C(2)), 142.55–139.22 (*s*, C(6)), 101.51–101.47 (*d*, C(5)) for **17–23**. [c]) Trityl: 146.03–126.91 (*s*, 3*d*, Ph_3C) for **2–11** and **17–21**, 87.75–85.27 (*s*, Ph_3CO) for **2–8** and **17–21**, and 72.09–71.44 (*s*, Ph_3CN) for **2–11**. [d]) 4-Methoxybenzyl: 159.63–113.77 (2*s*, 2*d*), 54.85–54.81 (*q*, MeO), and 43.35–43.34 (*t*, CH_2–N(3)) for **17–20**. [e]) Tosyl: 130.43–127.54 (2*s*, 2*d*, Ph) and 20.96–20.73 (*q*, Me) for **2**, **3**, **18**, and **19**. [f]) In $(CD_3)_2SO$. [g]) In CD_3CN.

Experimental Part

General. Solvents were dried and redistilled shortly before use. Extracts were dried (Na_2SO_4) and evaporated. Anal. samples were dried *i.v.* Flash column chromatography (FC): silica gel (*Merck 60*, 230–240 mesh ASTM); eluent CH_2Cl_2/MeOH 19:1. TLC: plastic sheets silica gel *60 F_{254}* (*Merck*); detection by UV light or I_2 vapours. Prep. TLC: silica gel *60 HF_{254}* (*Merck*) activated at 110° for 60 min; eluent CH_2Cl_2/MeOH 19:1 (*A*) or CH_2Cl_2/MeOH 99:1 (*B*). M.p.: *Kofler* hot-bench apparatus. Optical rotations $[\alpha]_D^{20-25°}$: *AA-10* automatic polarimeter (*Optical Activity Ltd.*, England). UV Spectra (λ_{max} (log ε) in nm): in 96% EtOH; *Philips-PU-8700* UV/VIS spectrophotometer. IR Spectra (in cm^{-1}): *Perkin-Elmer-297* spectrometer; solids in KBr pellets, liquids as thin films. NMR Spectra (δ in ppm rel. to Me_4Si and *J* in Hz): *Varian-Gemini-300* instrument; multiplicities from off-resonance decoupled spectra.

2′,3′-Bis-O-*(tolyl-4-sulfonyl)-5′*-O,N^6-*bis(triphenylmethyl)-2′,3′-secoadenosine* (= *9-{(1R)-2-[(Tol-4-yl)-sulfonyloxy]-1-{(1R)-2-[(tol-4-yl)sulfonyloxy]-1-[(triphenylmethoxy)methyl]ethoxy}ethyl}-6-[(triphenylmethyl)amino]purine*; **2**). To a soln. of 5′-*O*,N^6-bis(triphenylmethyl)-2′,3′-secoadenosine [7] (2.70 g, 3.58 mmol in pyridine (15 ml), toluene-4-sulfonyl chloride (2.73 g, 14.30 mmol) was added and the mixture stirred at r.t. overnight. The solvent was then evaporated, some H_2O added, and the product extracted into AcOEt. The org. layer was washed with H_2O, dried, and evaporated: 2.875 g (78%) of **2**. R_f 0.27 (*B*). M.p. 98–100°. $[\alpha]_D$ = +44.3 (*c* = 0.54, MeOH). IR. 3400*m*, 1600*s*, 1490*m*, 1470*m*, 1445*m*, 1365*m*, 1290*w*, 1220*m*, 1190*s*, 1175*s*, 1090*m*, 1000*m*, 810*m*, 695*s*. UV: 224.4 (4.08), 274.0 (3.72). Anal. calc. for $C_{62}H_{55}N_5O_8S_2$ (1062.27): C 70.10, H 5.22, N 6.59; found: C 70.11, H 5.19, N 6.50.

2′-Deoxy-3′-O-*[(tol-4-yl)sulfonyl]-5′*-O,N^6-*bis(triphenylmethyl)-2′,3′-secoadenosin-1′-ene* (= *9-{1-{(1R)-2-[(Tol-4-yl)sulfonyloxy]-1-[(triphenylmethoxy)methyl]ethoxy}vinyl}-6-[(triphenylmethyl)amino]purine*; **3**). *a*) To a soln. of **2** (508 mg, 0.48 mmol) in THF (15 ml), KO(*t*-Bu) (88 mg, 0.83 mmol) was added and stirred at 40° for

75 h. The solvent was then evaporated and the residue purified by prep. TLC (*B*): 358 mg (84%) of foamy **3**. R_f 0.50 (*B*). M.p. 101° (MeOH). $[\alpha]_D = -5.2$ ($c = 0.77$, MeOH). UV: 269.8 (4.36). IR: 3410*m*, 1670*w*, 1600*s*, 1490*m*, 1470*m*, 1445*m*, 1370*m*, 1280*w*, 1220*m*, 1190*s*, 1175*s*, 900*w*, 810*w*, 760*w*, 745*w*, 700*s*. Anal. calc. for $C_{55}H_{46}N_5O_5S$ (889.03): C 74.30, H 5.22, N 7.88; found: C 74.47, H 5.42, N 7.71.

b) To a soln. of **2** (140 mg, 0.13 mmol) in THF (4 ml), NaH (13 mg, 0.30 mmol) was added and stirred at 40° for 18 h. The solvent was then evaporated and the residue purified by prep. TLC (*B*): 56 mg (48%) of foamy **3**, identical to that described above.

2',3'-Dideoxy-5'-O,N⁶-bis(triphenylmethyl)-2',3'-secoadenosine-1',3'-diene (= *9-{1-{1-[(Triphenylmethoxy)-methyl]vinyloxy}vinyl}-6-[(triphenylmethyl)amino]purine*; **4**). As described for **3** (*Exper. a*), with **2** (300 mg, 0.28 mmol), THF (10 ml), and KO(*t*-Bu) (106 mg, 1.00 mmol; 100 h): 131 mg (65%) of foamy **4**. R_f 0.71 (*B*). M.p. 100–104° (CH_2Cl_2/MeOH). UV: 269.9 (4.25). IR: 3420*m*, 1650*w*, 1630*w*, 1600*s*, 1580*m*, 1490*w*, 1470*s*, 1450*m*, 1360*w*, 1280*m*, 1200*w*, 1050*w*, 1030*w*, 900*w*, 790*w*, 750*w*, 700*m*. Anal. calc. for $C_{48}H_{39}N_5O_2$ (717.83): C 80.31, H 5.48, N 9.76; found: C 80.34, H. 5.52, N 10.01.

3'-Azido-2',3'-dideoxy-5'-O,N⁶-bis(triphenylmethyl)-2',3'-secoadenosin-1'-ene (= *9-{1-{(1S)-2-Azido-1-[(triphenylmethoxy)methyl]ethoxy}vinyl}-6-[(triphenylmethyl)amino]purine*; **5**). To a soln. of **3** (60 mg, 0.07 mmol) in DMF (3 ml) under Ar, NaN_3 (13 mg, 0.20 mmol) was added and stirred at 85° for 21 h. The solvent was evaporated and the residue purified by prep. TLC (*B*): 40 mg (80%) of **5**. R_f 0.56 (*B*). M.p. 95–96° (MeOH). $[\alpha]_D = -14.1$ ($c = 0.92$, MeOH). UV: 270.0 (4.29). IR: 3400*m*, 2090*s*, 1670*m*, 1600*s*, 1490*m*, 1465*m*, 1445*m*, 1370*m*, 1275*s*, 1200*m*, 1070*m*, 895*w*, 790*w*, 760*w*, 740*m*, 700*s*. Anal. calc. for $C_{48}H_{40}N_8O_2$ (760.86): C 75.77, H 5.30, N 14.73; found: C 75.70, H 5.58, N 14.67.

3'-Chloro-2',3'-dideoxy-5'-O,N⁶-bis(triphenylmethyl)-2',3'-secoadenosin-1'-ene (= *9-{1-{(1R)-2-Chloro-1-[(triphenylmethoxy)methyl]ethoxy}vinyl}-6-[(triphenylmethyl)amino]purine*; **6**). To a soln. of **3** (55 mg, 0.06 mmol) in DMF (3 ml) under Ar, LiCl (11 mg, 0.26 mmol) was added and stirred at 85° for 25 h. The solvent was evaporated and the residue purified by prep. TLC (*B*): 40 mg (85%) of **5**. R_f 0.70 (*B*). M.p. 99–102° (CH_2Cl_2/MeOH). $[\alpha]_D = -5.3$ ($c = 0.95$, MeOH). UV: 269.9 (4.22). IR: 1675*m*, 1610*s*, 1500*s*, 1470*s*, 1450*m*, 1380*m*, 1280*s*, 1200*m*, 1060*m*, 900*w*, 750*m*, 700*s*. Anal. calc. for $C_{48}H_{40}ClN_5O_2$ (754.33): C 76.43, H 5.34, N 9.28; found: C 76.57, H 5.43, N 9.29.

2'-Deoxy-5'-O,N⁶-bis(triphenylmethyl)-2',3'-secoadenosin-1'-ene (= *9-{1-{(1S)-2-Hydroxy-1-[(triphenylmethoxy)methyl]ethoxy}vinyl}-6-[(triphenylmethyl)amino]purine*; **7**) *and 3,3'''-Oxybis[2',3'-dideoxy-5'-O,N⁶-bis(triphenylmethyl)-2',3'-secoadenosine-1'-ene]* (= *9,9'-{Oxybis{(1S)-1-[(triphenylmethoxy)methyl]ethane-2,1-diyl}bis(oxy)bis[(methylidene)methylene]}bis[6-[(triphenylmethyl)amino]purine]*; **8**). To a soln. of **3** (100 mg, 0.11 mmol) in 20% (*v*/*v*) H_2O/DMF (2.4 ml), $NaHCO_3$ (18.8 mg, 0.22 mmol) was added and heated to 100° for 18 h. The solvent was evaporated and the products separated by prep. TLC (*B*): 44 mg (54%) of **7** and 26 mg (32%) of **8**.

Data of **7**: R_f 0.21 (*B*). M.p. 125° (CH_2Cl_2). $[\alpha]_D = -10.4$ ($c = 0.77$, MeOH). UV: 272.5 (3.79). IR: 3420*m*, 3080*m*, 1755*m*, 1680*m*, 1620*s*, 1500*s*, 1480*s*, 1460*m*, 1350*m*, 1290*s*, 1270*s*, 1220*m*, 1165*m*, 1150*w*, 1065*s*, 1040*m*, 1015*m*, 1010*m*, 810*w*, 760*m*, 710*s*. Anal. calc. for $C_{48}H_{41}N_5O_3$ (735.85): C 78.34, H. 5.62, N 9.52; found: C 78.41, H 5.67, N 9.66.

Data of **8**: R_f 0.67 (*B*). M.p. 91–92° (CH_2Cl_2/MeOH 1:1). $[\alpha]_D = -1.4$ ($c = 0.71$, MeOH). UV: 270.1 (4.66). IR: 3400*m*, 1680*m*, 1620*s*, 1705*m*, 1480*s*, 1460*s*, 1385*s*, 1290*s*, 1210*m*, 1165*w*, 1070*m*, 1040*m*, 1010*w*, 910*m*, 850*w*, 755*m*, 710*s*. Anal. calc. for $C_{96}H_{80}N_{10}O_5$ (1453.68): C 79.31, H 5.55, N 9.64; found: C 79.44, H 5.52, N 9.60.

General Procedure for Monodetritylation. To a soln. of 2'-deoxy-5'-*O*,*N*⁶-bis(triphenylmethyl)-2',3'-secoadenosin-1'-ene **3**, or **5**–**7** (0.05 mmol) in CH_2Cl_2 (2 ml), 10 equiv. of $ZnBr_2$ (113 mg, 0.50 mmol) were added and stirred at r.t. for 1–6 h. More CH_2Cl_2 (20 ml) was then added, the mixture extracted with aq. Na_2HPO_4 soln., the org. layer dried and evaporated, and the foamy residue purified by prep. TLC (*B*).

3'-Azido-2',3'-dideoxy-N⁶-(triphenylmethyl)-2',3'-secoadenosin-1'-ene (= *9-{1-[(1S)-2-Azido-1-(hydroxymethyl)ethoxy]vinyl}-6-[(triphenylmethyl)amino]purine*; **9**). Yield 71%. R_f 0.35 (*A*). M.p. 85° (CH_2Cl_2/MeOH). $[\alpha]_D = -8.0$ ($c = 1.00$, MeOH). UV: 271.4 (4.21). IR: 3400*m*, 2920*m*, 2090*w*, 1700*s*, 1650*s*, 1605*s*, 1510*s*, 1460*m*, 1390*m*, 1340*m*, 1250*s*, 1175*w*, 1110*m*, 1055*m*, 1030*m*, 1000*w*, 900*w*, 830*m*. Anal. calc. for $C_{29}H_{26}N_8O_2$ (518.57): C 67.16, H 5.08, N 21.61; found: C 67.29, H 4.88, N 21.38.

3'-Chloro-2',3'-dideoxy-N⁶-(triphenylmethyl)-2',3'-secoadenosin-1'-ene (= *9-{1-[(1R)-2-Chloro-1-(hydroxymethyl)ethoxy]vinyl}-6-[(triphenylmethyl)amino]purine*; **10**). Yield 70%. R_f 0.10 (*B*). M.p. 104–107° (MeOH). $[\alpha]_D = -3.8$ ($c = 1.05$, MeOH). UV: 271.7 (4.20). IR: 3410*w*, 3050*w*, 1680*m*, 1610*s*, 1500*m*, 1475*s*, 1450*m*, 1380*m*, 1280*m*, 1200*m*, 1160*w*, 1070*m*, 900*w*, 810*w*. Anal. calc. for $C_{29}H_{26}ClN_5O_2$ (512.01): C 68.03, H 5.12, N 13.68; found: C 67.94, H 4.99, N 13.66.

2'-Deoxy-N^6-(triphenylmethyl)-2',3'-secoadenosin-1'-ene (= *9-{1-[2-Hydroxy-1-(hydroxymethyl)ethoxy]-vinyl}-6-[(triphenylmethyl)amino]purine*; **11**). Yield 80%. R_f 0.36 (*A*). M.p. 187–190° (MeOH). UV: 273.1 (4.46). IR: 3420*m*, 3060*m*, 1670*m*, 1610*s*, 1500*m*, 1475*m*, 1450*m*, 1380*m*, 1340*m*, 1295*m*, 1270*m*, 1200*m*, 1060*m*, 1005*w*, 905*m*, 800*w*, 750*m*, 700*s*. Anal. calc. for $C_{29}H_{27}N_5O_3$ (493.57): C 70.57, H 5.51, N 14.19; found: C 70.62, H 5.48, N 14.10.

General Procedure for Complete Detritylation. To a soln. of 2'-deoxy-5'-*O*,*N*^{6}-bis(triphenylmethyl)-2',3'-secoadenosin-1'-ene **3**–**7** (0.10 mmol) in CH_2Cl_2 (3 ml), 20 equiv. of $ZnBr_2$ (450 mg, 2.00 mmol) were added and stirred at r.t. for 18 h. The solvent was evaporated, the oily residue dissolved in AcOEt and washed with aq. Na_2HPO_4 soln., the org. layer dried and evaporated, and the foamy residue purified by prep. TLC (*A*).

3'-Azido-2',3'-dideoxy-2',3'-secoadenosin-1'-ene (= *6-Amino-9-{1-[(1S)-2-azido-1-(hydroxymethyl)ethoxy]-vinyl}purine*; **12**). Yield 85%. R_f 0.13 (*A*). M.p. 120° (MeOH). $[\alpha]_D = -7.4$ (*c* = 1.08, MeOH). UV: 258.8 (3.80). IR: 3360*s*, 3140*s*, 2100*s*, 1690*s*, 1610*s*, 1510*w*, 1475*s*, 1420*m*, 1385*m*, 1399*s*, 1285*s*, 1200*m*, 1150*m*, 1060*m*, 990*m*, 790*w*, 730*m*. Anal. calc. for $C_{10}H_{12}N_8O_2$ (276.26): C 43.48, H 4.38, N 40.56; found: C 43.60, H 4.42, N 40.60.

3'-Chloro-2',3'-dideoxy-2',3'-secoadenosin-1'-ene (= *6-Amino-9-{1-[(1R)-2-chloro-1-(hydroxymethyl)-ethoxy]vinyl}purine*; **13**). Yield 80%. R_f 0.26 (*A*). M.p. 191–192° (MeOH). $[\alpha]_D = -9.0$ (*c* = 0.33, MeOH). UV: 258.7 (3.87). IR: 3400*m*, 3130*s*, 2900*w*, 1690*s*, 1660*s*, 1615*s*, 1515*w*, 1480*m*, 1430*m*, 1390*s*, 1340*m*, 1300*s*, 1280*s*, 1220*m*, 1150*m*, 1070*m*, 1000*m*, 980*w*, 790*w*, 760*m*, 730*m*. Anal. calc. for $C_{10}H_{12}ClN_5O_2$ (269.69): C 44.53, H 4.49, N 25.97; found: C 44.71, H 4.42, N 26.19.

2'-Deoxy-2',3'-secoadenosin-1'-ene (= *6-Amino-9-{1-[2-hydroxy-1-(hydroxymethyl)ethoxy]vinyl}purine*; **14**). Yield 85%. R_f 0.06 (*A*). M.p. 187–190° (MeOH). UV: 259.5 (3.80). IR: 3380*s*, 3280*s*, 3140*s*, 2900*m*, 1690*s*, 1660*m*, 1620*s*, 1570*m*, 1520*w*, 1480*m*, 1430*m*, 1390*s*, 1350*m*, 1290*s*, 1205*s*, 1150*m*, 1060*m*, 1000*m*, 920*w*, 840*w*, 800*w*, 740*m*. Anal. calc. for $C_{10}H_{13}N_5O_3$ (251.24): C 47.81, H 5.22, N 27.87; found: C 47.73, H 5.33, N 27.93.

2',3'-Dideoxy-2',3'-secoadenosin-1',2'-diene (= *6-Amino-9-{1-[1-(hydroxymethyl)vinyloxy]vinyl}purine*; **15**). Yield 71%. UV, IR, and NMR: identical to those described in [16].

3-(4-Methoxybenzyl)-5'-O-(triphenylmethyl)-2',3'-secouridine (= *1-{(1R)-2-Hydroxy-1-{(1S)-2-hydroxy-1-[(triphenylmethoxy)methyl]ethoxy}ethyl}-3-(4-methoxybenzyl)pyrimidine-2,4(1H,3H)-dione*; **17**). To a soln. of 5'-*O*-(triphenylmethyl)-2',3'-secouridine (**16**) [7] [22] (450 mg, 0.90 mmol) in MeCN (7 ml) 4-methoxybenzyl chloride (0.22 ml, 1.60 mmol) and DBU (0.28 ml, 1.80 mmol) were added. The soln. was stirred at 60° for 1 h. The solvent was evaporated, the residue dissolved in CH_2Cl_2, the soln. washed with H_2O, dried, and evaporated, and the foamy residue submitted to FC: 504 mg (80%) of **17**. R_f 0.40 (*A*). M.p. 58–60° (CH_2Cl_2/light petroleum ether). $[\alpha]_D = 35.3$ (*c* = 0.68, MeOH). UV: 259.2 (3.90). IR: 3420*s*, 2930*m*, 1700*m*, 1655*s*, 1510*m*, 1445*s*, 1390*m*, 1245*m*, 1110*m*, 1070*m*, 1030*m*, 805*w*, 700*m*. Anal. calc. for $C_{36}H_{36}N_2O_7$ (608.66): C 71.03, H 5.96, N 4.60; found: C 71.22, H 6.00, N 4.71.

3-(4-Methoxybenzyl)-2',3'-bis-O-[(tol-4-yl)sulfonyl]-5'-O-(triphenylmethyl)-2',3'-secouridine (= *3-(4-Methoxybenzyl)-1-{(1R)-2-[(tol-4-yl)sulfonyloxy]-1-{(1S)-2-[(tol-4-yl)sulfonyloxy]-1-[(triphenylmethoxy)-methyl]ethoxy}ethyl}pyrimidine-2,4(1H,3H)-dione*; **18**). To a soln. of **17** (272 mg, 0.45 mmole) in pyridine (4 ml), toluene-4-sulfonyl chloride (229 mg, 1.20 mmol) was added and the mixture stirred at r.t. overnight. The solvent was then evaporated and the product separated by prep. TLC (*A*): 347 mg (84%) of foamy **17**. R_f 0.75. M.p. 75° (CH_2Cl_2). $[\alpha]_D = 18.4$ (*c* = 1.035, MeOH). UV: 223.6 (infl.; 4.69), 261.3 (3.93). IR: 3430*m*, 1705*m*, 1660*s*, 1510*m*, 1445*s*, 1360*m*, 1240*m*, 1190*s*, 1175*s*, 1090*m*, 1000*m*, 810*m*, 705*m*. Anal. calc. for $C_{50}H_{48}N_2O_{11}S_2$ (917.03): C 65.48, H 5.28, N 3.06; found: C 65.44, H 5.34, N 3.4.

2'-Deoxy-3-(4-methoxybenzyl)-3'-O-[(tol-4-yl)sulfonyl]-5'-O-(triphenylmethyl)-2',3'-secouridin-1'-ene (= *3-(4-Methoxybenzyl)-1-{1-{(1R)-2-[(tol-4-yl)sulfonyloxy]-1-[(triphenylmethoxy)methyl]ethoxy}vinyl}pyrimidine-2,4(1H,3H)-dione*; **19**). *a*) As described for **3** (*Exper. a*), with **18** (450 mg, 0.50 mmol), THF (15 ml), and KO(*t*-Bu) (114 mg, 1.08 mmol): 200 mg (44%) of **18** and 122 mg (33%) of the foamy product **19**. R_f 0.55 (*B*). M.p. 84–86° (CH_2Cl_2/MeOH). $[\alpha]_D = -13.0$ (*c* = 0.93, MeOH). UV: 220.3 (infl.; 4.39), 261.5 (3.96). IR: 1720*m*, 1675*s*, 1520*m*, 1455*s*, 1400*m*, 1250*m*, 1180*m*, 1125*m*, 1090*m*, 1035*m*, 710*m*. Anal. calc. for $C_{43}H_{40}N_2O_8S$ (744.86): C 69.34, H 5.41, N 3.76; found: C 69.08, H 5.25, N 3.79.

b) As described for **3**, with **18** (190 mg, 0.21 mmol), THF (4 ml), and NaH (18 mg, 0.41 mmol): 90 mg (47%) of **18** and 51 mg (33%) of **19**, identical to that described above.

3'-Azido-2',3'-dideoxy-3-(4-methoxybenzyl)-5'-O-(triphenylmethyl)-2',3'-secouridin-1'-ene (= *1-{1-{(1S)-2-Azido-1-[(triphenylmethoxy)methyl]ethoxy}vinyl}-3-(4-methoxybenzyl)pyrimidine-2,4(1H,3H)-dione*; **20**). As described for **5**, with **19** (37 mg, 0.05 mmol), DMF (1 ml), and NaN_3 (10 mg, 0.15 mmol; 18 h): 22 mg (70%) of **20**. R_f 0.70 (*B*). M.p. 53–56° (CH_2Cl_2/MeOH). $[\alpha]_D = -18.3$ (*c* = 0.60, MeOH). UV: 260.1 (3.89). IR: 2100*s*, 1725*m*,

1670*m*, 1515*m*, 1440*m*, 1390*m*, 1290*m*, 1250*s*, 1180*m*, 1100*m*, 1050*w*, 1000*m*, 800*m*, 780*m*, 750*m*, 710*m*. Anal. calc. for $C_{36}H_{33}N_5O_5$ (615.69): C 70.23, H 5.40, N 11.37; found: C 70.39, H 5.58, N 11.39.

3'-Azido-2',3'-dideoxy-5'-O-(triphenylmethyl)-2',3'-secouridin-1'-ene (= *1-{1-{(1S)-2-Azido-1-[(triphenylmethoxy)methyl]ethoxy}vinyl}pyrimidine-2,4(1H,3H)-dione;* **21**). *a*) To a soln. of **20** (26 mg, (0.035 mmol) in anisole (1 ml), $AlCl_3$ (38 mg, 0.28 mmol) was added and the mixture stirred at 60° for 1 h. The solvent was then evaporated, the oily residue dissolved in AcOEt, the soln. washed with aq. Na_2HPO_4 soln., dried, and evaporated, and the foamy residue purified by prep. TLC (*A*): 17 mg (77%) of **21**. R_f 0.35 (*A*). M.p. 56–59°. $[\alpha]_D$ = +0.05 (*c* = 0.60, MeOH). UV: 260.6 (3.89). IR: 3450*s*, 3070*m*, 2100*s*, 1700*m*, 1680*m*, 1300*m*, 1220*s*, 1100*m*, 780*m*. Anal. calc. for $C_{28}H_{25}N_5O_4$ (495.52): C 67.86, H 5.09, N 14.13; found: C 67.60, H 5.01, N 14.10.

b) To a soln. of 2,2'-anhydro-3'-azido-3'-deoxy-5'-*O*-(triphenylmethyl)-2',3'-secouridine (**22**; 370 mg, 0.72 mmol) in THF (10 ml), 1M KO(*t*-Bu) in THF (1 ml) was added and stirred at r.t. for 5 min. The solvent was evaporated and the product isolated by prep. TLC (*A*): 161 mg (44%) of **21**, identical to that described above.

2,2'-Anhydro-3'-azido-3'-deoxy-5'-O-(triphenylmethyl)-2',3'-secouridine (= *(3R)-3-{(1S)-2-Azido-1-[(triphenylmethoxy)methyl]ethoxy}-2,3-dihydro-7H-oxazolo-[3,2-a]pyrimidin-7-one;* **22**). As described for **5**, with 2,2'-anhydro-3'-*O*-(tolyl-4-sulfonyl)-5'-*O*-(triphenylmethyl)-2',3'-secouridine [20] (900 mg, 1.40 mmol), DMF (20 ml), and NaN_3 (278 mg, 4.20 mmol; 40° for 40 h). TLC (*B*) gave 519 mg (70%) of **22**. Spectral data: consistent with those reported [20].

3'-Azido-2',3'-dideoxy-2',3'-secouridin-1'-ene (= *1-{1-[(1S)-2-Azido-1-(hydroxymethyl)ethoxy]vinyl}pyrimidine-2,4(1H,3H)-dione;* **23**). As described for **12**–**14**, with **22** (80 mg, 0.16 mmol), CH_2Cl_2 (10 ml), and $ZnBr_2$ (362 mg, 1.60 mmol; 10 h). The foamy residue was crystallized from MeOH: 32 mg (88%) of **23**. R_f 0.22 (*A*). M.p. 62–65° (MeOH). $[\alpha]_D$ = −3.5 (*c* = 1.10, MeOH). UV: 263.7 (4.05). IR: 3400*m*, 3000*m*, 2100*s*, 1670*s*, 1440*s*, 1300*w*, 1220*m*, 1100*m*, 800*w*, 780*m*. Anal. calc. for $C_9H_{11}N_5O_4$ (253.22): C 42.67, H 4.38, N 27.67; found: C 42.60, H 4.29, N 27.82.

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