Synthesis of heterocyclic systems with a carbohydrate fragment
4.* Unusual reactivity of levoglucosenone with respect to α-aminoazoles and β-dicarbonyl compounds

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Levoglucosenone reacts with α-aminoazoles to yield azolo[1,5-*a*]pyrimidine systems fused with a carbohydrate fragment. The reaction occurs much more smoothly than in the case of other α,β-unsaturated ketones. The reactions of levoglucosenone with β-dicarbonyl compounds (dimedone, barbituric acid) in the presence of a base results in the pyran ring closure, which has never been observed earlier in reactions of β-dicarbonyl compounds with α,β-unsaturated ketones under the conditions of basic catalysis. The structures of products were established by IR and NMR spectroscopy.

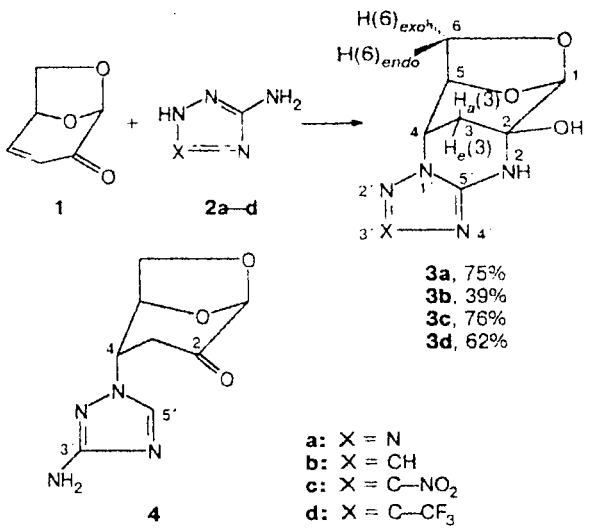
Key words: levoglucosenone, α-aminoazoles, dimedone, barbituric acid, 2-aminopyridine, ethyl β-aminocrotonate, stereoselective heterocyclization.

Our previous works[1,2] were devoted to the study of reactions of levoglucosenone (**1**) with 1,3-binucleophiles that yield heterocyclic compounds containing a fused carbohydrate fragment. In the present work, we studied the reaction of **1** with α-aminoazoles (N,N-binucleophiles) and β-dicarbonyl compounds (C,O-binucleophiles). We found that the behavior of levoglucosenone in these reactions differs (sometimes, appreciably) from that of α,β-unsaturated ketones studied previously.

The reactions of **1** with α-aminoazoles (**2a—d**) in the presence of a base lead to azolo[1,5-*a*]pyrimidine systems fused with carbohydrate fragments (**3a—d**) (Scheme 1).

The reactions with 5-aminotetrazole (**2a**) and 5-amino-3-nitro-1,2,4-triazole (**2c**) are completed over a period of several minutes at 70—80 °C to give compounds **3a,c** in high yields. The reactions with triazoles (**2b,d**) occur more slowly (for 30—60 min); in the case of **2b**, together with the tetracyclic compound (**3b**), a minor product is formed. Based on the NMR spectra, this product was identified as compound **4** (we were not able to isolate it in a pure state). Its ^{1}H NMR spectrum is similar to the spectra of the products resulting from addition of azoles to levoglucosenone[3] and differs markedly from those of the cyclization products like **3** (see Table 1 and Ref. 1); the signal of the NH_2 group is manifested at 5.5 ppm. The fact that compound **4** is built as a 1,3-disubstituted triazole is indicated by the chemical shifts of the carbon atoms in the azole ring, equal to 141.84 ppm (C-5′) and 163.87 ppm (C-3′). In the spectrum of compound **3b**, these chemical shifts are 148.77 (C-3′) and 156.48 ppm (C-5′) (Table 2), which can serve as evidence for its 1,5-disubstituted triazole structure (*cf.* Refs. 4 and 5). The ratio of products **3b** to **4** in the mixture is ~5 : 1 (according to ^{1}H NMR data).

Scheme 1



Reagents and conditions: a base, MeCN/EtOH, 70—80 °C.

The high reaction rate looks especially surprising if we compare the behavior of levoglucosenone (**1**) with that of other α,β-unsaturated ketones. In fact, according to published data,[6,7] reactions of 5-aminotetrazole and

* For Part 3, see Ref. 1

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Table 1. ^{1}H NMR spectra of compounds **3a—d**, **4—6**, **8a,b**, **9**, and **10**

Compound	δ, (*J*/Hz)							
	H(1)	H_e(3)	H_a(3)	H(4)	H(5)	$H(6)_{exo}$	$H(6)_{endo}$	Other H atoms
3a	5.12 (d, *J* = 1.9)	2.04 (ddt, *J* = 13.1, *J* = 3.0, *J* = 1.9)	2.65 (dd, *J* = 13.1, *J* = 3.0)	4.99 (q, *J* = 3.0)	4.67 (m)	3.89 (dd, *J* = 8.3, *J* = 4.8)	4.33 (d, *J* = 8.3)	7.38—7.44 (br.s), 5.5—7.0 (br.s) (NH, OH)
3b	5.06 (d, *J* = 1.9)	2.01 (ddt, *J* = 12.5, *J* = 3.0, *J* = 1.9)	2.55 (br.dd, *J* = 12.5, *J* = 3.0)	4.50 (q, *J* = 3.0)	4.55 (m)	3.89 (dd, *J* = 8.0, *J* = 4.8)	4.33 (dd, *J* = 8.0, *J* = 1.2	7.35 (s, H(3′)); 7.11 (br.s), 6.35—6.45 (br.s) (NH, OH);
3c	5.13 (d, *J* = 2.0)	2.17 (ddt, *J* = 13.0, *J* = 3.1, *J* = 2.0)	2.67 (dm, *J* = 13.0)	4.68—4.73 (m)		3.91 (dd, *J* = 8.2, *J* = 4.3)	4.33 (d, *J* = 8.2)	6.52—6.56 (br.s), 7.76—7.80 (br.s) (NH, OH)
3d	5.16 (d, *J* = 1.8)	2.19 (dm, *J* = 13.1)	2.74 (dd, *J* = 13.1, *J* = 2.6)	4.66—4.72 (m)		3.93 (dd, *J* = 8.2, *J* = 4.5)	4.36 (d, *J* = 8.2)	5.5—6.0 (br.s), 7.0—7.1 (br.s) (NH,OH);
4	5.14 (s)	2.76 (dm, *J* = 17.5)	3.31 (dd, *J* = 17.5, *J* = 7.7)	4.93 (d, *J* = 7.7)	5.01 (br.d, *J* = 5.6)	3.99 (dd, *J* = 8.2, *J* = 5.6)	4.33 (dd, *J* = 8.2, *J* = 1.2)	7.93 (s, H(5′)), 5.45—5.55 (br.s, NH_2);
5	4.83 (s)	2.33 (dm, *J* = 17.3)	3.05 (dd, *J* = 17.3, *J* = 7.9)	Overlap		3.96 (dd, *J* = 5.6, *J* = 7.8)	4.22 (dd, *J* = 7.8)	5.2—5.4 (br.s, NH), 6.49 (dd, H(5″), *J* = 5.0), 6.64 (d, H(3″), *J* = 8.7), 7.36 (ddd, H(4″), *J* = 8.7, *J* = 7.1 *J* = 2.0), 8.02 (dd, H(6″) *J* = 5.0, *J* = 2.0);
6*	5.04 (d, *J* = 1.9) [5.02 (s, H(1′))]	2.67 (ddt, *J* = 13.0, *J* = 2.9, *J* = 1.9) [3.24 (d, H(3′), *J* = 9.8]	2.20 (dd, *J* = 13.0, *J* = 3.8)	4.25 (dist.q) [4.83 (d, H(4′) *J* = 8.9)]	4.61—4.64 (m, H(5) and H(5′))	3.73 (dd, *J* = 4.8) [3.83 (dd, $H(6')_{exo}$, *J* = 7.4, *J* = 5.4)]	4.01 (d, *J* = 7.8, [4.15 (d, $H(6')_{endo}$, *J* = 7.4)]	4.50 (br.s, OH), *J* = 7.8) 6.66 (dd, H(5″), *J* = 7.1, *J* = 5.0), 6.82 (d, H(3″), *J* = 8.7), 7.56 (ddd, *J* = 8.7, H(4″), *J* = 7.1, *J* = 2.0), 8.15 (dd, H(6″), *J* = 5.0, *J* = 2.0)
8a	5.05 (d, *J* = 1.8)	1.58 (ddt, *J* = 12.7, *J* = 2.7, *J* = 1.8)	2.65 (dd, *J* = 12.7, *J* = 3.5)	3.02 (dist.q)	4.23 (m)	3.81 (dd, *J* = 7.5, *J* = 4.7)	4.21 (d, *J* = 7.5)	1.08 (s, 2 CH_3), 2.25 (br.s, 2 CH_2), 6.2—6.5 (br.s, OH)
8b	5.10 (d, *J* = 1.7)	1.73 (ddt, *J* = 13.2, *J* = 2.3, *J* = 1.7)	2.38 (dd, *J* = 13.2, *J* = 3.2)	3.00—3.05 (m)	4.33 (m)	3.81 (dd, *J* = 8.0, *J* = 4.6)	4.15 (d, *J* = 8.0)	7.6—8.0 (br.s, OH), 10.1—10.4 (br.s, NH), 11.0 (br.s, NH)
9	4.93 (s)	2.78 (dm, *J* = 17.5)	2.97 (dd, *J* = 17.5, *J* = 8.7)	3.00—3.05 (m)	4.63 (br.d, *J* = 5.7)	3.91 (dd, *J* = 5.7, *J* = 7.8)	4.22 (d, *J* = 7.8)	3.49 (d, H(7), *J* = 5.2), 10.7 (br.s, NH), 10.85 (br.s, NH)
10	4.87 (d, *J* = 1.9)	1.53 (dm, *J* = 11.3)	2.34 (ddd, *J* = 11.3, *J* = 3.6, *J* = 1.4)	2.94 (dist.q)	4.38 (m)	3.78 (dd, *J* = 7.4, *J* = 4.6)	4.14 (d, *J* = 7.4)	1.31 (t, ether CH_3), 2.29 (s, CH_3), 4.0—4.1 (m, ether CH_2)

* Characteristics of the H(1′), H(3′), H(4′), H(5′), $H(6')_{exo}$, and $H(6')_{endo}$ protons in compound **6** are given in brackets.

Table 2. ^{13}C NMR spectra of compounds **3a—c**, **6**, **8a,b**, **9**, and **10**

Compound	δ						
	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	Other C atoms
3a	104.94 (d)	81.87 (s)	29.82 (dd)	52.51 (d)	76.10 (d)	67.80 (dd)	156.81 (s)
3b	105.18 (d)	81.48 (s)	30.86 (dd)	53.37 (d)	76.13 (d)	67.90 (dd)	148.77 (d, C(3′)), 156.48 (s, C(5′))
3c	105.11 (d)	81.41 (s)	29.92 (dd)	54.96 (d)	76.91 (d)	68.25 (dd)	159.87 (s, C(3′)), 156.88 (s, C(5′))
6*	106.41 (d) [99.52 (d, C(1′))]	71.17 (s) [202.71 (s, C(2′))]	30.83 (dd) [50.19 (d, C(3′))]	53.49 (d) [55.17 (d, C(4′))]	79.26 (d) [73.51 (d, C(5′))]	66.77 (dd) [68.86 (dd, C(6′))]	108.06 (d, C(3″)), 113.55 (d, C(5″)), 138.15 (d, C(4″)), 148.49 (d, C(6″)), 157.87 (s, C(2″))
8a	103.31 (d)	100.18 (s)	28.96 (dd)	30.97 (d)	76.16 (d)	68.37 (dd)	28.09 (q, 2 CH_3), 32.78 (s, $\underline{C}(CH_3)_2$), 41.58; 50.01 (t, 2 CH_2), 112.55 (s, C(7)), 173.38 (s, C(8)), 195.00 (s, CO)
8b	102.51 (d)	102.51 (s)	29.27 (dd)	30.47 (d)	76.36 (d)	68.22 (dd)	88.36 (s, C(7)), 150.33; 160.67; 162.75 (2 CO and C(8))
9	100.73 (d)	197.59 (s)	34.97 (dd)	41.02 (d)	74.04 (d)	67.09 (dd)	50.10 (d, C(7)), 150.98 (s, CO), 170.07 (s, 2 CO)
10	105.81 (d)	81.46 (s)	29.79 (dd)	35.62 (d)	78.77 (d)	69.33 (dd)	14.74 (q, ether CH_3), 19.79 (q, CH_3), 57.83 (t, ether CH_2), 93.53 (s, C(8)), 157.41 (s, C(7)), 166.79 (s, CO)

* Characteristics of the C(1′), C(2′), C(3′), C(4′), C(5′), and C(6′) atoms in compound **6** are given in brackets.

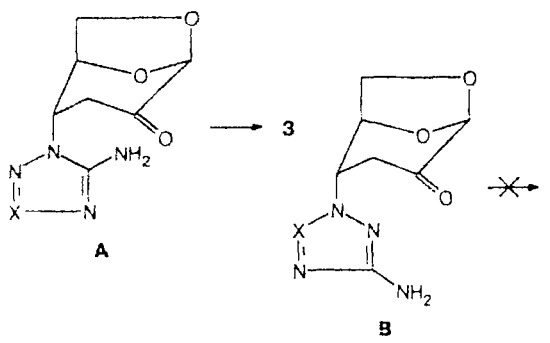
3-amino-1,2,4-triazole with chalcones require refluxing the reactants in DMF for many hours; this differs dramatically from the relatively mild conditions needed for their reactions with levoglucosenone.

The structures of **3a—d**, or, more precisely, the facts that the nitrogen atom in the heterocyclic ring is bound to the C(4) atom and the nitrogen atom in the exocyclic amino-group is bound to C(2), and not the reverse, are proved by the data of ^1H NMR spectroscopy. The signal of the H(4) proton in the ^1H NMR spectra of **3a—d** is an almost non-distorted quartet. This means that the spin-spin coupling constants of H(4) with the H(5), $H_a(3)$, and $H_e(3)$ protons are approximately equal to one another and that there is no NH group in the neighborhood of the C(4) atom: otherwise, the signal for H(4) would be additionally split at the NH-group proton (*cf.* Ref. 1). Thus, it is the NH group that is bound to C(2) and it is the azole ring that is bound to C(4). This is consistent with the published data on the structures of the products resulting from reactions of α-aminoazoles with α,β-unsaturated carbonyl compounds.[6,7] The magnitudes of spin-spin coupling constants ($J_{4,3a} \sim J_{4,3e} \sim J_{4,5} \sim 3$ Hz) indicate that the heterocyclic ring is closed from the side opposite to the 1,6-anhydro-bridge, as was also observed in our previous study.[1,2]

Apparently, the reaction mechanism includes the abstraction of a proton from the heterocyclic nitrogen atom and the attack of the anion thus formed on the C=C bond in levoglucosenone. If the C=C bond is attacked, after the proton abstraction, by the nitrogen atom closest to the amino group, the reaction does not stop at the formation of the addition product **A** but proceeds further as cyclization to give compound **3** (Scheme 2), because in this case, a six-membered ring is formed. Otherwise, if the C=C bond is attacked by the nitrogen atom remote from the amino group, the cyclization of product **B** does not occur (Scheme 2), since this cyclization would yield a seven-membered ring, and this is much less probable than the closure of a six-membered ring.

In this connection, the following should be noted. The amino group present as a substituent in the azole ring causes an electrophile to attack predominantly (and, sometimes, even exclusively) the nitrogen atom closest to it[8,9] (unlike, for example, a nitro group[3,9,10]). Therefore, the type **A** intermediate able to undergo cyclization predominates over non-cyclizable intermediate **B**. This

Scheme 2



accounts for the pathway observed for the reactions of **1** with α-aminoazoles **2a—d**.

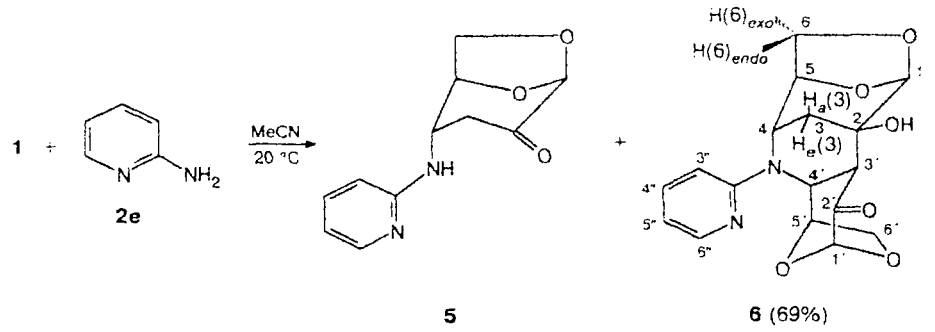
The reactions of levoglucosenone with α-aminoazoles are of interest for one more reason. The presence of the azole nucleus imposes stringent restrictions on the admissible geometry of molecules **3a—d**, because it requires a planar configuration of the C(4)—N(1′)—C(5′)—N(2) moiety (see Scheme 1). However, these restrictions were found not to prevent closure of the heterocyclic ring, and the reaction proceeds surprisingly smoothly. Apparently, this is due to the fact that the planar configuration of this moiety conforms well to the requirements imposed by the rigid bicyclic carbohydrate skeleton on the conformation of the newly closed heterocyclic ring (which, in turn, follow from the requirement for minimization of the energy of the tetracyclic structure formed). In fact, according to X-ray diffraction data obtained for the tricyclic product of the reaction of **1** with thiourea,[1] the pyrimidine ring acquires a sofa conformation in which five atoms (all, except for C(3)) lie in the same plane.

We also studied the reaction of levoglucosenone with 2-aminopyridine **2e**. This reaction gives no pyrido[1,2-*a*]pyrimidine system fused with the carbohyrate fragment that could be expected by analogy with the reaction described above. At an equimolar ratio of the reactants, a mixture consisting of the initial 2-aminopyridine, product of addition **5**, and compound **6** was obtained. In the case of a twofold molar excess of **1**, compound **6** was almost the only reaction product (Scheme 3).

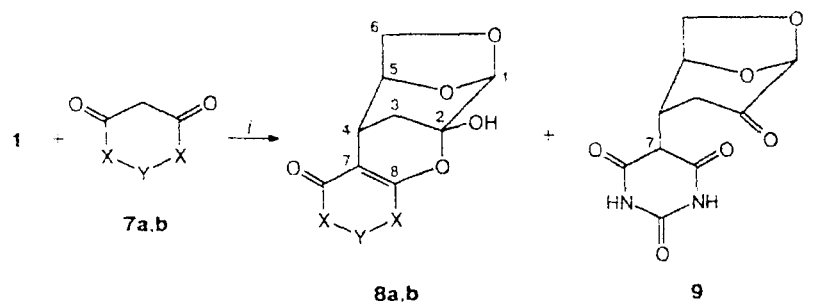
The structure of adduct **6** is very similar to that of the 2 : 1 adduct of levoglucosenone with nitromethane;[11] thus, the mechanism of its formation can also be the same, namely, the addition of two levoglucosenone molecules at the nucleophilic center followed by intramolecular aldol condensation.

The enol forms of 1,3-dicarbonyl compounds possess the same specific feature as the aminoazoles considered above: the presence of the C=C double bond in the —C=C—OH enol group dictates a planar configuration of the corresponding part of the molecule of the heterocyclization product (the C(4)—C(7)—C(8)—O fragment in molecule **8**, Scheme 4). However, as has

Scheme 3



Scheme 4



i. MeCN (dioxane), 20—70 °C

a: X = CH_2; Y = CMe_2
b: X = NH; Y = CO

been already mentioned, this fact by no means hampers the ring closure (but rather favors it).

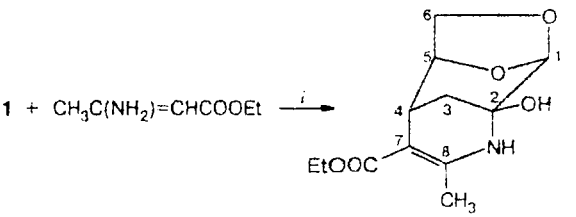
When compound **1** reacts with dimedone **7a** and barbituric acid **7b**, heterocyclization products **8a** (74%) and **8b** (58%) are formed. In the case of dimedone, **8a** is the only reaction product, whereas in the case of barbituric acid, the situation is more complex. The ^{1}H NMR spectrum of the products of its reaction with **1** indicates the presence of compound **9**, in addition to **8b**. The ^{1}H NMR spectrum of compound **9** is similar to those of the products obtained by the addition of nucleophiles to the C=C bond of levoglucosene,[3,12] and the ^{13}C NMR spectrum exhibits a signal for the carbonyl carbon atom (C-2) at 197.59 ppm. The fact that the barbituric acid residue exists in molecule **9** in the keto-form (rather than in the enol form) is confirmed by the presence of the signal corresponding to the H(7) proton (a doublet at 3.5 ppm) in the ^{1}H NMR spectrum of **9**.

It is of interest that the ratio of **8b** to **9**, determined from the ^{1}H NMR spectra, depends on the solvent in which the spectrum is recorded and on the time that has passed from dissolution of the crystals to the recording of the spectrum. For example, in DMSO-d_6, this ratio is 4 : 1, while in a mixture of DMSO-d_6 with CD_3CN (1 : 5), it is 2 : 1 within 5 h after the dissolution and 3 : 2 after 24 h. Meanwhile, the IR spectrum of the crystals (in pellets with KBr) contains no band at 1730—1750 cm^{-1} (corresponding to the carbonyl group at the C(2) atom) that is always observed in the IR spectra of the products of addition to compound **1**.[3] Thus, based on the IR and ^{1}H NMR spectra, it can be concluded that during the reaction of **1** with **7b** compound **8b** is formed and crystallizes from the reaction mixture, while compound **9** is formed from the latter in the solution as time passes. This is the first example of ring—chain isomerization observed in the series of heterocyclization products derived from levoglucosenone.

The most interesting aspect in the reactions of compounds **1** and **7** is the following. Formation of pyrans has never been observed previously in the reactions of dimedone or barbituric acid with α,β-unsaturated ketones catalyzed by bases. Reactions of this type have always afforded the Michael addition products,[13,14] while their cyclization to pyrans required acid catalysis[15,16] (to the best of our knowledge, no examples of cyclization of 1,5-diketones to pyrans under the conditions of basic catalysis have been reported). This unusual behavior of levoglucosenone may be due either to the increased reactivity of its carbonyl group (for instance, this compound is known to be easily converted into *gem*-diols or ketals under the action of water or alcohols, respectively[3,17]) or to the steric factors that are favorable for cyclization (see above).

However, reactions of **1** with β-dicarbonyl compounds do not necessarily result in the closure of a pyran ring. In fact, levoglucosenone reacts with ethyl acetoacetate to give the Michael addition product.[18] However, in the case of ethyl β-aminocrotonate (the nitrogen analog of the enol form of ethyl acetoacetate), a pyridine ring is readily closed and compound **10** is formed (Scheme 5).

Scheme 5



10 (71%)

i. Et_3N; MeCN, 40–50 °C

Obviously, this difference in the behavior of ethyl acetoacetate and the corresponding enamine is due to the higher nucleophilicity of the NH_2 group in the enamine compared to the OH group of the enol.

Experimental

^{1}H NMR spectra were obtained on a Bruker WM-250 spectrometer operating at 250.13 MHz, ^{13}C NMR spectra were recorded on a Bruker AM-300 instrument operating at 75.47 MHz, and IR spectra were measured on a Specord M-80 spectrophotometer for pellets with KBr. Products **3a—c** were recrystallized from ethanol, compounds **3d**, **6**, **8a**, and **10** were recrystallized from MeCN, and **8b** were recrystallized from 80% aqueous dioxane (compound **3c** is a yellow crystalline solid, and the other compounds are colorless). The NMR spectra for compounds **3a,c** and **3b** (pure and containing some **4**) were recorded in $(CD_3)_2SO$, and those for compounds **8b** and **9** were obtained in $(CD_3)_2SO$ or a mixture of $(CD_3)_2SO$ and CD_3CN (see the text); the spectra of compounds **3d**, **5** (mixed with **2e**), **6**, **8a**, and **10** were obtained in $(CD_3)_2CO$. Triazoles **2c** and **2d** were prepared by the procedures described in Refs. 19 and 20, respectively.

(1*S*,8*S*,9*R*,12*S*)-10,14-Dioxa-2,3,4,5,7-pentaazatetracyclo[6.4.1.1^{9,12}.0^{2,6}]tetradeca-3,5-dien-8-ol (3a).* The dihydrate of 5-aminotetrazole **2a** (1.21 g, 0.01 mol) was dissolved with heating in 20 mL of MeCN; seven drops of Et_3N (10 mol.%) and then compound **1** (1.26 g, 0.01 mol) were added to the resulting solution. Five minutes later, the precipitated crystals of **3a** were filtered off. Yield 1.59 g (75%), m.p. 185 °C (decomp.). IR, ν/cm^{-1}: 3355, 3180, 1590. Found (%): C, 39.55; H, 4.39; N, 33.30. $C_7H_9N_5O_3$. Calculated (%): C, 39.80; H, 4.30; N, 33.17.

(1*S*,8*S*,9*R*,12*S*)-4-Nitro-10,14-dioxa-2,3,5,7-tetraazatetracyclo[6.4.1.1^{9,12}.0^{2,6}]tetradeca-3,5-dien-8-ol (3c) was prepared in a similar way from 5-amino-3-nitro-1,2,4-triazole (**2c**); yield 76%, m.p. 218—221 °C (decomp.). IR, ν/cm^{-1}:

* The IUPAC nomenclature and the relevant atom numbering, used in the names of the compounds, are not used in any other part of this paper.

3300, 1595, 1520, 1310. Found (%): C, 37.57; H, 3.69; N, 27.54. $C_8H_9N_5O_5$. Calculated (%): C 37.65, H, 3.56; N, 27.45.

(1*S*,8*S*,9*R*,12*S*)-4-Trifluoromethyl-10,14-dioxa-2,3,5,7-tetraazatetracyclo[6.4.1.1^{9,12}.0^{2,6}]tetradeca-3,5-dien-8-ol (3d) was prepared from 5-amino-3-trifluoromethyl-1,2,4-triazole (**2d**) and **1** (0.01 mol each) in 5 mL of MeCN. The mixture was refluxed for 1 h in the presence of Et_3N, and cooled, and the precipitate of **3d** was filtered off. Yield 1.72 g (62%), m.p. 237—240 °C (decomp.). IR, ν/cm^{-1}: 3300, 1590. Found (%): C 39.06; H, 3.25; N, 19.97; F, 19.92. $C_9H_9F_3N_4O_3$. Calculated (%): C, 38.85; H, 3.27; N, 20.14; F, 20.49.

(1*S*,8*S*,9*R*,12*S*)-10,14-Dioxa-2,3,5,7-tetraazatetracyclo[6.4.1.1^{9,12}.0^{2,6}]tetradeca-3,5-dien-8-ol (3b) and (1*S*,5*R*)-2-(3-amino-1,2,4-triazol-1-yl)-6,8-dioxabicyclo[3.2.1]octan-4-one (4). a. 3-Amino-1,2,4-triazole (**2b**) (0.84 g, 0.01 mol) was dissolved with heating in 6 mL of EtOH. Six drops of piperidine (10 mol.%) and then levoglucosenone (1.26 g, 0.01 mol) were added to the resulting solution. The reaction mixture was refluxed for 30 min and concentrated with heating approximately by half until precipitation began. The resulting suspension was cooled to 0 °C, and the precipitate of **3b** was filtered off. Yield 0.82 g (39%), m.p. 184—187 °C (decomp.). IR, ν/cm^{-1}: 3300—3360, 3135, 1580. Found (%): C, 45.92; H, 4.70; N, 26.52. $C_8H_{10}N_4O_3$. Calculated (%): C, 45.70; H, 4.80; N, 26.66.

b. The procedure was similar to that described for the synthesis of **3a,c** (MeCN, Et_3N). After the reactants had been mixed and the mixture had been kept for 30 min at 40—50 °C, the reaction mixture was placed in a refrigerator for 30 min (because the product, unlike **3a,c**, did not precipitate from the warm solution). The precipitate formed upon cooling was filtered off and dried; overall yield 81%. According to NMR data, it was a mixture of compound **3b**, addition product **4**, and unreacted **2b** in a ratio of 5 : 1 : 1. Recrystallization from ethanol gave pure **3b** in 35% yield. Compound **4** could not be isolated in a pure state.

(1*R*,2*S*,4*R*,7*S*,8*S*,10*S*,11*S*,14*R*)-1-Hydroxy-9-(2-pyridyl)-5,13,16,17-tetraoxa-9-azapentacyclo[8.4.1.1^{4,7}.1^{11,14}.0^{2,8}]-heptadecan-3-one (6) and (1*S*,5*R*)-2-(2-pyridylamino)-6,8-dioxabicyclo[3.2.1]octan-4-one (5). a. 2-Aminopyridine (**2e**) (0.94 g, 0.01 mol) was dissolved at 40 °C in 3 mL of MeCN, and levoglucosenone (1.26 g, 0.01 mol) was added to the solution. The reaction mixture was allowed to stand for 12 h and then subjected to column chromatography (silica gel; chloroform—ethyl acetate, 2 : 1, as the eluent) to give 0.95 g of compound **6** as crystals and 1.16 g of a nonseparable mixture of addition product **5** with unreacted **2e** (3 : 2) as a yellow oil.

b. The reaction was carried out by a procedure similar to that described in **a** but using 5 mmol (0.47 g) of 2-aminopyridine. The chromatography gave 1.19 g (69%) of compound **6**, m.p. 156—158 °C (decomp.). IR, ν/cm^{-1}: 3435, 1710—1740, 1595. Found (%): C, 59.13; H, 5.21; N, 8.16. $C_{17}H_{18}N_2O_6$. Calculated (%): C, 58.95; H, 5.25; N, 8.09.

(1*R*,9*R*,10*R*,13*S*)-9-Hydroxy-5,5-dimethyl-8,11,15-trioxa-tetracyclo[7.4.1.1^{10,13}.0^{2,7}]pentadec-2(7)-en-3-one (8a). Dimedone (**7a**) (1.40 g, 0.01 mol) was dissolved at 40 °C in 4 mL of MeCN, and 7 drops of Et_3N (10 mol.%) were added. Then levoglucosenone (1.26 g, 0.01 mol) was added dropwise over a period of 30 min. The reaction mixture was kept for 2 h at 40 °C, diluted with 6 mL of ether, and placed in a refrigerator for 30 min. The precipitated crystals of **8a** were filtered off. Yield 1.97 g (74%), m.p. 203—204 °C. IR, ν/cm^{-1}: 3220, 1620, 1590. Found (%): C, 63.00; H, 6.99. $C_{14}H_{18}O_5$. Calculated (%): C, 63.13; H, 6.83.

(1*R*,9*R*,10*R*,13*S*)-9-Hydroxy-8,11,15-trioxa-4,6-diaza-tetracyclo[7.4.1.1^{10,13}.0^{2,7}]pentadec-2(7)-ene-3,5-dione (8b). The dihydrate of barbituric acid **7b** (1.64 g, 0.01 mol) was dissolved at 70 °C in 8 mL of 85% aqueous dioxane. Then levoglucosenone (1.26 g, 0.01 mol) was added. The reaction mixture was kept for 5 h at 20 °C and for 2 days in a refrigerator. The resulting crystals were filtered off, yield 1.09 g (43%). After concentration and cooling of the mother liquor, an additional 0.38 g of the product was isolated. The overall yield of compound **8b** was 1.47 g (58%). The product decomposes above 225 °C. IR, ν/cm^{-1}: 3420, 3270, 3085, 1695—1720, 1655, 1620. Found (%): C, 46.95; H, 4.11; N, 11.11. $C_{10}H_{10}N_2O_6$. Calculated (%): C, 47.24; H, 3.97; N, 11.02.

Ethyl (1*S*,2*R*,5*S*,6*R*)-1-hydroxy-8-methyl-3,11-dioxa-9-azatricyclo[4.3.1.1^{2,5}]undec-7-ene-7-carboxylate (10). Ethyl β-aminocrotonate (1.29 g, 0.01 mol) was dissolved in 4 mL of MeCN, and 2 drops of Et_3N were added. Then levoglucosenone (1.26 g, 0.01 mol) was added, and the reaction mixture was kept for 3 h at 40—50 °C and cooled. The precipitate was filtered off. Yield 1.81 g (71%), m.p. 175—176 °C. IR, ν/cm^{-1}: 3320, 1605, 1560. Found (%): C, 56.49; H, 6.83; N, 5.57. $C_{12}H_{17}NO_5$. Calculated (%): C, 56.45; H, 6.73; N, 5.49.

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