Total Synthesis of (2*Z*)-[(4*R*,5*R*,6*S*)-6-(β-D-Glucopyranosyloxy)-4,5-dihydroxycyclohex-2-en-1-ylidene]ethanenitrile, a Cyanoglucoside from *Ilex warburgii*

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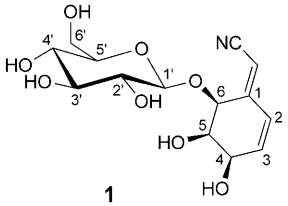
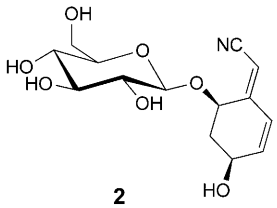
The total synthesis of the noncyanogenic cyanoglucoside **1**, originally isolated from *Ilex warburgii*, was achieved in nine steps (9% overall yield), starting from an optically pure *Diels–Alder* adduct ((+)-**3**). The key step of the synthesis, the glycosidation, was carried out under *Koenigs–Knorr* conditions closely related to those developed for the total syntheses of (−)-lithospermoside and (−)-bauhinin. We had to tune the protecting groups used for the two free *cis*-configured OH groups of the aglycone, which afforded the desired β-D-glucoside intermediate **15** in very good yield (62%).

Introduction. – The noncyanogenic cyanoglucoside **1** (=(2*Z*)-[(4*R*,5*R*,6*S*)-6-(β-D-glucopyranosyloxy)-4,5-dihydroxycyclohex-2-en-1-ylidene]ethanenitrile) [1] was first isolated in 1983 by *Ueda* and co-workers [1a] from the fruit of *Ilex warburgii*, an endemic plant growing in Iriomote Island (southern part of the Ryukyu Islands, Okinawa, Japan). The berries of *I. warburgii* were also found to contain (−)-menisdaurin (**2**) [2], another noncyanogenic cyanoglucoside, which had been isolated before in 1978 from *Menispermum dauricum* [2a]. Regarding the structure of **1**, it is noteworthy that the three OH functions of the aglycone have the 4,5,6-*cis* relative configuration [1].

A number of other noncyanogenic cyanoglucosides of related structure, *e.g.*, lithospermoside, dasycarponin, bauhinin, and purshianin, have been isolated from various medicinal plants [3]. Therefore, they appear to be interesting targets for total synthesis, as numerous other natural glycosides [4]. Herein, we report the first total synthesis of compound **1**. The versatility of our glycosidation conditions developed during the syntheses of (−)-bauhinin and (−)-lithospermoside [5] allowed us to prepare the desired β-D-glucoside with the unusual all-*cis* relative configuration.



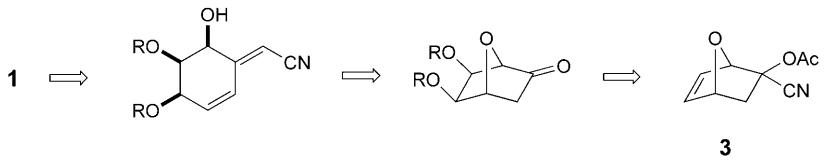
1



2

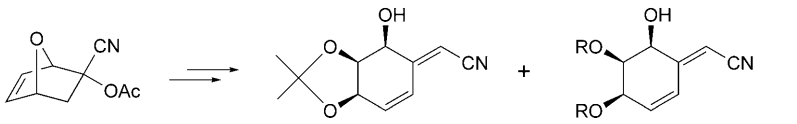
Results and Discussion. – We chose to prepare the protected aglycone of **1** from the optically pure *Diels–Alder* cycloadduct (+)-**3**, a *Vogel*'s 'naked sugar', which can be easily obtained [6] and whose powerful synthetic potential has been demonstrated during the syntheses of many biologically active substances [6]. A simple retrosynthetic analysis (*Scheme 1*) showed that the glycosidation reaction would be the key step.

Scheme 1



As reported recently in the literature [7], the selective formation with acceptable yields of β-D-glucosides of many secondary alcohols remains a challenge [7]. Therefore, at the outset of this work, we tried to glycosidate, according to our previously optimized *Koenigs–Knorr* conditions [8], the aglycones (±)-**4**, (±)-**5**, and (±)-**6** (*Scheme 2*). These three substrates had been prepared in preliminary experiments by *Vieira* and *Vogel* from the *Diels–Alder* cycloadduct (±)-**7** [9]. For example, (±)-**4** was obtained in 44% overall yield under the following reaction conditions: *a*) OsO_4, H_2O_2, acetone; *b*) CH_2O, MeONa; *c*) $(EtO)_2P(O)CHNaCN$; *d*) $(Me_3Si)_2NLi$.

Scheme 2



(±)-**7** (±)-(*E*)-**4** (±)-(*E*)-**5** R = Ac
(±)-(*E*)-**6** R = ^{t}BuMe$_2$Si

Despite numerous attempts, only poor results could be obtained with (±)-**5** and (±)-**6**: glycosidation of (±)-**5**, even under acidic conditions [7], gave mainly orthoesters, and aglycone (±)-**6** was almost completely unreactive. Only the bicyclic aglycone (±)-**4** afforded the expected β-D-glucosides **8** and **9** as a 1:1 diastereoisomeric mixture (*Scheme 3*). However, the yields were only moderate to fair, depending on the amount of base present at the outset of the reaction, since the formation of the isomeric β-D-glucosides **10** and **11** (1:1 diastereoisomeric mixture) and of the orthoesters **12** and **13** (mixture of isomers) was also observed (*Table 1*).

It appeared to us that the isopropylidene acetal (acetonide) was not stable enough under 'acidic' glycosidation conditions ($\leq$0.3 equiv. of base at the outset), which are required to decrease, or even avoid, the formation of orthoesters, an often significant side reaction [8]. We could, therefore, use only glycosidation conditions ranging from 'weakly acidic' (*Table 1*, *Entry 1*) to 'almost neutral' (*Entry 4*). The best conditions (*Entry 3*) gave fair results, but were only a compromise. Therefore, we decided to change the protection groups of the two OH groups at C(4) and C(5) of the aglycone,

Scheme 3

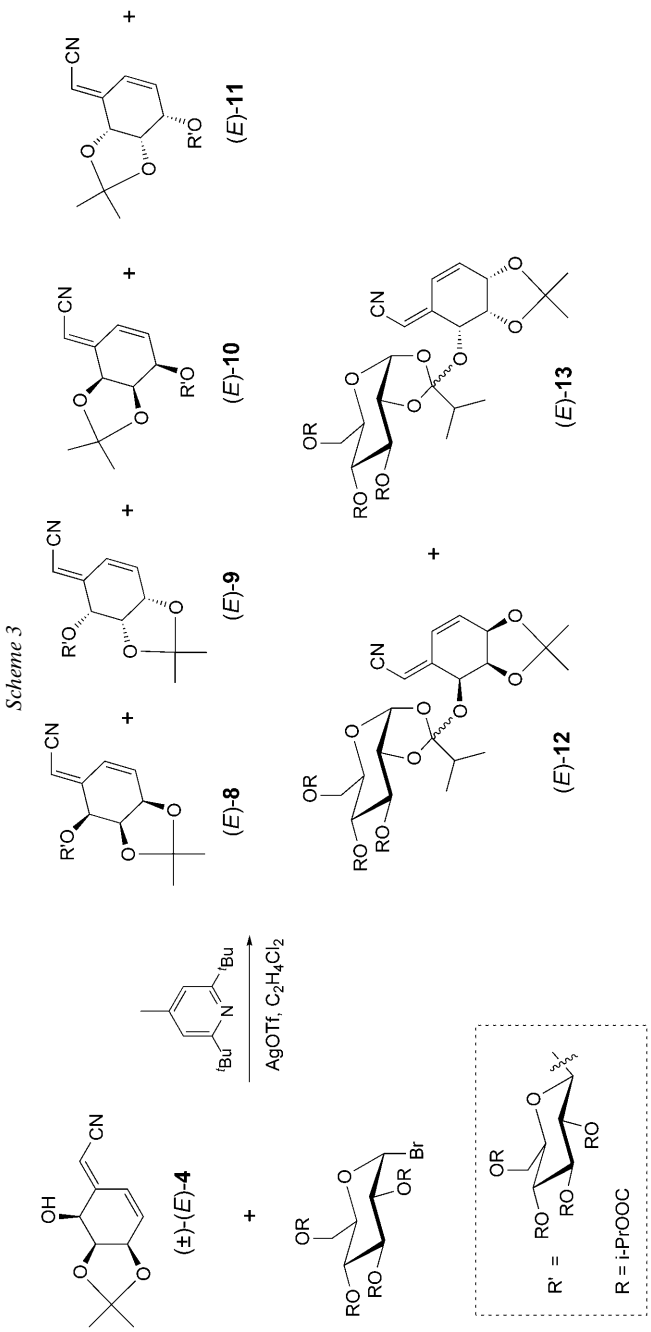


Table 1. *Glycosidation of the Aglycone* (±)-**4**

Entry	Base equiv. at the reaction outset	**8**+**9** [%][a])	**12**+**13** [%]	**10**+**11** [%][a])
1	0.45	34	25	16
2	0.59	42	30	10
3	0.68	50	31	<5
4	1.06	30	35	<5

[a]) 1:1 Mixture of isomers.

which then would be more stable in acidic media. Since the glycosidations of (±)-**5** and (±)-**6** failed, we chose another cyclic acetal, the known cyclohexylidene acetal [10a], which is much less labile than the acetonide, but can still be cleaved in the presence of a glycosidic bond. Besides, this acetal has been extensively used in carbohydrate and cyclitol chemistry [10].

For the first experiments, the aglycone (±)-**14**, prepared from (±)-**7**, was tested. It turned out that in the presence of an amount of base, at the outset of the glycosidation reaction, which is small enough to avoid the formation of orthoesters, transacetalization was still kept to a minimum (*Scheme 4*; *Table 2*, *Entry 3*). Since a very good yield of the 1:1 diastereoisomeric mixture of the β-D-glucosides **15** and **16** could be secured, with only minor amounts of the side products **17**–**20** being formed, the cyclohexylidene acetal seemed to us to be the protective group of choice for the total synthesis of **1** from an *optically pure* starting material.

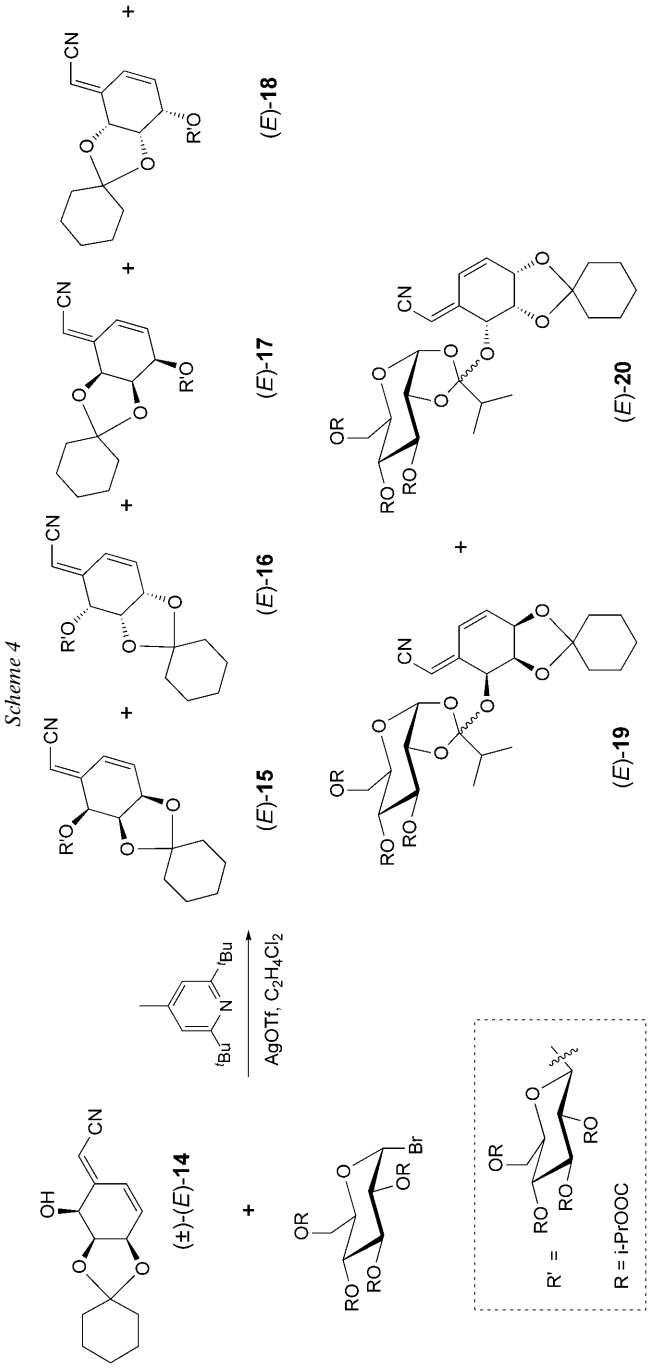
Table 2. *Glycosidation of the Aglycone* (±)-**14**

Entry	Base equiv. at reaction outset	**15**+**16** [%][a])	**19**+**20** [%]	**17**+**18** [%][a])
1	0	55	<5	25
2	0.06	56	<5	24
3	0.12	65	<5	15
4	0.20	44	25	12
5	0.34	38	43	<5

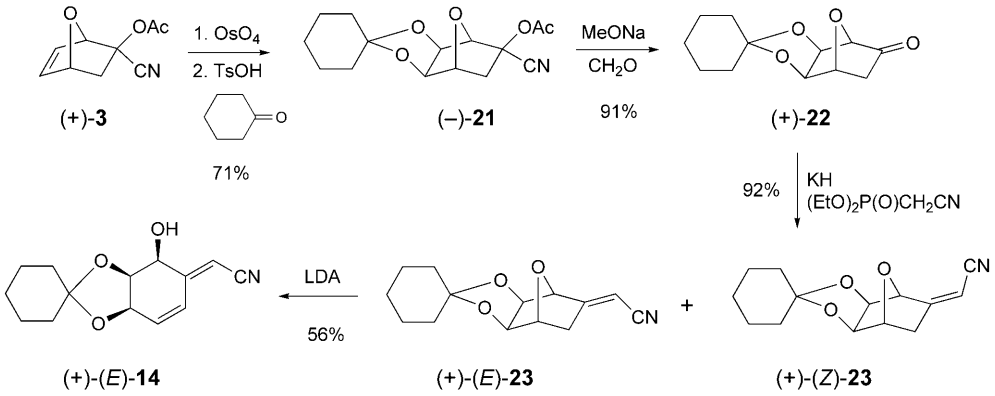
[a]) 1:1 Mixture of isomers.

The synthesis of the optically pure, protected aglycone (+)-**14** is presented in *Scheme 5*. Direct osmylation of the easily obtained optically pure (+)-**3** [6p,q,s], followed by protection with cyclohexanone, afforded the desired acetal (−)-**21** in 71% yield. Hydrolysis to the ketone (+)-**22** and *Wittig–Horner* reaction afforded in 92% yield an (*E*/*Z*)-mixture of the protected nitrile (+)-(*Z*)-**23**, which was directly used in the next reaction, since identical results were obtained with both the (*E*)- and the (*Z*)-isomer. We found that the opening of the oxa bridge in **23** was very sensitive to changes in reaction conditions such as nature of the base ((i-Pr)$_2$NLi, (Me$_3$Si)$_2$NK, (Me$_3$Si)$_2$NLi), solvent, temperature, reaction time, *etc*. Degradation products were always formed in sizable amounts. After many optimization attempts, we found conditions ((i-Pr)$_2$NLi , 45 s at 4°) that reproducibly afforded (+)-**14**, but only in 56% yield. It

Scheme 4



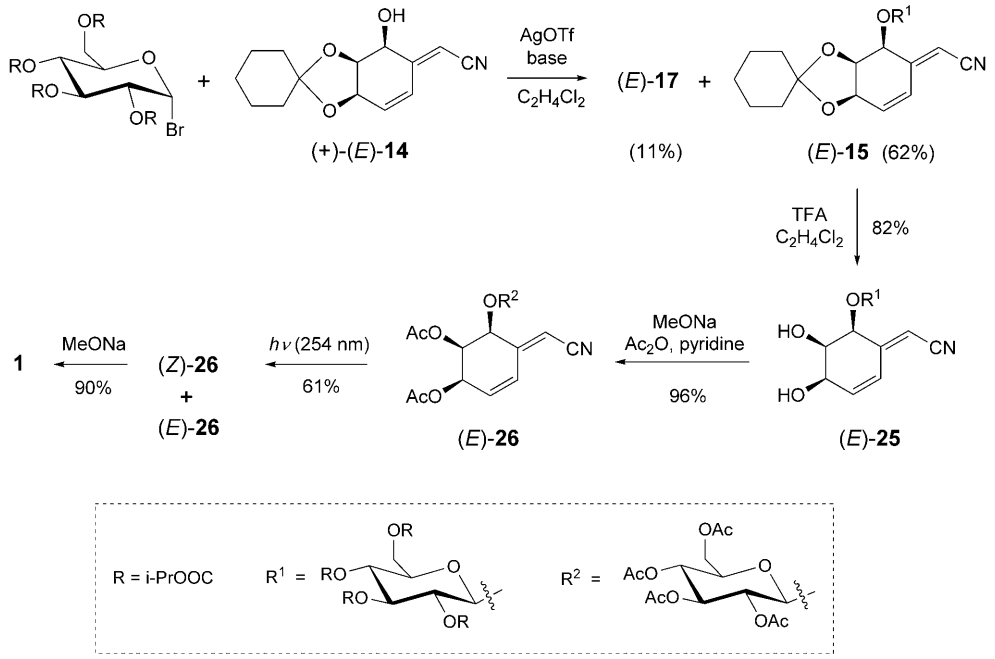
Scheme 5



should be noted that, contrary to our observations in related cases [5], no (*Z*)-isomer of (+)-**14** was observed.

Glycosidation of the aglycone (+)-**14** afforded the desired *β*-D-glucoside **15** in 62% yield, with only 11% yield of the isomeric glucoside **17** (*Scheme 6*). Then, cleavage of the cyclohexylidene acetal of **15** in the presence of CF_3CO_2H (TFA) in 1,2-dichloroethane afforded the diol **25**, which was converted into the hexaacetate (*E*)-**26**. Irradiation of (*E*)-**26** with a Hg lamp in MeCN afforded a mixture of its (*E*)- and (*Z*)-isomers. Irradiation was stopped well before the stationary state between the two isomers was

Scheme 6



reached: in a typical single run, 29% of (*Z*)-**26** was obtained, and 59% of (*E*)-**26**/(*Z*)-**26** 96 : 4 was recovered. Four successive irradiations thus allowed us to isomerize (*E*)-**26** to its (*Z*)-isomer in 61% yield (see *Exper. Part*). It should be noted that sizable degradation was observed when the photoisomerization was run in the typical solvent 1,4-dioxane. Finally, hydrolysis of (*Z*)-**26** in basic medium yielded **1**. The physical and spectroscopic data of (*Z*)-**26** were identical to those reported in the literature, and the data of **1** were very similar to the few reported ones for this natural product [1].

In summary, the total synthesis of the cyanoglucoside **1** isolated from *Ilex warburgii* was achieved in nine steps and in an overall yield of 9% from the *Diels–Alder* cycloadduct (+)-**3**, thanks to our versatile glycosidation procedure.

The senior author (*C. L. D.*) would like to thank Prof. *P. Vogel*, University of Lausanne, Switzerland, in whose laboratory the work on cyanoglucosides was begun. Special thanks are due to Dr. *E. Vieira*, who worked out the synthesis of many aglycones during his Ph.D. thesis in Prof. *Vogel*'s laboratory. We are also grateful to the *Centre National de la Recherche Scientifique* (UMR 7015) for financial support, and to Dr. *D. Le Nouen* for recording NMR spectra.

Experimental Part

General. See [8][11]. Systematic compound names are given in parentheses.

General Procedure for Glycosidation. To a stirred suspension of AgOTf (2 equiv.) in 1,2-dichloroethane (3–5 ml) protected from light, activated 4-Å molecular sieves (500 mg, powder) and 2,6-di(*tert*-butyl)-4-methylpyridine (*n* equiv. at the outset of the reaction) were added at 20°. The aglycone (1 equiv.) and tetra-*O*-isobutyrylglucosyl bromide (2 equiv.) were successively added at 20° under a stream of Ar gas. Then, a soln. of additional 2,6-di(*tert*-butyl)-4-methylpyridine (2 – *n* equiv.) in 1,2-dichloroethane (3 ml) was added at a rate of 75 µl/min over 40 min at 20°. The mixture was stirred for 14 h, and then filtered over *Celite*, which was washed with AcOEt (20 ml), and the combined filtrates were concentrated under reduced pressure. The resulting oil was purified by column chromatography (CC) (SiO_2; AcOEt/petroleum ether (PE)) to yield the glycosidated compounds.

*(2*E*)-{(4*R*,5*R*,6*S*)-4,5-(Isopropylidenedioxy)-6-[(2,3,4,6-tetra*-O*-isobutyryl-β-*D*-glucopyranosyl)oxy]-cyclohex-2-en-1-ylidene}ethanenitrile* (= *(2E)-[(3aR,4S,7aR)-2,2-Dimethyl-4-{[2,3,4,6-tetrakis*-O*-(2-methylpropanoyl)-β-*D*-glucopyranosyl]oxy}-3a,7a-dihydro-1,3-benzodioxol-5(4*H*)-ylidene]ethanenitrile*; **8**) *and (2*E*)-{(4*S*,5*S*,6*R*)-4,5-(Isopropylidenedioxy)-6-[(2,3,4,6-tetra*-O*-isobutyryl-β-*D*-glucopyranosyl)-oxy]cyclohex-2-en-1-ylidene}ethanenitrile* (= *(2E)-[(3a*S*,4*R*,7a*S*)-2,2-Dimethyl-4-{[2,3,4,6-tetrakis*-O*-(2-methylpropanoyl)-β-*D*-glucopyranosyl]oxy}-3a,7a-dihydro-1,3-benzodioxol-5(4*H*)-ylidene]ethanenitrile*; **9**). Purified by CC (SiO_2; AcOEt/PE 1 : 9 → 3 : 7).

Data of the Less-Polar Isomer (**8** or **9**). Colorless solid. M.p. 161–163°. $[\alpha]_D^{25} = -46$ ($c = 0.3$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 250 MHz)[1]): 1.24–1.26 (*m*, 4 *Me*$_2$CH); 1.33, 1.35 (2*s*, Me$_2$C); 2.30–2.50 (*m*, 4 Me$_2$C*H*); 3.74 (*ddd*, $^3J = 9.7$, 5.2, 2.2, H–C(5′)); 4.10 (*dd*, $^2J = 12.3$, $^3J = 5.2$, 1 H of CH_2(6′)); 4.25 (*dd*, $^2J = 12.3$, $^3J = 2.2$, 1 H of CH_2(6′)); 4.45–4.51 (*m*, 1 H (agl)); 4.67–4.73 (*m*, 2 H (agl)); 4.77 (*d*, $^3J = 7.6$, H–C(1′)); 5.11 (*dd*, $^3J = 9.3$, 9.2, H–C(4′)); 5.20 (*dd*, $^3J = 9.2$, 7.6, H–C(2′)); 5.29 (*dd*, $^3J = 9.3$, 9.2, H–C(3′)); 5.51 (br. *s*, C=CHCN); 5.96 (br. *d*, $^3J = 10.1$, H–C(2)); 6.62 (br. *d*, $^3J = 10.1$, H–C(3)). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): 18.75, 18.84, 18.92, 18.95 (4 *Me*$_2$CH); 26.81, 27.61 (*Me*$_2$C); 29.68, 33.80, 33.84 (4 Me$_2$*C*H); 61.73 (C(6′)); 67.60, 71.78, 72.18, 72.63 (C(2′), C(3′), C(4′), C(5′)); 73.68, 75.83 (C(4), C(6)); 77.61 (C(5)); 95.22 (C=*C*HCN); 101.86 (C(1′)); 111.48 (Me$_2$C); 115.92 (CN); 123.77 (C(3)); 134.14 (C(2)); 151.90 (C(1)); 175.12, 175.21, 176.05, 176.56 (4 C=O).

Data of the More-Polar Isomer (**9** or **8**). Colorless solid. M.p. 205–207°. $[\alpha]_D^{25} = +41$ ($c = 0.35$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 250 MHz): 0.90–1.20 (*m*, 4 *Me*$_2$CH); 1.29, 1.31 (2*s*, Me$_2$C); 2.3–2.5 (*m*, Me$_2$C*H*);

[1]) The term 'agl' refers to aglycone.

3.70–3.74 (*m*, H–C(5′)); 4.10–4.22 (*m*, CH_2(6′)); 4.52–4.64 (*m*, 2 H (agl)); 4.70–4.76 (*m*, 1 H (agl)); 4.83 (*d*, ^3J = 7.9, H–C(1′)); 5.10 (*dd*, ^3J = 9.7, 7.9, H–C(2′)); 5.16 (*dd*, ^3J = 9.7, 9.4, H–C(3′)); 5.31 (*t*, ^3J = 9.4, H–C(4′)); 5.71 (br. *s*, C=CHCN); 5.92 (br. *d*, ^3J = 10.1, H–C(2)); 6.63 (br. *d*, ^3J = 10.1, H–C(3)). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): 18.74, 18.81, 18.85, 18.89 (4 *Me*$_2$CH); 27.03, 27.70 (*Me*$_2$C); 33.82, 32.90 (4 Me$_2$*C*H); 61.32 (C(6′)); 67.62, 70.65, 71.93, 72.45 (C(2′), C(3′), C(4′), C(5′)); 73.49, 73.83, 74.85 (C(4), C(5), C(6)); 96.54 (C=*C*HCN); 98.96 (C(1′)); 111.40 (Me$_2$*C*); 116.29 (CN); 124.19 (C(3)); 133.33 (C(2)); 151.70 (C(1)); 175.19, 176.11, 176.57 (4 CO).

*(1*R*,2*R*,4*R*,5*R*,6*R*)-2-Acetoxy-5,6-(cyclohexylidenedioxy)-7-oxabicyclo[2.2.1]heptane-2-carbonitrile* (= *(3a′*R*,4′*R*,5′*R*,7′*R*,7a′*R*)-5′-Cyanohexahydrospiro[cyclohexane-1,2′-[1,3,8]trioxa[4,7]epoxy[1,3]benzodioxol]-5′-yl Acetate*; (–)-**21**). To a soln. of (+)-**3** (6.55 g, 36.55 mmol) in acetone (150 ml), OsO_4 (0.02M soln. in *t*-BuOH; 4 ml, 0.08 mmol) and H_2O_2 (30% soln. in H_2O, 60 ml, 0.6 mol) were successively added. The dark-yellow mixture was left at 20° until it decolorized (5 d). The acetone was evaporated under reduced pressure, and $NaHSO_3$ (40% soln. in H_2O, 40 ml) was added. The aq. phase was extracted with AcOEt (3×200 ml), and the combined org. phases were washed with sat. aq. NaCl soln. (200 ml), dried ($MgSO_4$), and evaporated to dryness. To a soln. of the residue (11.4 g) in toluene (350 ml), cyclohexanone (35 ml, 0.34 mol) and *para*-toluenesulfonic acid monohydrate (TsOH·H_2O; 1.5 g, 7.9 mmol) were added. The mixture was heated for 4 h in a *Dean–Stark* apparatus. Then, it was concentrated by evaporating 200 ml of toluene under reduced pressure. Sat. aq. Na_2CO_3 soln. (130 ml) was added, and the diphasic mixture was extracted with AcOEt (3×200 ml). The combined org. phases were washed with sat. aq. NaCl soln. (200 ml), dried ($MgSO_4$), and evaporated. The resulting oil was purified by CC (SiO_2; AcOEt/PE 1:9 → 3:7) to afford (–)-**21** (7.61 g, 71%). Colorless crystals (AcOEt/PE). M.p. 110–111°. UV (MeCN): 275.0 (370), 202.7 (620). $[\alpha]_D^{25} = -32$ (c = 0.5, $CHCl_3$). IR (KBr): 2954, 2936, 2862, 2850, 2361, 2342, 1772, 1757, 1444, 1430, 1372, 1246, 1235, 1210, 1166, 1115, 1065, 1043, 1022, 938. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.30–1.40 (*m*, 2 H of cyclohexylidene); 1.45–1.51 (*m*, 4 H of cyclohexylidene); 1.55–1.63 (*m*, 2 H of cyclohexylidene); 1.65–1.71 (*m*, 2 H of cyclohexylidene); 2.12 (*s*, OCOMe); 2.15 (*d*, ^2J = 14.5, H_{endo}–C(3)); 2.22 (*dd*, ^2J = 14.5, ^3J = 5.6, H_{exo}–C(3)); 4.33 (*d*, ^3J = 5.5, H–C(5) or H–C(6)); 4.55 (*d*, ^3J = 5.6, H–C(4)); 4.70 (*s*, H–C(1)); 4.78 (*d*, ^3J = 5.5, H–C(6) or H–C(5)). ^{13}C-NMR ($CDCl_3$, 100 MHz): 20.85 (OCO*Me*); 23.77, 24.01, 25.08, 34.51, 35.42 (5 C of cyclohexylidene); 40.86 (C(3)); 71.82 (C(2)); 77.80, 79.11, 80.70 ((C(4), C(5), C(6)); 84.13 (C(1)); 113.65 (1 C of cyclohexylidene); 116.19 (CN); 169.24 (O*C*OMe). Anal. calc. for $C_{15}H_{19}NO_5$ (293.32): C 61.42, H 6.53, N 4.78; found: C 61.22, H 6.61, N 4.69.

*(1*R*,4*R*,5*R*,6*R*)-5,6-(Cyclohexylidenedioxy)-7-oxabicyclo[2.2.1]heptan-2-one* (= *(3a′*R*,4′*R*,7′*R*,7a′*R*)-Tetrahydrospiro[cyclohexane-1,2′-[1,3,8]trioxa[4,7]epoxy[1,3]benzodioxol]-5′(4′*H*)-one*; (+)-**22**). To a soln. of (–)-**21** (4.4 g, 15.0 mmol) in anh. MeOH (120 ml), MeONa (900 mg, 16.7 mmol) was added. The mixture was stirred for 2 h at 20°, then 40% aq. formalin (CH_2O; 14 ml, 49 mmol) was added, and the soln. was stirred at 20° for an additional 2 h. Then, H_2O (80 ml) was added, and the soln. was extracted with AcOEt (3×120 ml). The combined org. phases were washed with sat. aq. NaCl soln. (120 ml), dried ($MgSO_4$), and evaporated. The resulting oil was purified by CC (SiO_2; AcOEt/PE 1:9 → 3:7) to afford (+)-**22** (3.07 g, 91%) as a colorless solid[2]), which was washed with PE. M.p. 67–69°. $[\alpha]_D^{25} = +123$ (c = 0.6, $CHCl_3$). IR (KBr): 2936, 2862, 1772, 1737, 1454, 1374, 1292, 1227, 1163, 1132, 1104, 1081, 1070, 1051, 938. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.30–1.40 (*m*, 2 H of cyclohexylidene); 1.45–1.55 (*m*, 4 H of cyclohexylidene); 1.56–1.65 (*m*, 2 H of cyclohexylidene); 1.67–1.75 (*m*, 2 H of cyclohexylidene); 1.81 (*d*, ^2J = 17.7, H_{endo}–C(3)); 2.40 (*dd*, ^2J = 17.7, ^3J = 6.6, H_{exo}–C(3)); 4.25 (*s*, H–C(1)); 4.43, 4.48 (2*d*, ^3J = 5.5, H–C(5), H–C(6)); 4.79 (*d*, ^3J = 6.6, H–C(4)). ^{13}C-NMR ($CDCl_3$, 100 MHz): 23.77, 24.00, 25.09, 34.58, 35.46 (5 C of cyclohexylidene); 38.21 (C(3)); 77.86, 79.83, 81.68 ((C(4), C(5), C(6)); 83.77 (C(1)); 114.57 (1 C of cyclohexylidene); 209.30 (C(2)). Anal. calc. for $C_{12}H_{16}O_4$ (224.25): C 64.27, H 7.19; found: C 64.24, H 7.12.

*(2*E*)- and (2*Z*)-[(1*S*,4*R*,5*R*,6*S*)-5,6-(Cyclohexylidenedioxy)-7-oxabicyclo[2.2.1]hept-2-ylidene]ethanenitrile* (= *(2*E*)- and (2*Z*)-(3a′*S*,4′*S*,7′*R*,7a′*R*)-Tetrahydrospiro[cyclohexane-1,2′-[1,3,8]trioxa[4,7]epoxy[1,3]benzodioxol]-5′(4′*H*)-ylideneethanenitrile*; (+)-(*E*)-**23** and (+)-(*Z*)-**23**, resp.). Anh. THF (15 ml)

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[2]) Note that (±)-**22**, prepared from (±)-**7**, was obtained as a colorless *oil*.

was added to KH (270 mg, 6.73 mmol), purified by three successive washings with PE of a 20% dispersion in oil. Under a stream of Ar gas, the suspension was cooled to 0°, and $(EtO)_2P(O)CH_2CN$ (1.07 ml, 6.79 mmol) was added dropwise under stirring. At the end of H_2 evolution (*ca.* 15 min), a soln. of (+)-**22** (812 mg, 3.62 mmol) in THF (10 ml) was added dropwise. The cooling bath was removed, and the mixture was stirred for 30 min at 20°. The reaction was quenched with sat. aq. NH_4Cl soln. (30 ml), and the mixture was extracted with AcOEt (3×40 ml). The combined org. phases were washed with sat. aq. NaCl soln. (40 ml), dried ($MgSO_4$), and concentrated under reduced pressure. The resulting oil was purified by CC (SiO_2; AcOEt/PE 1:9 → 3:7) to afford (+)-(*E*)-**23** (422 mg, 47%) followed by (+)-(*Z*)-**23** (408 mg, 45%) as colorless solids, which were washed with PE.

*Data of (+)-(*E*)-*(**23**). M.p. 94–95°[3]). UV (MeCN): 214.2 (13700). $[\alpha]_D^{25} = +10$ ($c = 1.2$, $CHCl_3$). IR (KBr): 3062, 2936, 2922, 2864, 2222, 1448, 1374, 1295, 1162, 1103, 1080, 1046, 1002, 923. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.34–1.42 (*m*, 2 H of cyclohexylidene); 1.45–1.56 (*m*, 4 H of cyclohexylidene); 1.58–1.63 (*m*, 2 H of cyclohexylidene); 1.65–1.75 (*m*, 2 H of cyclohexylidene); 2.24 (br. *d*, $^2J = 17.6$, H_{endo}–C(3)); 2.60 (*ddd*, $^2J = 17.6$, $^3J = 5.8$, $^4J = 3.0$, H_{exo}–C(3)); 4.23, 4.33 (2*d*, $^3J = 5.5$, H–C(5), H–C(6)); 4.63 (*d*, $^3J = 5.8$, H–C(4)); 4.71–4.74 (br. *s*, H–C(1)); 5.43–5.47 (*m*, C=CHCN). ^{13}C-NMR ($CDCl_3$, 100 MHz): 23.85, 24.06, 25.13, 33.67, 34.67 (5 C of cyclohexylidene); 35.53 (C(3)); 79.60, 80.56, 81.58 ((C(4), C(5), C(6)); 83.03 (C(1)); 92.95 (C=*C*HCN); 113.68, 115.76 (1 C of cyclohexylidene, CN); 162.75 (C(2)). Anal. calc. for $C_{14}H_{17}NO_3$ (247.29): C 68.00, H 6.93, N 5.66; found: C 67.73, H 7.02, N 5.65.

*Data of (+)-(*Z*)-*(**23**): M.p. 98–99°[3]). UV (MeCN): 214.2 (12900). $[\alpha]_D^{25} = +151$ ($c = 0.9$, $CHCl_3$). IR (KBr): 2939, 2908, 2855, 2220, 1370, 1162, 1135, 1105, 1052, 1003, 926. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.32–1.45 (*m*, 2 H of cyclohexylidene); 1.46–1.57 (*m*, 4 H of cyclohexylidene); 1.58–1.67 (*m*, 2 H of cyclohexylidene); 1.68–1.77 (*m*, 2 H of cyclohexylidene); 2.12 (br. *d*, $^2J = 17.4$, H_{endo}–C(3)); 2.53 (br. *dd*, $^2J = 17.4$, $^3J = 5.8$, H_{exo}–C(3)); 4.30 (br. *s*, H–C(5), H–C(6)); 4.60 (*d*, $^3J = 5.8$, H–C(4)); 5.01 (br. *s*, H–C(1)); 5.32 (br. *s*, C=CHCN). ^{13}C-NMR ($CDCl_3$, 100 MHz): 23.87, 24.08, 25.17, 33.98, 34.72 (5 C of cyclohexylidene); 35.58 (C(3)); 79.95, 80.27, 81.53 (C(4), C(5), C(6)); 82.63 (C(1)); 92.70 (C=*C*HCN); 113.69, 115.37 (1 C of cyclohexylidene, CN); 162.75 (C(2)). Anal. calc. for $C_{14}H_{17}NO_3$ (247.29): C 68.00, H 6.93, N 5.66; found: C 67.72, H 7.05, N 5.62.

*(*2E*)-[(4*R*,5*S*,6*S*)-4,5-(Cyclohexylidenedioxy)-6-hydroxycyclohex-2-en-1-ylidene]ethanenitrile* (=*(*2E*)-[(3a*S*,4*S*,7a*R*)-4-Hydroxy-3a,7a-dihydrospiro[1,3-benzodioxole-2,1′-cyclohexan]-5(4*H*)-ylidene]ethanenitrile*; (+)-(*E*)-**14**). A mixture of $(i\text{-}Pr)_2NH$ (1.07 ml, 7.5 mmol) and BuLi (8.75 ml of a 1.6M soln. in hexane, 14 mmol) in anh. THF (40 ml) was stirred at 4° under Ar gas for 20 min. Then, a soln. of (+)-(*E*)-**23**/(+)-(*Z*)-**23** (1.25 g, 5.05 mmol) in THF (12 ml) was added within *ca.* 20 s, and the mixture was stirred for 45 s at 4°. Then, sat. aq. NH_4Cl soln. (35 ml) was rapidly added to the mixture, which was extracted with AcOEt (3×50 ml), and the combined org. phases were washed with sat. aq. NaCl soln. (35 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The resulting oil was purified by CC (SiO_2; AcOEt/PE 2:8 → 3:7) to afford (+)-(*E*)-**14** (703 mg, 56%). Slightly yellow oil[4]). UV (MeCN): 253.8 (15900). $[\alpha]_D^{25} = +115$ ($c = 0.8$, $CHCl_3$). IR (film): 3527, 3074, 2962, 2940, 2932, 2907, 2858, 2212, 1748, 1632, 1591, 1360, 1233, 1165, 1118. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.27–1.42 (*m*, 2 H of cyclohexylidene); 1.44–1.65 (*m*, 8 H of cyclohexylidene); 2.65 (br. *s*, 6-OH); 4.45–4.47 (br. *s*, H–C(6)); 4.56 (br. *t*, $J = 3.6$, H–C(5)); 4.75 (br. *t*, $J = 3.6$, H–C(4)); 5.71 (br. *s*, C=CHCN); 5.98 (*dt*, $^3J = 10.1$, $^4J = 1.3$, H–C(2)); 6.61 (br. *d*, $^3J = 10.1$, H–C(3)). ^{13}C-NMR ($CDCl_3$, 100 MHz): 23.84, 23.98, 24.89, 36.43, 37.37 (5 C of cyclohexylidene); 69.39, 73.15, 75.87 ((C(4), C(5), C(6)); 95.20 (C=*C*HCN); 111.77, 116.56 (1 C of cyclohexylidene, CN); 123.85, 134.42 (C(2), (C(3)); 156.02 (C(1)). Anal. calc. for $C_{14}H_{17}NO_3$ (247.29): C 68.00, H 6.93, N 5.66; found: C 67.83, H 7.09, N 5.47.

*(*2E*)-{(4*R*,5*R*,6*S*)-4,5-(Cyclohexylidenedioxy)-6-[(2,3,4,6-tetra-*O*-isobutyryl-β-D-glucopyranosyl)oxy]-cyclohex-2-en-1-ylidene}ethanenitrile* (=*(*2E*)-[(3a*R*,4*S*,7a*R*)-4-{[2,3,4,6-Tetrakis-*O*-(2-methylpropanoyl)-β-D-glucopyranosyl]oxy}-3a,7a-dihydrospiro[1,3-benzodioxole-2,1′-cyclohexan]-5(4*H*)-ylidene]etha-

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[3]) M.p. of racemic (*E*)-**23** and (*Z*)-**23** (obtained from (±)-**22**): 138–140° and 93–95°, resp.

[4]) Racemic (±)-(*E*)-**14** (obtained from (±)-(*E*/*Z*)-**23**), was obtained as a yellow solid melting at 124–125°.

nenitrile; (*E*)-**15**) *and (2*E*)-[(4*R*,5*R*,6*S*)-5,6-(Cyclohexylidenedioxy)-4-[(2,3,4,6-tetra*-O*-isobutyryl-β-*D*-glucopyranosyl)oxy]cyclohex-2-en-1-ylidene}ethanenitrile* (=*(2*E*)-[(3a*S*,7*R*,7a*R*)-7-{[2,3,4,6-Tetrakis*-O*-(2-methylpropanoyl)-β-*D*-glucopyranosyl]oxy}-7,7a-dihydrospiro[1,3-benzodioxole-2,1′-cyclohexan]-4(3a*H*)-ylidene]ethanenitrile*; (*E*)-**17**). To a stirred suspension of AgOTf (=$CF_3SO_3^-Ag^+$; 195 mg, 0.76 mmol) in 1,2-dichloroethane (4 ml), protected from light, activated 4-Å molecular sieves (700 mg, powder) and 2,6-di(*tert*-butyl)-4-methylpyridine (18 mg, 0.09 mmol) were added at 20°. Then, a soln. of (+)-(*E*)-**14** (94 mg, 0.38 mmol) in 1,2-dichloroethane (1 ml) and tetra-*O*-isobutyrylglucosyl bromide (405 mg, 0.77 mmol) as a solid were successively added at 20° under a stream of Ar gas. Then, additional 2,6-di(*tert*-butyl)-4-methylpyridine (140 mg, 0.68 mmol) in 1,2-dichloroethane (3 ml) was added at a rate of 75 µl/min over 40 min at 20°. The mixture was stirred for 14 h. Then, the mixture was filtered over *Celite*, which was washed with AcOEt (20 ml), and the combined filtrates were concentrated under reduced pressure. The resulting oil was purified by CC (SiO_2; AcOEt/PE 1:9 → 3:7) to afford (*E*)-**17** (27 mg, 11%) as a slightly yellow solid, followed by (*E*)-**15** (162 mg, 62%) as a colorless solid.

Data of Isomer (*E*)-**17**. M.p. 148–150° (MeOH/H_2O). UV (MeCN): 264.0 (24800). $[\alpha]_D^{25} = -18$ ($c = 2.8$, $CHCl_3$). IR (KBr): 2977, 2938, 2879, 2215, 1754, 1753, 1471, 1462, 1390, 1365, 1345, 1251, 1188, 1151, 1113, 1097, 1071, 1037. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.05–1.25 (*m*, 4 Me_2CH); 1.43–1.60 (*m*, 10 H of cyclohexylidene); 2.40–2.62 (*m*, 4 Me_2CH); 3.71–3.75 (*m*, H–C(5′)); 4.11–4.20 (*m*, CH_2(6′)); 4.47–4.50 (*m*, H–C(5)); 4.65 (br. *s*, H–C(6)); 4.68 (br. *dd*, $^3J = 4.7$, 2.2, H–C(4)); 4.87 (*d*, $^3J = 7.8$, H–C(1′)); 5.10–5.17 (*m*, H–C(2′), H–C(4′)); 5.29 (*t*, $^3J = 9.4$, H–C(3′)); 5.53 (br. *s*, C=CHCN); 6.17 (br. *d*, $^3J = 10.6$, H–C(2)); 6.67 (br. *dd*, $^3J = 10.6$, 2.2, H–C(3)). ^{13}C-NMR ($CDCl_3$, 100 MHz): 18.80, 18.83, 18.86, 18.89, 18.91, 18.97, 19.01, 19.08 (4 Me_2CH); 23.83, 23.92, 25.00 (3 C of cyclohexylidene); 33.92, 33.97, 34.04 (4 Me_2CH); 35.76, 37.18 (2 C of cyclohexylidene); 61.99 (C(6′)); 67.89, 70.65 (C(4′), C(2′)), 72.36 (C(3′)), 72.70 (C(5′)); 73.25, 73.34, 73.89 (C(4), C(5), C(6)); 98.41 (C=*C*HCN); 100.57 (C(1′)); 111.94 (1 C of cyclohexylidene); 116.28 (CN); 124.48 (C(3)); 135.34 (C(2)); 155.09 (C(1)); 175.38, 175.40, 176.16, 176.71 (4 C=O). Anal. calc. for $C_{36}H_{51}NO_{12}$ (689.80): C 62.68, H 7.45, N 2.03; found: C 62.24, H 7.52, N 1.80.

Data of Isomer (*E*)-**15**. M.p. 217–219° (MeOH/H_2O) (dec.). UV (MeCN): 260.0 (21000). $[\alpha]_D^{25} = +15$ ($c = 1.25$, $CHCl_3$). IR (KBr): 2976, 2939, 2879, 2219, 1751, 1471, 1450, 1387, 1367, 1345, 1249, 1189, 1150, 1112, 1069. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.00–1.30 (*m*, 4 Me_2CH); 1.40–1.60 (*m*, 10 H of cyclohexylidene); 2.40–2.60 (*m*, 4 Me_2CH); 3.72–3.75 (*m*, H–C(5′)); 4.14–4.17 (*m*, CH_2(6′)); 4.55–4.61 (*m*, 2 H (agl)); 4.72 (br. *s*, 1 H (agl)); 4.83 (*d*, $^3J = 8.1$, H–C(1′)); 5.10–5.19 (*m*, H–C(2′), H–C(4′)); 5.31 (*t*, $^3J = 9.6$, H–C(3′)); 5.67 (br. *s*, C=CHCN); 5.92 (br. *d*, $^3J = 10.1$, H–C(2)); 6.60 (br. *d*, $^3J = 10.1$, H–C(3)). ^{13}C-NMR ($CDCl_3$, 100 MHz): 18.85, 18.87, 18.90, 18.93, 18.99, 19.03 (Me_2CH); 23.88, 23.89, 24.93 (3 C of cyclohexylidene); 33.96, 33.97, 34.04 (4 Me_2CH); 36.69, 37.30 (2 C of cyclohexylidene); 61.48 (C(6′)); 67.82 (C(4′)), 70.83 (C(2′)), 72.05 (C(3′)), 72.58 (C(5′)); 72.95, 73.64, 74.75 (C(4), C(5), C(6)); 96.34 (C=*C*HCN); 98.71 (C(1′)); 112.15 (1 C of cyclohexylidene); 116.48 (CN); 124.24 (C(3)); 133.67 (C(2)); 152.03 (C(1)); 175.29, 175.36, 176.20, 176.65 (4 C=O). Anal. calc. for $C_{36}H_{51}NO_{12}$ (689.80): C 62.68, H 7.45, N 2.03; found: C 62.15, H 7.58, N 1.91.

*(2*E*)-[(4*R*,5*R*,6*S*)-4,5-Dihydroxy-6-{[2,3,4,6-tetrakis*-O*-(2-methylpropanoyl)-β-*D*-glucopyranosyl]oxy}-cyclohex-2-en-1-ylidene]ethanenitrile* ((*E*)-**25**). CF_3CO_2H (TFA; 6 ml) was added dropwise to a soln. of (*E*)-**15** (400 mg, 0.58 mmol) in anh. 1,2-dichloroethane (7 ml). The mixture was stirred at 20° for 12 h, diluted with AcOEt (15 ml), and treated with sat. aq. $NaHCO_3$ soln. until gas evolution ceased. The mixture was extracted with AcOEt (3×20 ml), and the combined org. phases were washed with sat. aq. NaCl soln. (20 ml), dried ($MgSO_4$), and evaporated. The resulting oil was purified by CC (SiO_2; AcOEt/PE 2:8 → 1:1) to afford, besides starting material (*E*)-**15** (27 mg, 6.7%), compound (*E*)-**25** (270 mg, 76%) as colorless crystals. Global yield: 82%. M.p. 182–184°. UV (MeCN): 260.5 (30500). $[\alpha]_D^{25} = -7$ ($c = 1.5$, $CHCl_3$). IR (KBr): 3550–3450, 2977, 2939, 2880, 2217, 1750, 1471, 1388, 1371, 1345, 1249, 1187, 1149, 1111, 1089, 1082, 1019. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.00–1.18 (*m*, 4 Me_2CH); 2.44–2.60 (*m*, 4 Me_2CH); 3.67–3.73 (*m*, H–C(5′)); 4.03–4.05 (br. *s*, H–C(5)); 4.08–4.14 (*m*, CH_2(6′)); 4.29–4.32 (br. *s*, H–C(4)); 4.38–4.41 (br. *s*, H–C(6)); 4.76 (*d*, $^3J = 7.6$, H–C(1′)); 5.05 (*dd*, $^3J = 9$, 7.6, H–C(2′)); 5.11 (*t*, $^3J = 9.5$, H–C(4′)); 5.30 (*dd*, $^3J = 9.5$, 9.0, H–C(3′)); 5.61 (br. *s*, C=CHCN); 6.13 (br. *d*, $^3J = 9.7$, H–C(2)); 6.67 (br. *d*, $^3J = 9.7$, H–C(3)). ^{13}C-NMR ($CDCl_3$, 100 MHz): 18.83, 18.87, 18.97, 19.01, 19.06 (4 Me_2CH); 33.94, 34.12 (4 Me_2CH); 61.49 (C(6′)); 67.72, 67.73, 69.56, 71.33, 71.87, 72.62, 78.68 (C(2′),

C(3′), C(4′), C(5′), C(4), C(5), C(6)); 98.02, 100.54 (C(1′), C=*C*HCN); 116.02 (CN); 124.72 (C(3)); 136.63 (C(2)); 152.32 (C(1)); 175.34, 175.93, 176.04, 176.70 (4 C=O). Anal. calc. for $C_{30}H_{43}NO_{12}$ (609.67): C 59.10, H 7.11, N 2.30; found: C 59.06, H 7.20, N 2.40.

*(2*E*)-{(4*R*,5*R*,6*S*)-4,5-Diacetoxy-6-[(2,3,4,6-tetra*-O*-acetyl-β-*D*-glucopyranosyl)oxy]cyclohex-2-en-1-ylidene}ethanenitrile* (*=(1*R*,2*R*,5*E*,6*S*)-5-(Cyanomethylidene)-6-[(2,3,4,6-tetra*-O*-acetyl-β-*D*-glucopyranosyl)oxy]cyclohex-3-ene-1,2-diyl Diacetate*; (*E*)-**26**). MeONa (130 mg, 2.4 mmol) was added to a stirred soln. of (*E*)-**25** (215 mg, 0.35 mmol) in anh. MeOH (20 ml) at 0° under Ar gas. The cooling bath was removed, and the mixture was stirred for 1 h at 20°. Then, sufficient *Amberlite IRC-50* was added to reach neutral pH. MeOH (40 ml) was added, the mixture was filtered, and the filtrate was evaporated under reduced pressure. The residue was dissolved in Ac_2O (50 ml), DMAP (=4-(dimethylamino)pyridine; 20 mg, 0.16 mmol) was added, and the mixture was stirred for 3 h at 20°. The mixture was evaporated to dryness, and the resulting oil was purified by CC (SiO_2; AcOEt/PE 1:1) to afford (*E*)-**26** (197 mg, 96%). Colorless syrup. UV (MeCN): 252.3 (15000). $[\alpha]_D^{25} = +0.5$ ($c = 1.4$, $CHCl_3$). IR (film): 2979, 2961, 2942, 2922, 2361, 2217, 1752, 1736, 1432, 1374, 1230, 1169, 1068, 1038, 908. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.98, 2.00, 2.01, 2.04, 2.08 (5*s*, 6 AcO); 3.69–3.73 (*m*, H–C(5′)); 4.12 (*dd*, $^2J = 12.3$, $^3J = 2.0$, 1 H of CH_2(6′)); 4.22 (*dd*, $^2J = 12.3$, $^3J = 4.6$, 1 H of CH_2(6′)); 4.56–4.58 (br. *s*, H–C(6)); 4.70 (*d*, $^3J = 7.9$, H–C(1′)); 5.00 (*dd*, $^3J = 9.6$, 7.9, H–C(2′)); 5.08 (*dd*, $^3J = 9.8$, 9.3, H–C(4′)); 5.19 (*dd*, $^3J = 9.6$, 9.3, H–C(3′)); 5.65 (br. *s*, C=CHCN, H–C(5)); 5.71 (br. *s*, H–C(4)); 5.89 (*dd*, $^3J = 10.3$, $^4J = 1.5$, H–C(2)); 6.78 (br. *d*, $^3J = 10.3$, H–C(3)). ^{13}C-NMR ($CDCl_3$, 100 MHz): 20.54, 20.62, 20.65, 20.74, 20.78 (6 *Me*CO); 61.55 (C(6′)); 68.14 (C(4′)); 68.33, 68.69 (C(4), C(5)); 70.90 (C(2′)); 72.19 (C(5′)); 72.55 (C(3′)); 74.88 (C(6)); 97.53 (C=*C*HCN); 99.47 (C(1′)); 116.24 (CN); 126.18 (C(3)); 132.02 (C(2)); 151.53 (C(1)); 169.41, 169.49, 170.06, 170.17, 170.49, 170.63 (6 C=O). Anal. calc. for $C_{26}H_{31}NO_{14}$ (581.53): C 53.70, H 5.37, N 2.41; found: C 52.97, H 5.32, N 2.34.

*(2*Z*)-{(4*R*,5*R*,6*S*)-4,5-Diacetoxy-6-[(2,3,4,6-tetra*-O*-acetyl-β-*D*-glucopyranosyl)oxy]cyclohex-2-en-1-ylidene}ethanenitrile* (*=(1*R*,2*R*,5*Z*,6*S*)-5-(Cyanomethylidene)-6-[(2,3,4,6-tetra*-O*-acetyl-β-*D*-glucopyranosyl)oxy]cyclohex-3-ene-1,2-diyl Diacetate*; (*Z*)-**26**). In a disk-shaped quartz flask (63-mm i.d., 11-mm width), a soln. of (*E*)-**26** (88 mg, 0.15 mmol) in freshly dist. MeCN (30 ml) was irradiated with a medium-pressure Hg lamp (*Philips HPK-125*). The reaction was monitored by HPLC on a *Zorbax-Sil* column (250×4.6 mm) eluting with AcOEt/hexane 1:1 at a flow rate of 1.8 ml/min, with detection at 254 nm: t_R 15 *vs.* 24 min for (*E*)- *vs.* (*Z*)-(**26**), resp. After a total of 13 min of irradiation, an (*E*/*Z*)-ratio of 2:1 was obtained. The irradiation was stopped, the solvent was evaporated, and the resulting oil was purified by CC (SiO_2; AcOEt/PE 1:1) to afford 52 mg (59%) of (*E*/*Z*)-**26** 96:4, and 26 mg (29%) of pure (*Z*)-**26**. This experiment was carried out four times, each time using the recovered (*E*/*Z*)-mixture from the previous run. Thus, a total of 10 mg (11%) of (*E*/*Z*)-**26** was recovered, together with 54 mg (61%) of (*Z*)-**26**. The title compound was obtained as a syrup, which afforded colorless crystals after crystallization from MeOH/H_2O. M.p. 73–74° (MeOH/H_2O). UV (MeCN): 253.1 (21100) (lit.: 253 nm (EtOH) [1]). $[\alpha]_D^{25} = -84$ ($c = 0.8$, $CHCl_3$). IR (KBr): 2961, 2924, 2853, 2218, 1758, 1755, 1432, 1375, 1240, 1136, 1064, 1038. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.99, 2.02, 2.06, 2.08, 2.09 (5*s*, 6 Ac); 3.73–3.78 (*m*, H–C(5′)); 4.10 (*dd*, $^2J = 12.3$, $^3J = 4.5$, 1 H of CH_2(6′)); 4.34 (*dd*, $^2J = 12.3$, $^3J = 2.2$, 1 H of CH_2(6′)); 4.79–4.81 (br. *s*, H–C(6)); 4.85 (*d*, $^3J = 7.5$, H–C(1′)); 5.13–5.25 (*m*, H–C(2′), H–C(3′), H–C(4′)); 5.33–5.38 (*m*, H–C(5)); 5.44 (br. *s*, C=CHCN); 5.62–5.64 (br. *s*, H–C(4)); 5.98 (br. *d*, $^3J = 9.8$, H–C(3)); 6.33 (*d*, $^3J = 9.8$, H–C(2)). ^{13}C-NMR ($CDCl_3$, 100 MHz): 20.71, 20.74, 20.81, 20.95 (6 *Me*CO); 61.51 (C(6′)); 66.03 (C(4)); 68.14 (C(5)); 68.18 (C of Glc); 70.95 (C of Glc); 72.33 (C(5)); 72.97 (C of Glc); 74.90 (C(6)); 100.63, 100.92 ((C(1′), C=*C*HCN); 115.93 (CN); 129.38 (C(2)); 131.49 (C(3)); 151.17 (C(1)); 169.02, 169.49, 170.05, 170.38, 170.65, 170.81 (6 C=O). Anal. calc. for $C_{26}H_{31}NO_{14}$ (581.52): C 53.70, H 5.37, N 2.41; found: C 53.85, H 5.83, N 2.12.

*(2*Z*)-[(4*R*,5*R*,6*S*)-6-(β-*D*-Glucopyranosyloxy)-4,5-dihydroxycyclohex-2-en-1-ylidene]ethanenitrile* (**1**). MeONa (10 mg, 0.19 mmol) was added to a stirred soln. of (*Z*)-**26** (16 mg, 0.027 mmol) in anh. MeOH (5 ml) at 0° under Ar gas. After 5 min at 0°, the mixture was allowed to warm to 20°, and after 1 h, sufficient *Amberlite IRC-50* (*ca.* 1 g) was added to reach neutral pH. Then, MeOH (10 ml) was added, and the mixture was filtered and evaporated under reduced pressure. The resulting oil was purified by CC (SiO_2; MeOH/AcOEt 1:9) to afford 8.2 mg (92%) of **1** as a slightly yellow oil. Unfortunately, all crystallization attempts were unsuccessful (lit. m.p. 221–223° [1]). $[\alpha]_D^{25} = -223$ ($c = 0.8$, MeOH) (lit.

$[\alpha]_D^{25} = -247$ ($c = 0.61$, MeOH) [1]). ^{1}H-NMR (D_2O, 400 MHz, 25°; δ(HOD) 4.79): 3.44–3.50 (*m*, H–C(4′), H–C(5′)); 3.51–3.57 (*m*, H–C(2′), H–C(3′)); 3.75 (*dd*, $^2J = 12.1$, $^3J = 7.1$, 1 H of CH_2(6′)); 3.92 (br. *d*, $^2J = 12.1$, 1 H of CH_2(6′)); 4.29–4.33 (*m*, H–(5)); 4.50–4.54 (*m*, H–C(4)); 4.75 (br. *d*, $^3J = 7.3$, H–C(1′)); 4.97–5.01 (*m*, H–C(6)); 5.66 (br. *s*, C=CHCN); 6.07 (*dd*, $^3J = 10.1$, 2.0, H–C(3)); 6.36 (*dd*, $^3J = 10.1$, $^4J = 2.0$, H–C(2)). ^{13}C-NMR (D_2O, 100 MHz): 61.46 (C(6′)); 68.30 (C(4)); 70.00 (C(5)); 70.38 (C(5′)); 73.40 (C(2′)); 76.50 (C(4′)); 76.69 (C(6)), 76.90 (C(3′)); 97.74 (C=*C*HCN); 101.04 (C(1′)); 118.63 (CN); 128.13 (C(2)), 136.92 (C(3)), 155.48 (C(1)).

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