Total Synthesis of (−)-Bauhinin

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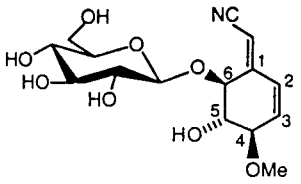
The total synthesis of the naturally occurring cyanoglucoside (−)-bauhinin (**1**) was achieved starting from the optically pure oxatrinorbornenone **2** in 12 steps and 8% overall yield. The aglycone of (−)-bauhinin was easily obtained from the optically pure oxatrinorbornenone derivative **6** by a *Wittig-Horner* reaction followed by the opening of the oxa bridge. Glycosidation with tetra-*O*-isobutyryl-D-glucosyl bromide **9** as the reagent in the *Koenigs-Knorr* reaction afforded glucoside **10** in 58% yield, which, after photoisomerization and deprotection, gave (−)-bauhinin (**1**).

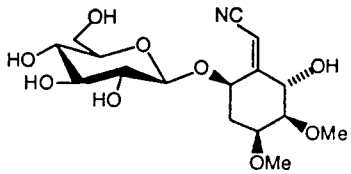
Introduction. – (−)-Bauhinin (**1**) was first isolated by *C. C. Chen et al.* in 1985 from the roots of *Bauhinia Championii*, a plant belonging to the *Leguminosae* family, which grows in the mountainous area and dense forests of Taiwan [1]. A number of other non-cyanogenic cyanoglucosides of related structure have been isolated from various plants, *e.g.* simmondsin, menisdaurin, purshianin, and lithospermoside [2]. Simmondsin is the only non-cyanogenic cyanoglucoside that has been prepared so far: its partial synthesis has been carried out in *ca.* 19 steps from a natural cyclitol, L-quebrachitol [3]. Since these cyanoglucosides are of biological importance, they appeared to us to be interesting targets for total synthesis.

We will report here the first total synthesis of a member of this 'class', (−)-bauhinin (**1**), from a very versatile, enantiomerically pure starting material.

Synthesis. – We chose to prepare the protected aglycone of (−)-bauhinin (**1**) from the oxatrinorbornenone **2**. This *Vogel*'s 'naked sugar' is easily obtained enantiomerically pure [4] and could be used for the syntheses of the aglycones of several other cyanoglucosides. The powerful synthetic potentialities of **2** have already been demonstrated during the syntheses of many biologically active substances [5].



1 (-)-bauhinin

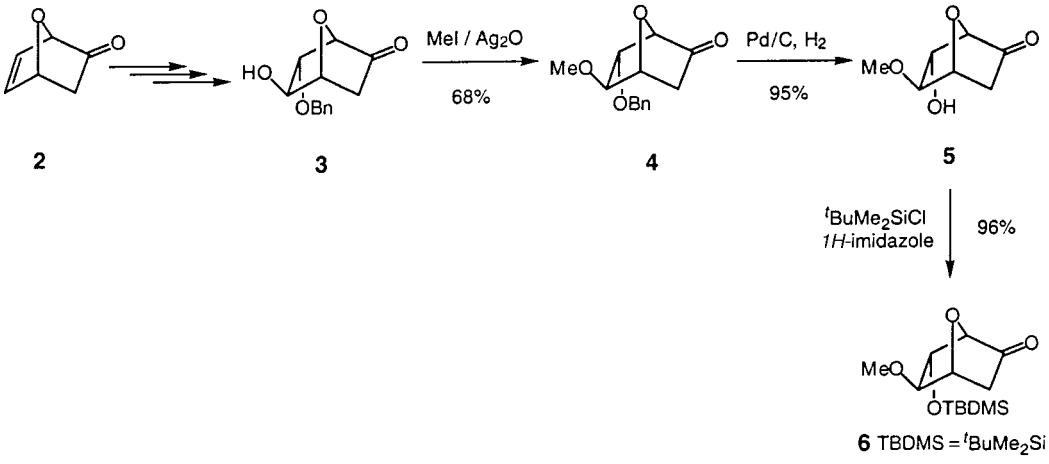


simmondsin

The partially protected dihydroxy ketone **3** (obtained [6] in 3 steps and 66% total yield from **2**) possesses the required configuration. The MeO group present at C(4) of (−)-bauhinin was easily introduced (→ **4**; see *Scheme 1*). Anticipating that the benzyl protecting group would be very difficult to remove towards the end of the synthesis in the presence of an α,β and γ,δ diunsaturated nitrile, we replaced it with a silyl group (→ **5** → **6**). This protecting group was chosen because of its stability both under basic conditions (opening of the oxa bridge, *Wittig-Horner* reaction) and under the weakly acidic conditions of the glycosidation, whereas its cleavage remains possible under conditions innocuous to the glycosidic bond.

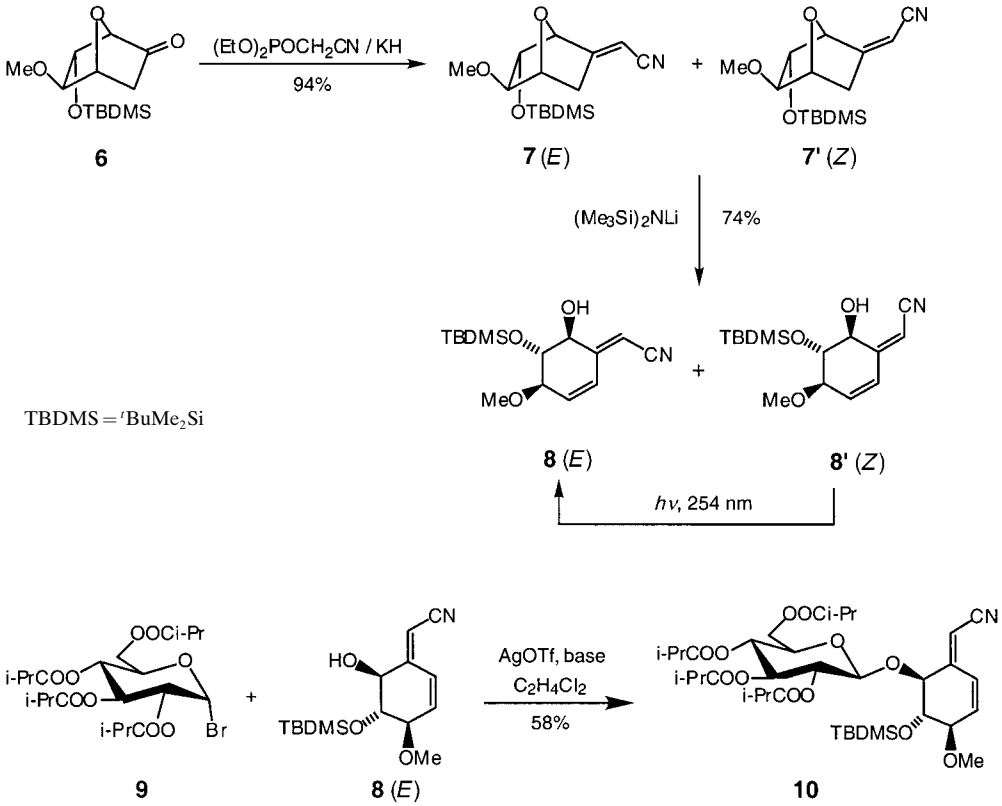
In preliminary experiments, the opening of the oxa bridge of ketone **6** was found to yield a complex mixture [7]. Therefore, we decided to introduce first the cyanomethylene group by a *Wittig-Horner* reaction (see *Scheme 2*). The opening of the oxa bridge of the thus-obtained nitriles **7**/**7′** could be achieved in good yield, but this reaction was very sensitive to the experimental conditions (solvent, base, temperature, *etc.*), and $(Me_3Si)_2NLi$ in THF afforded the best results. A *ca.* 1:1 mixture of **8** (*E*) and **8′** (*Z*) was obtained, irrespectively of the configuration of the C=C bond in the starting material. Therefore, the unseparated *Wittig-Horner* product **7**/**7′** 7:3 was used without separation to yield 38% of **8** (*E*) and 36% of **8′** (*Z*). The configuration of the C=C bond of **8′** (*Z*) corresponds to that of natural (−)-bauhinin; however, isomer **8′** is considerably less stable (*vs.* light, temperature, *etc.*) than the (*E*)-isomer **8**, and its glycosidation afforded only a very low yield of the desired β-D-glucoside (*ca.* 7%). Therefore, we decided to carry out the synthesis with the (*E*)-isomer **8**, which subsequently would be photoisomerized [8]. Consequently, the (*Z*)-isomer **8′** had to be isomerized into the (*E*)-isomer **8** by irradiation with an Hg lamp. To keep degradation to a minimum and thus to achieve maximal recovery, irradiation was stopped well before the stationary state between the two isomers was reached[1]): in a typical single

Scheme 1



[1]) Isomerization experiments starting from both pure (*E*)- and (*Z*)-isomers **8** and **8′**, respectively, turned out to give identical results: if degradation is to be kept under 10%, irradiation should be stopped in both cases once a 2:1 mixture of starting material/other isomer is obtained.

Scheme 2



run, 27% of **8** (*E*) were obtained and 60% of **8′** (*Z*) recovered. Five successive irradiations allowed us to transform the (*Z*)-isomer **8′** into the (*E*)-isomer **8** with a 64% yield (see *Exper. Part*). The global yield of **8** (*E*) from **7**/**7′** was thereby increased from 38% to 61%. Then β-D-glucoside **10** was obtained by a modified *Koenigs-Knorr* reaction in very good yield compared to literature precedents[2]).

Hydroxy nitrile **11** was derived from the silyloxy derivative **10** on treatment with aqueous HF solution (*Scheme 3*). Under these conditions, no cleavage of the glycosidic bond or of the ester moieties could be observed; it should be noted, however, that when aqueous HF solution was replaced with $Bu_4NF \cdot 3\ H_2O$, the ester groups were partially hydrolyzed. Irradiation of **11** with a Hg lamp afforded a mixture of the (*E*)- and (*Z*)-isomers **11** and **12**, respectively. To keep degradation to a minimum and thus achieve maximal recovery, irradiation was stopped well before the stationary state between the two isomers was reached[3]): in a typical single run, 23% of **12** was obtained and 71% of

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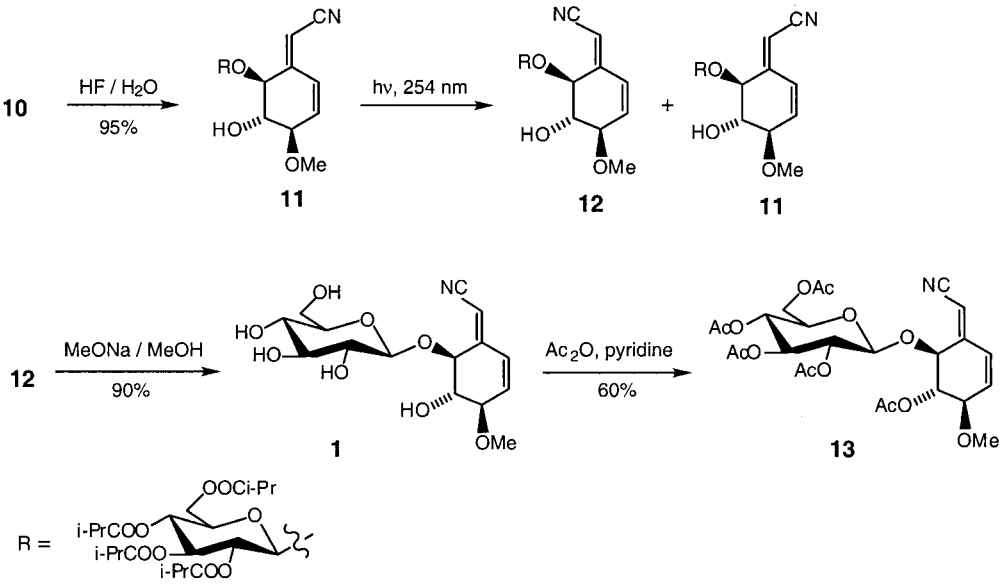
[2]) For a discussion of other glycosidation attempts of this aglycone, see the preceding paper [9].

[3]) As for the **8**/**8′** isomers, irradiation experiments starting from both pure (*E*)- and (*Z*)-isomers **11** and **12**, respectively, were found to give identical results: if degradation is to be kept under 8%, irradiation should be stopped in both cases once a 2.5 : 1 mixture of starting material/other isomer is obtained.

Scheme 3



11 recovered. Successive experiments allowed us to obtain 71% of **12** after 7 runs (see *Exper. Part*). Basic hydrolysis of tetraester **12** yielded (−)-bauhinin (**1**), which was acetylated to **13** for characterization purposes. The data of **1** and **13** were identical with those reported [1] for the natural compound.

Conclusion. – The first total synthesis of a cyanoglucoside, (−)-bauhinin, was achieved in 12 steps and with 8% overall yield. The experimental conditions of the key reaction, the glycosidation, were optimized to afford a good yield of the desired β-D-glucoside, while remaining compatible with the presence of a silyl-ether moiety.

We hope that our methodologies for the glycosidation and for the preparation of these cyclitol-derived aglycones will be useful examples for the synthesis of other β-D-glucosides.

The senior author began to work on this subject at the University of Lausanne in the laboratory and under the scientific guidance of Prof. *Pierre Vogel*, who deserves, therefore, very special thanks. We would like to thank also the former members of *P. Vogel*'s group (especially Dr. *E. Vieira*, now in Basle) who performed considerable work on similar aglycones (*Wittig-Horner* reaction, opening of the oxa bridge, *etc.*) and, finally, *D. Reingpach* who, as an undergraduate student in Mulhouse, worked with enthusiasm and dedication on the synthesis of this aglycone. We are grateful also to the *Centre National de la Recherche Scientifique* (UPRES-A Q7015), for financial support, and to Dr. *D. Le Nouen* and Dr. *S. Bourg* for the recording of many NMR spectra.

Experimental Part

General. See [9]. Moreover, solvents were freshly distilled, dried, and kept under Ar over 4 Å molecular sieves or over Na wire [10].

*(−)-(1*R,*4*R,*5*R,*6*S*)-6*-endo-*(Benzyloxy)-5*-exo-*methoxy-7-oxabicyclo[2.2.1]heptan-2-one* (**4**). Silver oxide (7.55 g, 32.6 mmol) was added under stirring to a soln. of **3** (7.64 g, 32.6 mmol) and MeI (15 ml, 0.24 mol) in anh.

MeCN (8 ml), protected from light. The mixture was stirred for 4 h at 55° and then evaporated. The resulting oil was purified by CC (silica gel, AcOEt/petroleum ether 2:8): **4** (5.50 g, 68%). Colorless oil. $[\alpha]_D^{25} = -40.5$ ($c = 10$, $CHCl_3$). IR (CCl_4): 2933, 2898, 1774, 1497, 1455, 1406, 1372, 1271, 1202, 1134, 1111, 1025, 947, 895, 806, 793, 753, 697. ^{1}H-NMR ($CDCl_3$, 250 MHz): 2.10 (*d*, $^2J = 17.7$, H_{endo}–C(3)); 2.52 (*ddd*, $^2J = 17.7$, $^3J = 6.7$, $^4J = 1.3$, H_{exo}–C(3)); 3.36 (*s*, MeO); 3.59 (*d*, $^3J = 0.8$, H–C(5)); 3.99 (br. *d*, $^3J = 5.4$, H–C(6)); 4.45 (br. *d*, $^3J = 5.4$, H–C(1)); 4.56 (*AB*, $^2J = 11.3$, $\nu_o\delta = 37.6$, PhCH_2); 4.78 (br. *d*, $^3J = 6.7$, H–C(4)); 7.3–7.4 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): 39.00 (C(3)); 56.73 (MeO); 72.50 (Ph*C*H$_2$); 79.47 (C(4)); 80.43 (C(1)); 81.92 (C(6)); 87.45 (C(5)); 128.07 (arom. C); 128.10 (arom. C); 128.46 (arom. C); 136.67 (arom. C); 207.41 (C(2)). Anal. calc. for $C_{14}H_{16}O_4$ (248.27): C 67.72, H 6.49; found: C 67.64, H 6.46.

*(+)-(1*R*,4*R*,5*S*,6*S*)-6*-endo-*Hydroxy-5*-exo-*methoxy-7-oxabicyclo[2.2.1]heptan-2-one* (**5**). To a soln. of **4** (5.5 g, 22.1 mmol) in AcOEt, 10% Pd/C (200 mg) was added. The mixture was stirred for 15 h under H_2 at 20°. After filtration over *Celite*® and washing of the *Celite*® with AcOEt, the combined filtrates were evaporated. The resulting oil was purified by CC (silica gel, AcOEt/petroleum ether 1:1): **5** (3.33 g, 95%). Colorless oil. $[\alpha]_D^{25} = +11.2$ ($c = 10.5$, $CHCl_3$). IR (CCl_4): 3613, 3493, 3014, 2992, 2933, 2826, 1774, 1588, 1565, 1467, 1406, 1386, 1216, 1201, 1108, 1074, 1023, 981, 944, 806, 796, 764. ^{1}H-NMR ($CDCl_3$, 250 MHz): 2.11 (*d*, $^2J = 17.8$, H_{endo}–C(3)); 2.54 (*ddd*, $^2J = 17.8$, $^3J = 6.6$, $^4J = 1.2$, H_{exo}–C(3)); 3.44 (*s*, MeO); 3.54 (*d*, $^3J = 0.7$, H–C(5)); 4.28 (*ddd*, $^3J = 6.5$, 0.7, $^4J = 1.2$, H–C(6)); 4.30 (br. *d*, $^3J = 6.6$, H–C(4)); 4.79 (br. *d*, $^3J = 6.5$, H–C(1)). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): 39.22 (C(3)); 56.59 (MeO); 75.30 (C(1)); 79.68 (C(4)); 88.48 (C(6)); 88.84 (C(5)); 209.59 (C(2)). Anal. calc. for $C_7H_{10}O_4$ (158.15): C 53.16, H 6.37; found: C 52.86, H 6.40.

*(−)-(1*R*,4*R*,5*R*,6*S*)-6*-endo-*{[(*tert-*Butyl)dimethylsilyl]oxy}-5*-exo-*methoxy-7-oxabicyclo[2.2.1]heptan-2-one* (**6**). A soln. of **5** (2.8 g, 17.7 mmol), ^{t}BuMe$_2$SiCl (3.32 g, 22 mmol) and ^1H-imidazole (1.84 g, 27 mmol) in DMF was stirred at 20° for 1 h. AcOEt (150 ml) and sat. aq. $NaHCO_3$ soln. (50 ml) were added. The org. phase was dried ($MgSO_4$) and evaporated and the resulting oil purified by CC (silica gel, AcOEt/petroleum ether 5:95): **6** (4.63 g, 96%). Colorless oil. $[\alpha]_D^{25} = -13.5$ ($c = 10$, $CHCl_3$). IR (CCl_4): 2931, 2897, 2859, 1776, 1463, 1406, 1390, 1362, 1252, 1200, 1135, 1110, 1023, 938, 856, 840, 753, 672. ^{1}H-NMR ($CDCl_3$, 250 MHz): 0.10, 0.11 (2*s*, Me_2Si); 0.86 (*s*, ^{t}BuSi); 2.03 (*d*, $^2J = 17.6$, H_{endo}–C(3)); 2.47 (*ddd*, $^2J = 17.6$, $^3J = 6.7$, $^4J = 1.2$, H_{exo}–C(3)); 3.41 (*s*, MeO); 3.44 (*d*, $^3J = 0.6$, H–C(5)); 4.16 (br. *d*, $^3J = 5.6$, H–C(6)); 4.20 (br. *d*, $^3J = 5.6$, H–C(1)); 4.75 (*ddd*, $^3J = 6.7$, $^4J = 1.2$; 0.6, H–C(4)). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): −5.21, −4.99 (Me_2Si); 17.74 (Me_3*C*Si); 25.48 (*Me*$_3$CSi); 38.72 (C(3)); 56.95 (MeO); 76.28 (C(6)); 79.34 (C(4)); 81.37 (C(1)); 89.94 (C(5)); 206.90 (C(2)). Anal. calc. for $C_{13}H_{24}O_4Si$ (272.41): C 57.31, H 8.87; found: C 57.27, H 8.91.

*(−)-(2*E*)-{(1*S*,4*R*,5*R*,6*R*)-6*-endo-*{[(*tert-*Butyl)dimethylsilyl]oxy}-5*-exo-*methoxy-7-oxabicyclo[2.2.1]hept-2-yliden}acetonitrile* (**7**) *and (+)-(2*Z*)-{(1*S*,4*R*,5*R*,6*R*)-6*-endo-*{[(*tert-*Butyl)dimethylsilyl]oxy}-5*-exo-*methoxy-7-oxabicyclo[2.2.1]hept-2-yliden}acetonitrile* (**7′**). Anh. THF was added to KH (1.34 g, 33.4 mmol) prepared by 3 successive washings with petroleum ether of a 20% KH dispersion in oil. Under a stream of Ar, the suspension was cooled to 0°, and $(EtO)_2P(O)CH_2CN$ (5.3 ml, 33.69 mmol) was added dropwise under stirring. At the end of H_2 evolution (*ca.* 10 min), a soln. of **6** (4.6 g, 16.88 mmol) in THF (10 ml) was added dropwise. The cooling bath was removed and the mixture left for 15 min at 20° under stirring. The reaction was quenched with sat. aq. NaCl soln. and the mixture extracted twice with AcOEt (100 ml). The org. phase was dried ($MgSO_4$) and evaporated. The resulting oil was purified by CC (silica gel, AcOEt/petroleum ether 5:95) to yield first **7** (3.24 g, 65%) and then **7′** (1.45 g, 29%), both as colorless oils.

*Data of (*E*)-Isomer* **7**: $[\alpha]_D^{25} = -87.5$ ($c = 10$, DMSO). IR (CCl_4): 2931, 2859, 2223, 1773, 1664, 1463, 1378, 1252, 1202, 1137, 1111, 1022, 940, 859, 839, 759, 734, 673, 611. ^{1}H-NMR ($CDCl_3$, 250 MHz): 0.06, 0.08 (2*s*, Me_2Si); 0.84 (*s*, ^{t}BuSi); 2.39 (*dd*, $^2J = 17.6$, $^4J = 2.1$, H_{endo}–C(3)); 2.62 (*ddd*, $^2J = 17.6$, $^3J = 6.0$, $^4J = 2.9$, H_{exo}–C(3)); 3.19 (*d*, $^3J = 1.5$, H–C(5)); 3.26 (*s*, MeO); 3.99 (*dd*, $^3J = 5.4$, 1.5, H–C(6)); 4.63 (br. *d*, $^3J = 6.0$, H–C(4)); 4.77 (br. *d*, $^3J = 5.4$, H–C(1)); 5.66 (*m*, H–C(7)). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): −5.03, −4.87 (Me_2Si); 17.77 (Me_3*C*Si); 25.57 (*Me*$_3$CSi); 35.13 (C(3)); 57.14 (MeO); 78.52 (C(6)); 80.00 (C(4)); 82.11 (C(1)); 89.58 (C(5)); 92.95 (C(7)); 116.05 (CN); 163.22 (C(2)). Anal. calc. for $C_{15}H_{25}NO_3Si$ (295.45): C 60.97, H 8.52, N 4.74; found: C 61.06, H 8.52, N 4.60.

*Data of (*Z*)-Isomer* **7′**: $[\alpha]_D^{25} = +95.5$ ($c = 10$, $CHCl_3$). IR (CCl_4): 2930, 2896, 2859, 2224, 1666, 1463, 1379, 1253, 1201, 1132, 1111, 1020, 987, 941, 918, 858, 840, 674, 622. ^{1}H-NMR ($CDCl_3$, 250 MHz): 0.11, 0.14 (2*s*, Me_2Si); 0.88 (*s*, ^{t}BuSi); 2.28 (*dd*, $^2J = 17.3$, $^4J = 1.3$, H_{endo}–C(3)); 2.64 (*ddd*, $^2J = 17.3$, $^3J = 6.1$, $^4J = 2.3$, H_{exo}–C(3)); 3.14 (*d*, $^3J = 1.4$, H–C(5)); 3.37 (*s*, MeO); 4.16 (*ddd*, $^3J = 5.4$; 1.4, $^4J = 1.2$, H–C(6)); 4.60 (*dd*, $^3J = 6.1$, $^4J = 1.2$, H–C(4)); 4.95 (br. *d*, $^3J = 5.4$, H–C(1)); 5.35 (*dd*, $^4J = 2.3$, 1.3, H–C(7)). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): −5.23, −5.11 (Me_2Si); 17.92 (Me_3*C*Si); 25.68 (*Me*$_3$CSi); 35.14 (C(3)); 57.39 (MeO); 78.71 (C(6)); 79.82 (C(4)); 81.40 (C(1)); 89.42 (C(5)); 93.10 (C(7)); 116.24 (CN); 162.91 (C(2)). Anal. calc. for $C_{15}H_{25}NO_3Si$ (295.45): C 60.97, H 8.52, N 4.74; found: C 61.05, H 8.56, N 5.13.

*(+)-(1*E*)-{(4*R*,5*R*,6*S*)-5-[[(*tert*-Butyl)dimethylsilyl]oxy}-6-hydroxy-4-methoxycyclohex-2-en-1-yliden}acetonitrile* (**8**) *and (−)-(1*Z*)-{(4*R*,5*R*,6*S*)-5-[[(*tert*-Butyl)dimethylsilyl]oxy}-6-hydroxy-4-methoxycylohex-2-en-1-yliden}acetonitrile* (**8′**). 1. *Opening of the Oxa Bridge.* At 0°, 1M $(Me_3Si)_2NLi$ in THF (23.5 ml, 1.5 equiv.) was added to a stirred soln. of **7**/**7′** (4.64 g, 15.7 mmol) in THF (10 ml) at 0° under Ar. The mixture was stirred for 20 min at 0°, and then sat. aq. NH_4Cl soln. (30 ml) and aq. 1M HCl (25 ml) were added. The residue was extracted with AcOEt (200 ml) and the org. phase washed with sat. aq. $NaHCO_3$ soln. (50 ml), dried ($MgSO_4$), and evaporated. The resulting oil was purified by CC (silica gel, AcOEt/petroleum ether 1:9): **8** (1.76 g, 38%) and **8′** (1.67 g, 36%).

*Data of (*E*)-Isomer* **8**: White crystals. M.p. 86–87°. $[\alpha]_D^{25} = +17.7$ ($c = 11$, $CHCl_3$). IR (KBr): 3433, 2930, 2858, 2213, 1629, 1585, 1472, 1419, 1386, 1249, 1091, 1066, 998, 942, 903, 836, 780, 735. ^{1}H-NMR ($CDCl_3$, 250 MHz): 0.12, 0.14 (2*s*, Me_2Si); 0.93 (*s*, ^{t}BuSi); 2.74 (*d*, $^3J = 2.2$, OH); 3.43 (*s*, MeO); 3.57 (*dd*, $^3J = 10$, 7.7, H–C(5)); 3.79 (br. *d*, $^3J = 7.7$, H–C(4)); 4.18 (br. *d*, $^3J = 10$, H–C(6)); 5.57 (*m*, H–C(7)); 6.18 (br. *d*, $^3J = 10.1$, H–C(2)); 6.65 (*dd*, $^3J = 10.1$, 1.9, H–C(3)). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): −4.94, −4.38 (Me_2Si); 18.16 (Me_3CSi); 25.87 (*Me*$_3$CSi); 57.06 (MeO); 72.33 (C(6)); 76.52 (C(4)); 81.65 (C(5)); 92.97 (C(7)); 116.55 (CN); 124.16 (C(3)); 134.76 (C(2)); 156.29 (C(1)). Anal. calc. for $C_{15}H_{25}NO_3Si$ (295.45): C 60.97, H 8.52, N 4.74; found: C 61.29, H 8.65, N 4.84.

*Data of (*Z*)-Isomer* **8′**: Colorless oil. $[\alpha]_D^{25} = -103$ ($c = 11$, $CHCl_3$). IR (CCl_4): 3426, 2929, 2902, 2856, 2222, 1621, 1592, 1466, 1399, 1349, 1252, 1150, 1096, 1061, 948, 913, 835, 783. ^{1}H-NMR ($CDCl_3$, 250 MHz): 0.13, 0.14 (2*s*, Me_2Si); 0.89 (*s*, ^{t}BuSi); 3.22 (*d*, $^3J = 5.5$, OH); 3.44 (*s*, MeO); 3.73 (*dd*, $^3J = 5.9$, 2.5, H–C(4)); 3.86 (*dd*, $^3J = 7.5$, 5.9, H–C(5)); 4.46 (*ddd*, $^3J = 7.5$, 5.5, $^4J = 1.7$, H–C(6)); 5.3 (br. *d*, $^4J = 1.7$, H–C(7)); 6.13 (*dd*, $^3J = 10.1$, 2.5, H–C(3)); 6.20 (*d*, $^3J = 10.1$, H–C(2)). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): −4.97, −4.72 (Me_2Si); 17.94 (Me_3CSi); 25.65 (*Me*$_3$CSi); 57.18 (MeO); 71.39 (C(6)); 73.39 (C(4)); 79.47 (C(5)); 96.76 (C(7)); 116.64 (CN); 127.25 (C(3)); 133.16 (C(2)); 155.79 (C(1)). Anal. calc. for $C_{15}H_{25}NO_3Si$ (295.45): C 60.97, H 8.52, N 4.74; found: C 60.91, H 8.57, N 4.81.

2. *Photoisomerization of* **8′** *into* **8**: In a disk-shaped (diameter *ca.* 63 mm, thickness 11 mm) quartz flask, a soln. of **8′** (*Z*) (150 mg, 0.507 mmol) in dioxane (30 ml) was irradiated with a *Philips-HPK-125* medium-pressure Hg lamp (HPLC monitoring: *Zorbax-Sil*, 250 × 4.6 mm; 2.28 ml/min, AcOEt/hexane 15:85; t_R 4.5 (**8**) and 11 min (**8′**); detection at 254 nm, peak area ratio of 1.3:1 for **8**/**8′** 1:1). After 10.5 min, **8**/**8′** 1:2.2 was obtained. The irradiation was stopped, the solvent evaporated, and the resulting oil purified by CC (silica gel, AcOEt/petroleum ether 1:9): first 41 mg (27%) of **8** as a white solid and then 90 mg (60%) of **8′** as an oil. This experiment was repeated 4 times, each time with the recovered (*Z*)-isomer **8′** from the previous run. Thus, a total of 96 mg (64%) of **8** (*E*) and 15 mg (10%) of **8′** (*Z*) were isolated.

*(−)-(1*E*)-{(4*R*,5*S*,6*S*)-5-[[(*tert*-Butyl)dimethylsilyl]oxy}-4-methoxy-6-[(2,3,4,6-tetra-*O*-isobutyryl-β-D-glucopyranosyl)oxy]cyclohex-2-en-1-yliden}acetonitrile* (**10**). To a stirred suspension of AgOTf (174 mg, 0.68 mmol) in 1,2-dichloroethane (2 ml) protected from light, activated 4-Å molecular sieves (500 mg, powder), 2,6-di(*tert*-butyl)-4-methylpyridine (94 mg, 0.46 mmol), aglycone **8** (100 mg, 0.34 mmol), and glucosyl bromide **9** (354 mg, 0.68 mmol) were successively added at 20° under a stream of N_2. Then, a soln. of additional 2,6-di(*tert*-butyl)-4-methylpyridine (44 mg, 0.214 mmol) in 1,2-dichloroethane (2.4 ml) was added at the rate of 80 µl/min within 30 min at 20°. The mixture was left for 14 h under stirring. After filtration over *Celite*® and washing of the *Celite*® with CH_2Cl_2 (10 ml), the combined filtrate was evaporated and the resulting oil purified by CC (silica gel, AcOEt/petroleum ether 1:9). The white solid obtained was recrystallized from MeOH/H_2O: 145 mg (58%) of **10**. M.p. 94–95°. $[\alpha]_D^{25} = -11.1$ ($c = 1.1$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 400 MHz): 0.12, 0.13 (2*s*, Me_2Si); 0.9 (*s*, ^{t}BuSi); 1.04–1.22 (*m*, 4 *Me*$_2$CH); 2.38–2.6 (*m*, 4 Me$_2$*CH*); 3.38 (*s*, MeO); 3.66 (*ddd*, $^3J = 10$, 4.8, 2.4, H–C(5′)); 3.75 (*m*, H–C(5), H–C(6)); 4.10 (*dd*, $^2J = 12.4$, $^3J = 4.8$, H–C(6′)); 4.20 (*dd*, $^2J = 12.4$, $^3J = 2.4$, H–C(6′)); 4.53 (*dd*, $^3J = 8.4$, 1.6, H–C(4)); 5.10 ('*dd*', $^3J = 9$, 7.6, H–C(2′)); 5.13 ('*dd*', $^3J = 10$, 9.6, H–C(4′)); 5.15 (*d*, $^3J = 7.6$, H–C(1′)); 5.24 ('*dd*', $^3J = 9.6$, 9, H–C(3′)); 5.58 (br. *s*, H–C(7)); 6.17 (br. *d*, $^3J = 10$, H–C(2)); 6.66 (*dd*, $^3J = 10$, 1.6, H–C(3)). ^{13}C-NMR ($CDCl_3$; 100.577 MHz): −4.15, −4.12 (Me_2Si); 18.30, 18.47, 18.71, 18.75, 18.80, 18.98, 19.25 (4 *Me*$_2$CH, Me_3CSi); 26.14 (*Me*$_3$CSi); 33.76, 33.80, 33.86 (4 Me$_2$*C*H); 56.56 (MeO); 61.33 (C(6′)); 68.16 (C(3′)); 71.47 (C(2′)); 72.11 (C(4′)); 72.37 (C(5′)); 74.65 (C(4)); 76.51 (C(5)); 82.28 (C(6)); 95.3 (C(7)); 99.15 (C(1′)); 116.69 (CN); 124.77 (C(3)); 133 (C(2)); 155.56 (C(1)); 175.29, 175.49, 175.88, 176.54 (4 CO). Anal. calc. for $C_{37}H_{59}NO_{12}Si$ (737.95): C 60.21, H 8.05, N 1.89; found: C 60.41, H 8.04, N 1.69.

*(+)-(1*E*)-{(4*R*,5*S*,6*S*)-5-Hydroxy-4-methoxy-6-[(2,3,4,6-tetra-*O*-isobutyryl-β-D-glucopyranosyl)oxy]cyclohex-2-en-1-yliden}acetonitrile* (**11**). At 20°, 40% aq. HF soln. (1.4 ml) was added to a soln. of **10** (400 mg, 0.54 mmol) in MeCN (20 ml). After stirring for 4 h at 20°, sat. aq. $NaHCO_3$ soln. (50 ml) was added, and the mixture was extracted with AcOEt (100 ml, 2 ×). The org. phase was washed with sat. aq. NaCl soln. (40 ml), dried ($MgSO_4$), and evaporated and the resulting oil purified by CC (silica gel, AcOEt/petroleum ether 1:1).

The white solid obtained was recrystallized from MeOH/H_2O: 320 mg (95%) of **11**. M.p. 146–147°. $[\alpha]_D^{25} = +3.5$ ($c = 1.1$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.03–1.29 (*m*, 4 *Me*$_2$CH); 2.41–2.63 (*m*, 4 Me$_2$C*H*); 2.71 (*d*, $^3J = 1.5$, OH–C(5)); 3.51 (*s*, MeO); 3.69–3.76 (*m*, H–C(5′), H–C(5)); 3.93 (br. *d*, $^3J = 8$, H–C(4)); 4.1–4.16 (*m*, CH_2(6′)); 4.28 (*dd*, $^3J = 10.2$, $^4J = 2$, H–C(6)); 4.98 (*d*, $^3J = 8$, H–C(1′)); 5.10 (‘*dd*’, $^3J = 9.5$, 8, H–C(2′)); 5.13 (*t*, $^3J = 9.5$, H–C(4′)); 5.24 (*t*, $^3J = 9.5$, H–C(3′)); 5.7 (br. *s*, H–C(7)); 6.16 (br. *d*, $^3J = 10.2$, H–C(2)); 6.65 (*dd*, $^3J = 10.2$, $^4J = 2$, H–C(3)). ^{13}C-NMR ($CDCl_3$, 100.577 MHz): 18.76, 18.80, 18.85, 18.91 (4 *Me*$_2$CH); 33.82, 33.84, 33.94 (4 Me$_2$*C*H); 57.59 (MeO); 61.31 (C(6′)); 67.73 (C(4′)); 71.28 (C(2′)); 72.13 (C(5′) or C(5)); 72.24 (C(3′)); 75.23 (C(5) or C(5′)); 78.87 (C(6)); 80.96 (C(4)); 95.93 (C(7)); 101.36 (C(1′)); 116.28 (CN); 124.67 (C(3)); 134.64 (C(2)); 154.01 (C(1)); 175.18, 175.24, 175.98, 176.58 (4 CO). Anal. calc. for $C_{37}H_{59}NO_{12}Si$ (623.96): C 59.69, H 7.27; found: C 59.77, H 7.48.

*(−)-(1*Z*)-[(4*R*,5*S*,6*S*)-5-Hydroxy-4-methoxy-6-[(2,3,4,6-tetra-*O*-isobutyryl-β-*D*-glucopyranosyl)oxy]cyclohex-2-en-1-yliden]acetonitrile* (**12**). As described for **8** and **8′**, **11** (120 mg, 0.19 mmol) was irradiated in dioxane (30 ml) (HPLC monitoring: *Zorbax-ODS*, 250 × 4.6 mm; 0.8 ml/min, MeOH/H_2O 4:1; t_R 7 (**12**) and 15 min (**11**); detection at 254 nm, peak area ratio of 0.84:1 for **12**/**11** 1:1). After 10 min, **11**/**12** 2.4:1 was obtained. The irradiation was stopped, the solvent evaporated, and the resulting oil purified by CC (silica gel, AcOEt/petroleum ether 1:1): first 85 mg (71%) of **11** and then 28 mg (23%) of **12** as white solids. This experiment was repeated 6 times, each time with the recovered (*E*)-isomer **11** from the previous run. Thus, a total of 85 mg (71%) of **12** and 8 mg (5%) of **11** were isolated. **12**: M.p. 126–127°. $[\alpha]_D^{25} = -19.6$ ($c = 0.92$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.05–1.24 (*m*, 4 *Me*$_2$CH); 2.41–2.66 (*m*, 4 Me$_2$C*H*); 3.50 (*s*, MeO); 3.73 (*ddd*, $^3J = 9.5$, 4.4, 2, H–C(5′)); 3.76 (*dd*, $^3J = 10$, 8, H–C(5)); 3.90 (*d*, $^3J = 8$, H–C(4)); 4.11 (*dd*, $^2J = 12.3$, $^3J = 4.4$, H–C(6′)); 4.25 (*dd*, $^2J = 12.3$, $^3J = 2$, H–C(6′)); 4.53 (*dd*, $^3J = 10$, $^4J = 2$, H–C(6)); 5.20 (*d*, $^3J = 7.5$, H–C(1′)); 5.24 (*t*, $^3J = 9.5$, H–C(3′)); 5.28 (br. *s*, H–C(7)); 5.31 (*t*, $^3J = 9.5$, H–C(4′)); 5.37 (‘*dd*’, $^3J = 9.5$, 7.5, H–C(2′)); 6.04 (br. *d*, $^3J = 10.2$, H–C(2)); 6.11 (br. *d*, $^3J = 10.2$, H–C(3)). ^{13}C-NMR ($CDCl_3$, 100.577 MHz): 18.70, 18.78, 18.81, 18.84 (4 *Me*$_2$CH); 33.85, 33.88, 33.90 (4 Me$_2$*C*H); 57.68 (MeO); 61.44 (C(6′)); 67.90 (C(3′)); 70.89 (C(2′)); 72.27 (C(5′)); 72.41 (C(4′)); 75.62 (C(5)); 75.78 (C(6)); 80.95 (C(4)); 97.64 (C(7)); 100.78 (C(1′)); 115.76 (CN); 127.86 (C(3)); 133.56 (C(2)); 152.63 (C(1)); 175.0, 175.05, 176.28, 176.77 (4 CO). Anal. calc. for $C_{37}H_{59}NO_{12}Si$ (623.96): C 59.69, H 7.27, N 2.24; found: C 59.40, H 7.28, N 2.26.

*(−)-(1*Z*)-[(4*R*,5*S*,6*S*)-6-(β-*D*-Glucopyranosyloxy)-5-hydroxy-4-methoxycyclohex-2-en-1-yliden]acetonitrile* (*=(−)-Bauhinin*; **1**). At 0°, 1M MeONa/MeOH (2 ml, 2 mmol) was added to a stirred soln. of **12** (75 mg, 0.12 mmol) in MeOH (4 ml) at 0° under Ar. After 1 h at 0°, sufficient *Amberlite® IRC-50* (*ca.* 0.5 g) was added to bring the pH to neutrality. MeOH (10 ml) was added, the mixture filtered, the filtrate evaporated, and the resulting oil purified by CC (silica gel, MeOH/AcOEt 1:9). For characterization purposes, the white solid obtained (**1**, 37 mg, 90%) was recrystallized in MeOH/Et_2O: 23 mg. M.p. 209–210° ([1]: 213–214° (−)-bauhinin dihydrate). $[\alpha]_D^{25} = -80$ ($c = 1.05$, MeOH). UV (MeOH): 258 (19700) ([1]: 256 (MeOH)). IR (KBr): 3481, 3417, 2921, 2874, 2216, 1629, 1594, 1458, 1406, 1375, 1348, 1218, 1081, 937, 888, 852, 659. ^{1}H-NMR (C_3D_6O, 250 MHz): 3.3, 3.5 (*m*, 4 H); 3.19 (*t*, $^3J = 6.7$, CH_2OH); 3.48 (*s*, MeO); 3.64 (*ddd*, $^2J = 11.1$, $^3J = 6.7$, 2.4, H–C(6′)); 3.81 (*ddd*, $^2J = 11.1$, $^3J = 6.7$, 4.9, H–C(6′)); 3.93 (*m*, H–C(4), H–C(5)); 4.22, 4.5 (2 br. *s*, OH); 4.65 (*dd*, $^3J = 7.6$, $^4J = 1.7$, H–C(6)); 4.8 (*d*, $^3J = 7.2$, H–C(1′)); 4.86 (br. *s*, OH); 5.63 (br. *s*, H–C(7)); 6.18 (*dd*, $^3J = 10$, 2.4, H–C(3)); 6.35 (br. *d*, $^3J = 10$, H–C(2)).

*(−)-(1*Z*)-[(4*R*,5*S*,6*S*)-5-Acetoxy-4-methoxy-6-[(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)oxy]cyclohex-2-en-1-yliden]acetonitrile* (*=(−)-Bauhinin Pentaacetate*; **13**). A soln. of **1** (16 mg, 0.046 mmol) in pyridine (0.5 ml) and Ac_2O (1 ml) was stirred for 2 h at 20°. After evaporation, the mixture was purified directly by CC (silica gel, AcOEt/petroleum ether 1:1): **13** (15.5 mg, 60%). Colorless crystals. M.p. 169–170° ([1]: 168–170°). $[\alpha]_D^{25} = -106.6$ ($c = 0.56$, $CHCl_3$). UV (MeCN): 255 (24500). IR (KBr): 2960, 2937, 2216, 1755, 1630, 1436, 1432, 1369, 1230, 1165, 1052, 946, 908. ^{1}H-NMR ($CDCl_3$, 250 MHz): 1.99, 2.01, 2.04, 2.08, 2.15 (5*s*, MeCO); 3.36 (*s*, MeO); 3.71 (*ddd*, $^3J = 9.8$, 3.8, 2.5, H–C(5′)); 4.02 (*ddd*, $^3J = 6.5$, 2.7, $^4J = 1.8$, H–C(4)); 4.08 (*dd*, $^2J = 12.2$, $^3J = 3.8$, H–C(6′)); 4.38 (*dd*, $^2J = 12.2$, $^3J = 2.5$, H–C(6′)); 4.62 (*dd*, $^3J = 8.8$, $^4J = 1.8$, H–C(6)); 4.84 (*d*, $^3J = 7.5$, H–C(1′)); 5.1 (*m*, H–C(3′), H–C(4′)); 5.28 (*dd*, $^3J = 9.8$, 7.5, H–C(2′)); 5.29 (*dd*, $^3J = 8.8$, 6.5, H–C(5)); 5.36 (br. *s*, H–C(7)); 6.08 (*dd*, $^3J = 10$, 2.7, H–C(3)); 6.22 (*dd*, $^3J = 10$, $^4J = 1.8$, H–C(2)). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): 20.47, 20.62, 20.84, 21.09 (4 *Me*CO); 56.27 (MeO); 61.23 (C(6′)); 68.32 (C(4′)); 70.48 (C(2′)); 71.89 (C(5)); 71.99 (C(5′)); 72.81 (C(3′)); 73.85 (C(6)); 77.23 (C(4)); 98.88 (C(7)); 100.91 (C(1′)); 115.68 (CN); 128.07 (C(3)); 133.84 (C(2)); 151.47 (C(1)); 169.01, 169.23, 169.35, 170.54 (4 Me*C*O). Anal. calc. for $C_{25}H_{31}NO_{13}$ (553.51): C 54.24, H 5.64, N 2.53; found: C 54.34, H 5.72, N 2.40.

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