gave 5.3 mg (58%) of colorless syrup: $[\alpha]^{20}_D$ -90.2 (c 0.27, ethyl acetate); ^{1}H NMR (400 MHz, C_6D_6) δ 4.37 (dd, H-1), 1.94 (ddd, H-2a), 2.27 (ddd, H-2e), 3.96 (ddd, H-3), 5.30 (dd, t, H-4), 3.36 (dq, H-5), 1.35 (d, CH_3-6), 4.08 (dd, H-1'), 1.59 (ddd, H-2a'), 1.68 (ddd, H-2e'), 3.39 (ddd, H-3'), 4.61 (dd ~ t, H-4'), 2.97 (dq, H-5'), 1.04 (d, CH_3-6'), 5.16 (d, H-1''), 4.03 (d, H-2''), 5.26 (d, H-4''), 3.85 (dq, H-5''), 1.21 (d, CH_3-6''), 1.44 (s, CH_3-3''), 4.51 and 4.90 (AB pattern, J = 11.9, PhCH_2), 1.60 and 1.71 (each s, each 3 H, OAc), 7.04-7.39 and 8.20-8.28 (m, 10 H, aryl-H), $J_{1,2a}$ = 9.6, $J_{1,2e}$ = 1.9, $J_{2a,2e}$ = 12.5, $J_{2a,3}$ = 12.0, $J_{2e,3}$ = 5.3, $J_{3,4}$ = 9.2, $J_{4,5}$ = 9.6, $J_{5,6}$ = 6.2, $J_{1',2a'}$ = 9.7, $J_{1'2e'}$ = 1.9, $J_{2a',2e'}$ = 12.3, $J_{2a',3'}$ = 11.8, $J_{2e',3'}$ = 5.3, $J_{3',4'}$ = 9.3, $J_{4',5'}$ = 9.5, $J_{5',6'}$ = 6.2, $J_{1'',2''}$ = 1.9, $J_{4'',5''}$ = 9.1, $J_{5'',6''}$ = 6.3 Hz.

Anal. Calcd. for $C_{37}H_{47}IO_{13}$ (826.7): C, 53.76; H, 5.73. Found: C, 53.46; H, 5.98.

Benzyl 3-*O*-[3-*O*-(4-*O*-Acetyl-2,6-dideoxy-3-*C*-methyl-α-L-*arabino*-hexopyranosyl)-4-*O*-acetyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl]-4-*O*-benzoyl-2,6-dideoxy-β-D-*arabino*-hexopyranoside (28). Compound **27** (3.1 mg, 3.7 μmol) in ethyl acetate (2 mL) was hydrogenated with 10% palladium/charcoal (10 mg) for 3 h at room temperature in the presence of triethylamine (1 drop). After the mixture was filtered over Celite and silica gel, evaporation led to 2.5 mg (95%) of colorless syrup: $[\alpha]^{20}_D$ -16.6 (c 0.25, ethyl acetate); ^{1}H NMR (400 MHz, C_6D_6) δ 4.36 (dd, H-1), 1.91 (ddd, H-2a), 2.25 (ddd, H-2e), 3.96 (ddd, H-3), 5.28 (dd ~ t, H-4), 3.36 (dq, H-5, 1.34 (d, CH_3-6), 4.11 (dd, H-1'), 1.77 (ddd, H-2e'), 3.56 (ddd, H-3'), 4.70 (dd ~ t, H-4'), 3.02 (dq, H-5'), 1.06 (d, CH_3-6'), 4.49 (dd, H-1''), 4.80 (d, H-4''), 3.82 (dq, H-5''), 1.23 (d, CH_3-6''), 1.37 (s, CH_3-3''), 4.50 and 4.89 (AB pattern, J = 11.8, PhCH_2), 1.68 and 1.78 (each s, each 3 H, OAc), 7.05-7.38 and 8.20-8.25 (m, 10 H, aryl-H), $J_{1,2a}$ = 9.7, $J_{1,2e}$ = 1.9, $J_{2a,2e}$ = 12.4, $J_{2a,3}$ = 12.2, $J_{2e,3}$ = 5.1, $J_{3,4}$ = 9.5, $J_{4,5}$ = 9.6, $J_{5,6}$ = 6.2, $J_{1',2a'}$ = 9.6, $J_{1',2e'}$ = 1.9, $J_{2a',2e'}$ = 12.4, $J_{2a',3'}$ = 11.6, $J_{2e',3'}$ = 5.1, $J_{3',4'}$ = 9.4, $J_{4',5'}$ = 9.5, $J_{5',6'}$ = 6.2, $J_{1'',2a''}$ = 3.9, $J_{1'',2e''}$ = 0.7, $J_{4'',5''}$ = 9.6, $J_{5'',6''}$ = 6.2 Hz.

Anal. Calcd for $C_{37}H_{48}O_{13}$ (700.8): C, 63.42; H, 6.90. Found: C, 63.89; H, 6.51.

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One-Pot Conversion of 6-Hydroxy-Δ^7-iridoid Glucosides into *cis*-2-Oxabicyclo[3.3.0]oct-7-enes and Transformation into Corey's Lactone Analogue

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A simple conversion of some iridoid glucosides into *cis*-2-oxabicyclo[3.3.0]oct-7-enes by a three-step "one-pot" sequence is described. Such important prostanoid intermediates have been obtained through intramolecular acid-catalyzed cyclization of the corresponding cyclopentenepolyols. An analogue (**17**) of Corey's lactone has been prepared by PCC oxidation of 2-oxabicyclo[3.3.0]oct-7-ene (**16**) together with other important derivatives.

Various routes have been devised to prepare optically active prostanoid intermediates, starting from naturally occurring materials.[1] In particular several syntheses have appeared using iridoid glucosides including aucubin (**1**).[2]

In this report we describe a one-pot, three-step transformation of 6-hydroxy-Δ^7-iridoid glucosides into *cis*-2-oxabicyclo[3.3.0]oct-7-enes,[3] which implies the easy inversion of the C-O linkage at C-6 from a β to an α configuration. Such bicyclic ethers are considered particularly attractive intermediates[4] for prostaglandin synthesis.[5] Along these lines we carried out the oxidation of the tetrahydrofuran ring to the corresponding lactone and obtained an analogue of Corey's lactone.

Results and Discussion

In previous communications on the reactivity of iridoid aglycons we described the acid-catalyzed rearrangement of aucubigenin (**2**)[6] as well as the $NaBH_4$ reductions in aqueous solution of **2**[7] and its 6-deoxy and 6,10-dideoxy

(1) Stork, G.; Raucher, S. *J. Am. Chem. Soc.* **1976**, *98*, 1583. Paul, K. G.; Johnson, F.; Favara, D. *J. Am. Chem. Soc.* **1976**, *98*, 1285. Johnson, F.; Paul, K. G.; Favara, D.; Ciabotti, R.; Guzza, U. *J. Am. Chem. Soc.* **1982**, *104*, 2190.

(2) (a) Naruto, M.; Ohno, K.; Naruse, N. *Chem. Lett.* **1978**, 1419. Naruto, M.; Ohno, K.; Naruse, N.; Takeuchi, H. *Tetrahedron Lett.* **1979**, 251. Naruto, M.; Ohno, K.; Naruse, N.; Takeuchi, H. *Chem. Lett.* **1978**, 1423. Ohno, K.; Naruto, M. *Ibid.* **1979**, 1015; **1980**, 175. (b) Weinges, K.; Eltz, H.; Tran Viet, D. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 628. (c) Berkowitz, W. F.; Sasson, I.; Sampathkumar, P. S.; Hrabie, J.; Choudhry, S.; Pierce, D. *Tetrahedron Lett.* **1979**, 1641. Berkowitz, W. F.; Choudhry, S. C. *Ibid.* **1981**, 1075. Berkowitz, W. F.; Choudhry, S. C.; Hrabie, J. A. *J. Org. Chem.* **1982**, *47*, 824. (d) Tixidre, A.; Rolland, Y.; Garnier, J.; Poisson, J. *Heterocycles* **1982**, *19*, 253. (e) Bonini, C.; Di Fabio, R. *Tetrahedron Lett.* **1982**, *23*, 5199.

(3) Bonini, C.; Di Fabio, R.; Iavarone, C.; Trogolo, C. Italian Pat. Appl. 1981, 49042 A/81.

(4) Robinson, G. H. Ger. Offen 2 633 559, Brit. Pat. Appl. 75/31, 927, *Chem. Abstr.* **1977**, *86*, 170942b. Newton, R. F. Eur. Pat. Appl. 5, 308; *Chem. Abstr.* **1980**, *93*, 25986j. Eggler, J. F.; Bindra, J. S.; Hess, H. J. E. S. African Pat. 76 06 204, *Chem. Abstr.* **1978**, *89*, 108449u. Yankee, E. W. Ger. Offen. 2 719 975; *Chem. Abstr.* **1978**, *88*, 62048x. Kienzle, F.; Perry, R. U.S. Pat. 4 004 005; *Chem. Abstr.* **1978**, *88*, 74110z.

(5) Specifically such intermediates can be utilized for elaboration to 11-deoxy-11-methyl or 11-deoxy-11-hydroxymethyl PG, derived from natural prostaglandins: in addition 11-deoxy-11-(hydroxymethyl)prostaglandin intermediates have been already transformed into the natural 11-hydroxy PG (see ref 2a).

(6) Bianco, A.; Guiso, M.; Iavarone, C.; Passacantilli, P.; Trogolo, C. *Tetrahedron* **1977**, *33*, 847; **1984**, *40*, 1191.

(7) Bianco, A.; Guiso, M.; Iavarone, C.; Passacantilli, P.; Trogolo, C. *Tetrahedron* **1977**, *33*, 851.

0022-3263/85/1950-0958$01.50/0

Table I. ^{1}H NMR Data[a]

	H-1	H-3	2H-4	H-5	H-6	H-7	H-8 2H-8	CH_2OH-4	CH_2OH-6	CH_2OH-7	CH_3-7
6	4.56 bd	3.75 *J* = 7.0 t	2.1–1.9 cm	2.52 d	2.70 bsg		5.55 bs		3.72 d		1.80 bs
8	4.93 *J* = 8.0 bd	3.72 *J* = 7.0 t	1.88 *J* = 6.0 q	2.6–2.9 *J* = 6.0	2.76 m		5.48 bs		3.70 o		1.74 bs
5	4.60 d	3.75 *J* = 6.6 t	2.3–1.7	2.3–1.7	2.85 bs		5.80 bs		3.71 *J* = 4.0 d	4.24 bs	
7	5.10 *J* = 8.0 d	3.76 t	1.90 *J* = 6.0 q	3.04 bs	3.20 *J* = 6.0 q		5.68 bs		3.78 o	4.20 bs	
13	4.80 bd	3.70 d	2.0 m	2.0 cm	2.88 bsg		5.76 bs	3.88 d	3.70 d	4.22 bs	
14	4.48 bd	4.0–3.5	2.15 m	1.85 bsg	2.78 bs		5.98 bs	3.9–3.5	3.9–3.5	4.24 bs	
15	5.16 *J* = 9.0 bd	3.73 o	2.45 cm	2.80 o	3.03 bs		5.67 bs	3.54 o	3.80 d	4.20 bs	
17[b]	5.43 bd		2.60 m	3.20 bs	3.30		6.00 bs		4.30 o	4.70 bs	
18[c]	5.08 bd	3.72 o	2.0–1.7 m	3.4–3.0	3.13		5.87 bs		4.40 o	4.15 bs	
20	4.48 m	3.9–3.4	2.1–1.4	3.1–2.1	3.1–2.1	3.1–2.1	2.1–1.4		3.9–3.4	3.9–3.4	
21	4.45 m	4.2–3.5	2.1–1.6	2.9–2.5	2.9–2.5	2.9–2.5	2.1–1.6		4.2–3.5	4.2–3.5	

[a] D_2O for all compounds except **8** **17**, **18**, and **21** ($CDCl_3$). Chemical shifts (δ) in ppm, coupling constants (*J*) in Hz; bd = broad doublet, bs = broad singlet, bsg = broad signal, cm = complex multiplet, d = doublet, m = multiplet, o = octet, q = quartet, t = triplet. [b] OAc, 2.12 and 2.03, s. [c] OMs, 3.04 s.

Table II. ^{13}C NMR Data in D_2O Solution

	C-1	C-3	C-4	C-5	C-6	C-7	C-8	C-6′	C-7′	C-4′
6	82.32 d	62.16 t	31.28 t	48.50 d	52.06 d	144.98 s	129.99 d	59.75 t	15.36 t	
8[c]	87.40 d	67.77 t	27.93 t	43.06 d	51.26 d	144.43 s	126.94 d	61.62 t	15.33 q	
5	81.84 d	62.02 t	31.07 t	48.55 d	48.74 d	147.26 s	130.77 d	60.17[a] t	60.36[a] t	
7	87.81 d	68.18 t	28.04 t	43.09 d	48.54 d	149.22 s	126.00 d	61.34[a] t	60.17[a] t	
13	78.83 d	62.03 t	41.91 d	47.85 d	49.82 d	146.60 s	131.08 d	60.09 t	60.09 t	61.84 t
14	73.93 d	61.43 t	39.73 d	44.43 d	46.69 d	150.29 s	129.17 d	60.05[a] t	57.61[a] t	61.43 t
15	88.02 d	69.26 t	43.01 d	46.03 d	48.55 d	150.14 s	125.60 d	61.37 t	60.09 t	64.31 t
20	86.04 d	69.64 t	28.62 t	44.25[a] d	44.93[a] d	45.91[a] d	34.97 t	60.46[b] t	63.00[b] t	
21[c]	87.75 d	69.36 t	27.99 t	46.02[a] d	45.92[a] d	45.75[a] d	36.22 t	70.57[b] t	74.04[b] t	

[a,b] The assignments can be reversed. [c] In $CDCl_3$ solution.

derivatives.[8] The latter reaction led to cyclopentenepolyols (e.g., **5** from **2**) with an α-oriented β-hydroxyethyl chain at C-5.[9]

In order to avoid the yield fall connected with the tedious and delicate procedure required for the isolation of the iridoid aglycons from the aqueous solution, we carried out their $NaBH_4$ reduction directly in the presence of the β-glucosidase. Cyclization of the cyclopentenepolyols to *cis*-2-oxa[3.3.0]oct-7-enes was carried out in the same vessel, by simple acidification of the reduction mixture: in this way a three-step synthesis of these important prostanoid synthons was realized in one pot with high yields (Chart I).

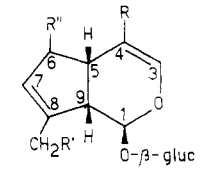
The $NaBH_4$ reduction of aglycons **2** and **4**, obtained from **1** and 10-deoxyaucubin (**3**) (prepared by Birch reduction of **1**), respectively, afforded the 5-(β-hydroxyethyl)-6,7-bis(hydroxymethyl)cyclopent-7-en-1-ol (**5**) and the 5-(β-hydroxyethyl)-6-(hydroxymethyl)-7-methylcyclopent-7-en-1-ol (**6**). By acidification (2 N HCl), **5** and **6** underwent, at room temperature, a fast and complete intramolecular cyclization to 6,7-bis(hydroxymethyl)-*cis*-2-oxabyciclo-[3.3.0]oct-7-ene (**7**) (66% overall yield from **1**) and 6-(hydroxymethyl)-7-methyl-*cis*-2-oxabyciclo[3.3.0]oct-7-ene (**8**) (47% overall yield from **3**), respectively.[10]

(8) Bianco, A.; Bonini, C.; Guiso, M.; Iavarone, C.; Trogolo, C. *Tetrahedron* **1981**, *37*, 1773.

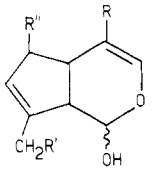
(9) In order to achieve a more immediate comparison for the spectral data of corresponding carbons, we used for the NMR analysis of the cyclopentenepolyols **5**, **6**, **13**, and **14** the IUPAC numbering of the bicyclo[3.3.0]octane system.

(10) This cyclization process also took place with other acidic catalysts (e.g., *p*-TSA or strong acidic resin in water at room temperature transformed completely **5** into **7** in 1 h); furthermore **6**, stored at −5 °C, still cyclized spontaneously.

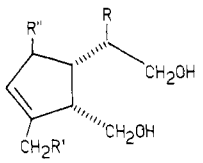
Chart I



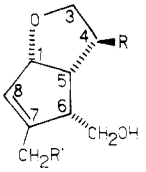
1 R=H, R'=OH, R''=βOH
3 R=R'=H, R''=βOH
9 R=COOCH$_3$, R'=OH, R''=βOH
10 R=COOCH$_3$, R'=OH, R''=αOH



2 R=H, R'=OH, R''=βOH
4 R=R'=H, R''=βOH
11 R=COOCH$_3$, R'=OH, R''=βOH
12 R=COOCH$_3$, R'=OH, R''=αOH

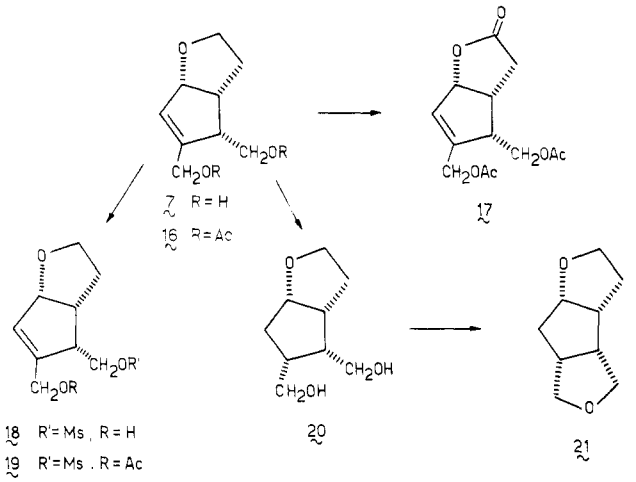


5 R=H, R=OH, R''=βOH
6 R=R'=H, R''=βOH
13 R=CH$_2$OH, R'=OH, R''=βOH
14 R=CH$_2$OH, R'=OH, R''=αOH



7 R=H, R'=OH
8 R=R'=H
15 R=CH$_2$OH, R'=OH

Scheme I



18 R'=Ms, R=H
19 R'=Ms, R=Ac
7 R=H
16 R=Ac
17
20
21

The ^{1}H and ^{13}C NMR spectra of **7** and **8** were in complete agreement with the proposed structures (see Tables I and II).

The inversion of the configuration of the C-1 center and the closure of the tetrahydrofuran ring which accompanied the transformations **5** → **7** and **6** → **8** caused conspicuous downfield shifts (^{13}C NMR) for both carbons linked to the ethereal oxygen C-1 (+5.97 and 5.08 ppm respectively for **7** and **8**); C-3 (+6.16 and 5.61 ppm). On the other hand, an upfield shift was observed for the three β carbons, C-4 (−3.03 and −3.35 ppm), C-5 (−5.46 and −5.44 ppm), and C-8 (−4.77 and −3.05 ppm).

The cyclization can be considered a typical S_N1 reaction proceeding through the allylic carbocation at C-1 which undergoes intramolecular nucleophylic attack by the α-oriented β-hydroxyethyl function at C-5 to form a fused tetrahydrofuran ring.

The above reaction pathway was verified by repeating the complete sequence with scandoside methyl ester **9** and 10-deacetylasperulosidic acid methyl ester **10**, both obtained by methylation of the corresponding natural acids isolated from *Asperula odorosa* (Rubiaceae) according to known procedures.[11] On the basis of the proposed mechanism, only one cyclization product **15** should be obtained starting from **9** and **10**, epimeric at C-6.

The "one-pot" $NaBH_4$ reduction of the aglycons **11** and **12** (obtained from **9** and **10**, respectively) gave in excellent yields the cyclopentenepolyols **13** and **14**, respectively. That **13** and **14** were C-1 epimers was evident from their ^{1}H and ^{13}C NMR data (Tables I and II).

Worthy of note in **13** (β epimer) was the deshielding of H-1 (0.32 ppm) and C-1 (4.90 ppm) compared with **14** (α epimer), in agreement with literature data.[12] Other chemical shift changes of the cyclopentane carbons of **13** were dependent on their distance from the C-1 center: deshielding was observed for the α carbons C-5 (+3.42 ppm) and C-8 (+1.91 ppm), while shielding for C-7 (−3.69 ppm).

As expected, both epimers **13** and **14**, by treatment with mineral acid (2 N HCl), gave the 4,6,7-tris(hydroxymethyl)-*cis*-2-oxabicyclo[3.3.0]oct-7-ene (**15**). The ^{1}H and ^{13}C NMR spectra of **15** (see Tables I and II) are in complete agreement with the proposed structure.[13]

Isolation of **15** from both **13** and **14** demonstrated unambiguously the proposed cyclization mechanism. Key structural features for this type of cyclization can be therefore identified with the presence on the cyclopentene ring of a vicinal allylic hydroxyl and β-hydroxyethyl groups.

The high yields of *cis*-2-oxabicyclo[3.3.0]oct-7-enes obtained simply from widely diffused natural products prompted us to test bicyclo ethers such as **7** as starting materials for an analogue (**17**) of Corey's lactone and other significant derivatives (see Scheme I).

Compound **16**, treated with PCC[14] in boiling CH_2Cl_2, afforded the corresponding lactone **17** in rather good yield (50%). The structure of **17** was substantiated by its IR spectrum (see Experimental Section) and ^{1}H NMR data (lack of the two H-3 signals, appearance of the two H-4 protons signals as the AB part of an ABX system).

Selective mesylation (MsCl/py, 0 °C) of **7** at the C-6 hydroxymethyl function only allows a differentiation between the two primary hydroxyl groups and consequently their different further elaboration. The structure proposed for **18** was confirmed by formation of the monoacetate **19**. Owing to the low reactivity of the primary hydroxyl group of **18**, the acetylation was carried out under rather drastic conditions.

Finally **7** was quantitatively and stereospecifically hydrogenated (Rh/Al_2O_3, 1 atm), without hydrogenolysis of the allylic hydroxyl functions, to 6,7-bis(hydroxymethyl)-*cis*-2-oxabicyclo[3.3.0]octane (**20**). The stereochemistry of **20** was confirmed by ring closure (TsCl in benzene) to the tricyclic derivative **21**, whose structure, 2,8-dioxatricyclo[6.3.0.0^{6,10}]undecane, was consistent with

(11) Inouye, H.; Inouye, S.; Shimokawa, N.; Okigawa, M. *Chem. Pharm. Bull.* **1969**, *17*, 1942.

(12) Chaudhuri, R. K.; Afifi-Yazar, F. Ü.; Sticher, O. *Helv. Chim. Acta* **1979**, *62*, 1603. Bianco, A.; Passacantilli, P.; Polidori, G.; Nicoletti, M.; Messana, I. *Gazz. Chim. Ital.* **1983**, *113*, 829.

(13) The stereochemistry of the C-4 center of **15** has been clarified by detailed ^{1}H NMR analysis and spin decoupling experiment. The value of 3.3 Hz found for the coupling constant $J_{4,5}$ indicates, in agreement with the Karplus rule, a dihedral angle of ca. 120° and therefore a trans arrangement between the H-5 (β) and the H-4 proton, permitting assignment to the latter an α configuration (β-CH_2OH). An opposite configuration at the C-4 center would have required a ratio $J_{4,5}/\Phi$ = 10 Hz/180°.

(14) This seems to be the first report of an oxidation by PCC of a cyclic ether to the corresponding lactone: the use of stronger oxidizing reagents, such as Jones or RuO_4, gave mainly the destruction of the starting material.

the ^1H and ^{13}C NMR data (see Tables I and II).

In conclusion a rapid and simple procedure adaptable to large-scale work allows facile preparation of important bicyclic intermediates from naturally occurring compounds with appropriate chirality and functionalities to be further elaborated into prostanoids by known routes.

Experimental Section

^1H NMR spectra were recorded at 60 or 90 MHz with HDO as internal standard (at 4.70 ppm) for D_2O solutions and Me_4Si as internal standard for $CDCl_3$ solutions. ^{13}C NMR spectra were registered at 20 or 22.63 MHz with dioxane (67.4 ppm from Me_4Si) as internal standard for D_2O solutions and Me_4Si as internal standard for $CDCl_3$ solutions. Silica gel SiF_{254} (Erba) plates were used for TLC and compounds were visualized by spraying with 2 N H_2SO_4 and heating at 120 °C. All new compounds described gave satisfactory elemental analyses.

Isolation and Purification of the Iridoid Glucosides. Aucubin (1) was isolated from *Eucommia ulmoides* (Eucommiaceae) and purified as already described (ref 2c). Isolation of scandoside and 10-deacetylasperulosidic acid from *Asperula odorosa* (Rubiaceae) and preparation of their Me esters **9** and **10** were carried out according to the procedures described in ref 11.

General "One-Pot" Preparation of *cis*-2-Oxabicyclo[3.3.0]oct-7-enes. A buffer solution (pH 5.4) of the iridoid glucoside and the β glucosidase (Fluka) in the molar ratio 10:1 was stored at 35 °C, and the reaction was checked by TLC ($CHCl_3$/MeOH (8:2) as eluent). Generally after 24 h the reaction was stopped, the solution was transferred to a large flask, and with vigorous magnetic stirring an excess of $NaBH_4$ was added during 1 h at room temperature. Then the solution was carefully bubbled with CO_2 until pH 8. To the neutralized solution was added dropwise 6 N HCl until the solution became 2 N in HCl. Checked periodically by TLC ($CHCl_3$/MeOH (9:1) as eluent), the reaction was stopped after 1 h by addition of 6 N NaOH until neutral. To the solution was added decolorizing charcoal to absorb all the organic products, and the suspension was then poured on a silica gel layer in a Gooch funnel. The inorganic salts were totally removed with water and finally the Gooch funnel was eluted with MeOH; evaporation in vacuo of the methanolic solution yielded a crude residue, generally purified by column chromatography (silica gel) with $CHCl_3$/MeOH (9:1) as eluent.

The overall yields of the described procedure for the different compounds were as follows: **7** from **1** (66%); **8** from **3** (47%); **15** from **9** (57%); and **15** from **10** (48%).

Isolation of Cyclopentenepolyol 13. A 140-mg (0.3 mmol) sample of **9** (ref 11) was treated as described above in the general "one-pot" procedure. After CO_2 bubbling, decolorizing charcoal (500 mg) was added to the solution. The suspension was then poured on a silica gel layer stratified in a Gooch funnel and eluted with water to eliminate the inorganic salts. The final elution with MeOH afforded, after evaporation in vacuo, 52 mg (69%) of almost pure **13** as an oil.

Isolation of Cyclopentenepolyol 14. A 340-mg (0.73 mmol) sample of **10** (ref 11) was worked up as described above for **9**. The final methanolic elution afforded, after evaporation, mg 130 of **14** (71%) as an oil.

Oxidation of 16: Lactone 17. A 20-mg (0.08 mmol) sample of **16** was stirred at 45 °C, in a dry apparatus with 10 mL of anhydrous CH_2Cl_2. Three portions of freshly prepared PCC (200 mg) were added in 2 h at room temperature to the mixture. After 48 h, the reaction, checked by TLC, was stopped and the brown suspension was poured on a silica gel column and eluted with ether. The evaporation of the ether solution afforded 20 mg of crude products. Column chromatography (silica gel, $CHCl_3$/MeOH (95:5) as eluent) yielded 10 mg of **17** (50%) and 8 mg of unreacted **16**. **17** (oil): IR ($CHCl_3$) 1780, 1750 cm^{-1}.

Hydrogenation of 7: Compound 20. 5% Rh on Al_2O_3 (Fluka) was added in catalytic amount to a solution of 30 mg (0.18 mmol) of **7** in 5 mL of MeOH. The heterogeneous solution was stirred, under a hydrogen atmosphere at normal pressure, for 8 h at room temperature. Filtration and concentration of the suspension gave a crude residue of 30 mg which was chromatographed on a silica gel column (MeOH/$CHCl_3$ (9:1) as eluent), affording 23 mg (73%) of pure **20** as a colorless oil.

Ring Closure of 20: Compound 21. To a solution of 23 mg (0.13 mmol) of **20** in 10 mL of dry benzene was added 10 mg of TsCl, and the mixture was refluxed for 8 h. After evaporation of benzene, the crude residue was chromatographed on silica gel (CH_2Cl_2), yielding 17 mg of **21** (85%) as a colorless oil.

Monomesyl Derivative 18. To a solution of 90 mg (0.53 mmol) of **7** in 0.5 mL of dry pyridine was carefully added, at 0 °C, 1 mL of MsCl (6 mmol). The temperature was then raised to room temperature during 1 h. After addition of Et_2O, the solution was acidified at 0 °C with 2 N HCl. The ethereal solution was extracted twice with water and then dried over Na_2SO_4. Evaporation of the ether solution afforded a residue of 88 mg which, chromatographed on a silica gel column (hexane/ether (3:7) as eluent), yielded 75 mg of pure **18** (54%) as an oil.

Acetyl Derivative 19. To a solution of 75 mg (0.30 mmol) of **18** in dry pyridine (0.5 mL) was added 1 mL of acetic anhydride (9 mmol) and 0.02 mL of NEt_3 (0.2 mmol). The reaction mixture was kept at 50 °C for 20 h and then was diluted with Et_2O (20 mL) and extracted with 2 N H_2SO_4 and H_2O until neutral. The organic layer, dried over Na_2SO_4, afforded after evaporation 73 mg of residue. Silica gel chromatography (hexane/ether (3:7) as eluent) yielded 58 mg of pure **19** (66%) as an oil.

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A New Efficient Total Synthesis of Vindorosine and Vindoline[1]

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Highly stereoselective total syntheses of indole alkaloids vindorosine (**1a**) and vindoline (**1b**) are described. An imino Diels–Alder reaction, a stereospecific alkylation, and a rearrangement induced by the Pummerer reaction are the key steps of these short and high overall yield sequences.

Aspidosperma alkaloid vindoline (**1b**)[2] is with catharanthine (**2a**)[3] the direct biogenetic precursor[4] of the antitumor alkaloids of *Catharanthus roseus* like vinblastine (**3**).[5] The discovery in our laboratory[6] of a hemisynthetic

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