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TAXOIDS FROM THE ROOTS OF *TAXUS* × *MEDIA* cv. HICKSII[1]

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ABSTRACT.—The roots of *Taxus*×*media* cv. Hicksii gave two new pseudoalkaloidal taxoids, identified as *N*-debenzoyl-*N*-butanoyl taxol [**1**] and 7β-acetoxy-9-acetylspicataxine [**2a**]. A new baccatin IV derivative [**7a**] and the lignans hydroxymatairesinol [**8**] and (−)-epinortrachelogenin [**9**] were also isolated. The epoxidation of $\Delta^{4(20),11}$ taxadienes was investigated, disclosing an unusual reactivity of the bridgehead double-bond towards peracids. Regiochemically and stereochemically unnatural epoxides of taxoids were obtained. Nmr data for these compounds were compared with literature values on the natural epoxides. No significant correlation between the configuration of the 4(20)-oxirane ring and the chemical shift of H-5 was found.

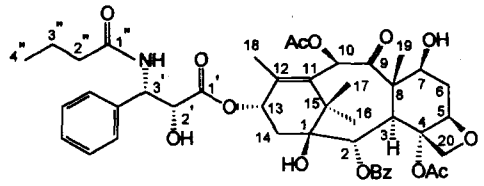
The stem bark and the needles of several species of yew have been thoroughly investigated (2), but very few studies have been done on the constituents of the roots (3,4). As part of a study aimed at assessing the availability of taxol and taxol-equivalent diterpenoids from cultivated yew species, we investigated the constituents of the roots of *T.* ×*media* Rehd. cv. Hicksii (5). This yew was developed for ornamental purposes and is popular as landscape material. Extensive cultivations exist in nurseries, and the needles have been studied as a potential source of taxol (6). A previous study has shown the presence of taxol and two novel analogs in the roots (7). We report here the isolation of three new taxoids [**1**, **2a**, **7a**] and of a lignan not previously described as a natural product [**9**].

RESULTS AND DISCUSSION

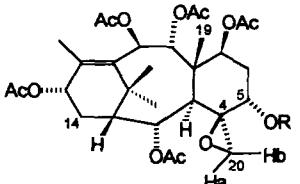
Compound **1** has the molecular formula $C_{44}H_{53}NO_{14}$ (cims). Its ^{1}H-nmr spectrum was similar to that of taxol C (*N*-debenzoyl-*N*-hexanoyl taxol) (7). The only significant difference was the absence of the ω-2 and ω-3 methylene protons of the *N*-acyl residue. The ^{13}C-nmr spectrum was almost superimposable on that of taxol C (7) except for the absence of the ω-2 and ω-3 carbons. These data suggested that **1** differs from taxol C by the substitution of a *n*-butanoyl group for the *n*-hexanoyl residue on the nitrogen. This conclusion was supported by cims, which showed a base peak at *m/z* 269 (*N*-butanoylphenylisoserine+NH_4)$^+$ and a prominent peak at *m/z* 586, corresponding to the loss of *N*-butanoylphenylisoserine from the molecular ion at *m/z* 837 $(M+NH_4)^+$. The virtual identity of all the ^{1}H- and ^{13}C-nmr chemical shifts and of all the scalar proton-proton couplings suggested that the relative configurations of **1** and taxol C are the same (syn- configuration of the amino acid side-chain; baccatin III stereoparent for the taxane moiety). A *n*-butanoyl residue has not previously been reported for a taxoid, and we have named **1** taxol D.

Compound **2a** has the molecular formula $C_{41}H_{55}NO_{13}$. Its ^{1}H-nmr spectrum showed the signals of a Winterstein acid residue (β-dimethylamino-β-phenylpropionic

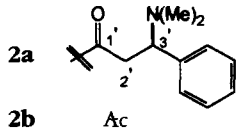
[1]Part 14 in the series "The Chemistry and Occurrence of Taxane Derivatives." For part 13, see Appendino *et al.* (1).



1

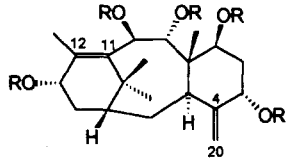


R



2a

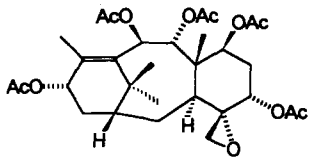
2b Ac



R

3a Ac

3b H



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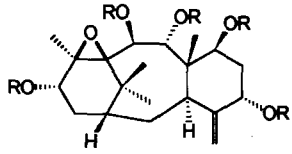


R

5a Ac

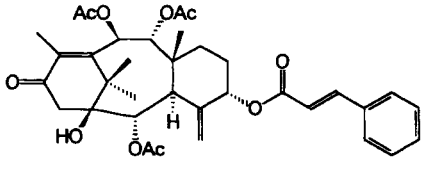
5b H

acid) and five acetyls. The ^{13}C-nmr spectrum displayed six resonances in the region of the hydroxylated carbons. The multiplicity of these signals (all doublets) indicated that the ester groups were all secondary. In the ^{1}H-nmr spectrum, the protons adjacent to the acylated hydroxyls could be easily identified from their splitting pattern. Although the chemical shifts of H-2, H-7, H-9, H-10, and H-13 were normal, H-5 resonated at unusually high field for an acylated methine of a taxoid (δ 4.21), suggesting the presence of an epoxide group at C-4–C-20. This was confirmed by the presence of an upfield AB system (doublets at δ 3.47 and 2.30, J=5.3 Hz). The chemical shift of H-6α (δ 1.14) showed shielding from the aromatic ring of the amino acid side-chain. The Winterstein acid residue was thus located at O-5 (8), in accordance with the structures of all the other taxoids of this type isolated to date (9). The β-orientation of the epoxide oxygen of **2a** was established by the detection of a rOe-effect between H-20a and H-14α (10). Thus, **2a** is 7β-acetoxy-9-acetylspicataxine.

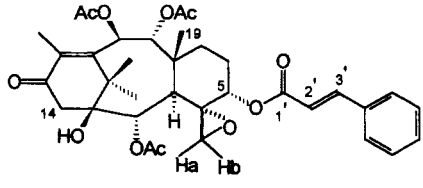
Almost twenty taxoids with the 4(20) double bond oxidized to the epoxide level are known (9,11), and a plausible biogenetic relationship between compounds of this type and oxetane-type taxoids has been proposed (9). All naturally occurring 4(20)-epoxides have been formulated as β-epoxides. In most cases this stereochemistry has been assigned solely by comparison with the spectrum of baccatin I [**2b**] (12). In this compound the β-epoxide oxygen causes a downfield shift of the angular methyl (H-19) and an upfield

shift of H-5β compared to the corresponding $\Delta^{4(20)}$-olefin. Comparison with the C-4 epimer of baccatin I, the major product from the epoxidation of the corresponding allylic ester (12), might also be useful. However, neither the spectroscopic characterization of this compound, nor that of any other 4(20)-α-epoxide, has ever been published. Examination of systems closely related to ring C of baccatin I shows an upfield shift of the proton corresponding to H-5 of taxoids in both the isomeric epoxides (13). Furthermore, the assignment of the 19-methyl group of taxoids by 1D nmr measurements alone is not always straightforward, since its chemical shift is subject to substituent and transannular effects (14). To check the consistency of the literature data on the stereochemistry of the naturally occurring C-4(20) epoxides of taxoids, we explored the preparation of α-epoxides.

Treatment of the pentaacetate **3a** (15) with *meta*-chloroperbenzoic acid gave an inseparable 4:1 mixture of two regioisomeric epoxides [**4** and **5a**]. The corresponding pentaol [**3b**], however, gave the bridge-headed epoxide **5b** as the major reaction product. The presence of rOe-effects between the 18-methyl and H-10 and H-3, established a β-configuration for the epoxide. Normally, the Δ^{11} double bond of taxoids is unaffected by catalytic hydrogenation, ozonolysis or osmylation (9) and is considered stereochemically almost inaccessible. Attack by peracids, however, has been observed as a minor reaction pathway (12). Thus, the outcome of the epoxidation of **3a** and **3b** was surprising. It showed that double allylic activation by hydroxyls can invert the usual order of reactivity of the taxoid double bonds. This unforeseen regioselectivity problem was overcome by the epoxidation of the taxicin derivative **6a** (14) to give a single reaction product [**6b**] in almost quantitative yield. The α-stereochemistry of the epoxidic oxygen was established by the observation of a rOe effect between H-20a and the 19-methyl, whereas no rOe effect between H-14α and H-20a could be detected. The observed facial diastereoselectivity (attack from the concave α-face of the molecule) is presumably the result of the presence of the angular β-methyl at C-8.

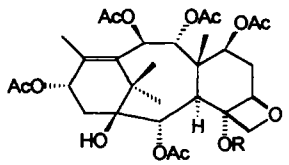


6a



6b

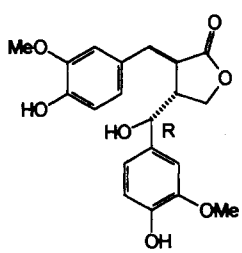
Comparison of the ^{1}H-nmr data of **6a** and **6b** revealed an upfield shift for H-5 ($\Delta\delta -1.00$ ppm) in **6b**, whereas H-19 was moved downfield ($\Delta\delta +0.08$ ppm). These shifts are comparable to those observed between $\Delta^{4(20)}$-taxenes and their naturally occurring β-epoxides (12). More interesting, however, is the comparison of the ^{1}H-nmr features of the C-20 protons in **6b** and **2a,b**. In the β-epoxy derivatives [**2a,b**], H-20b resonates at a much higher field (δ ca. 2.30) than H-20a (δ ca. 3.50). As a result, a large chemical shift difference between the geminal epoxidic protons is apparent ($\Delta\delta$ ca. 1.20 ppm). In the α-epoxide **6b**, these protons resonate at δ 2.90 and 2.57, and their chemical shift is much closer ($\Delta\delta$ 0.33 ppm). This difference is presumably the result of anisotropic effects associated with the oxygen functions at C-2α (apparently deshielding) and C-5α (apparently shielding). A similar, but not as marked trend, could be found between C-4 epimers of C-2 and C-5 deoxygenated synthetic models of taxoid 4(20)-epoxides (16). Inspection of the reported ^{1}H-nmr data on naturally occurring 4(20)-epoxide bearing ester groups at O-2 and O-5, shows a large difference (>1 ppm) in the



	R
7a	H
7b	Ac

chemical shift of the epoxide protons, thus supporting the assignment of the β-stereochemistry of the epoxide in all cases. In **4**, where C-2 is not oxygenated, the stereochemistry of the epoxide was tentatively assigned as α by analogy with the facial selectivity (attack from the concave face) observed in the epoxidation of **6a**. In **4**, the epoxide protons were almost isochronous (Δδ 0.05 ppm).

Compound **7a** has the molecular formula $C_{30}H_{42}O_{13}$. The ^{1}H-nmr spectrum (Table 1) showed the presence of five acetyls and an oxetane moiety on ring C. Five signals in the region of the protons adjacent to oxygen functions could be assigned to H-2, H-7, H-9, H-10, and H-13 on the basis of their splitting patterns. Chemical shift considerations suggested that their corresponding oxygens are acylated. This was confirmed by long-range (^{3}J) ^{1}H-^{13}C correlation experiments, and the failure to acetylate **7a** under standard conditions (Ac_2O, pyridine). Thus, the two free hydroxyls required by the molecular formula must be at C-1 and C-4, and **7a** is 4-deacetylbaccatin IV. Comparison of the spectral features of **7a** and baccatin IV [**7b**] (17) revealed upfield shifts for H-3, H-10, and H-5 in **7a**, an observation consistent with the removal of the anisotropic effects associated with the carbonyl of the *O*(4)-acetate. The upfield chemical shift of H-13 in **7a** (δ 5.72 vs δ 6.20 in **7b** (17)) is somewhat surprising. It is probably related to modifications in the conformation of ring A caused by the formation of an intramolecular hydrogen bonding between the hydroxyl at C-4 and the acetyl at C-13. The isolation of taxoids with an oxetane ring and a free hydroxyl at C-4 is unusual, but a precedent does exist with derivatives of baccatin IV (18).



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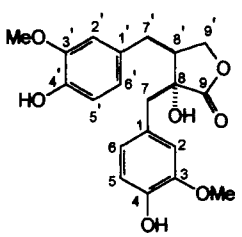

9

The fractions containing **1**, **2a**, and **7a** also gave two lignans of the dibenzylbutyrolactone type. These compounds were identified as hydroxymatairesinol [**8**] and (−)-epinortrachelogenin [**9**] by comparison of their physical and spectroscopic data with those reported in the literature (19,20). Compound **9** had been obtained by synthesis (20,21), but has not yet been isolated from any natural source.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined on a Büchi SMP 20 apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 141 automatic

TABLE 1. ^{1}H-Nmr Data (300 MHz, TMS as Reference, $CDCl_3$, *J* in Hz) for Compounds **1**, **2a**, **5b**, **6b**, and **7a**.[a]

Proton	Compound				
	1[b]	**2a**[c]	**5b**[d]	**6b**[f]	**7a**
H-1	—	1.72 d (8.4)	[e]	5.62 d (3.9)	5.64 d (5.5)
H-2	5.68 d (7.0)	5.54 d (3.7)	[e]	3.49 d (3.9)	2.69 d (5.5)
H-3	3.79 d (7.0)	2.86 d (3.7)	2.57 br s	4.35 br s	4.80 dd (8.1, 2.6)
H-5	4.94 br d (9.2)	4.21 t (3.1)	4.14 t (3.0)	[e]	2.35 m
H-6α	2.54 m	1.14 m	1.71 m	[e]	1.90 m
H-6β	1.86 m	1.96 m	1.41 m	[e]	5.25 t (9.2)
H-7	4.40 ddd (11.0, 6.3, 4.0)	5.40 dd (12.0, 4.3)	4.19 dd (11.0, 5.0)	5.95 d (10.2)	5.84 d (11.0)
H-9	—	5.97 d (11.2)	3.61 d (10.2)	6.09 d (10.2)	6.05 d (11.0)
H-10	6.29 s	6.24 d (11.2)	4.03 d (10.2)	—	5.72 br dd (9.7, 3.3)
H-13	6.24 br t (9.0)	5.83 br t (8.3)	3.88 t (8.7)	3.22 d (19.4)	2.40 dd (15.5, 9.7)
H-14α ...	2.30 m	1.29 dd (15.0, 7.0)	0.99 dd (14.7, 8.8)	2.74 d (19.4)	2.25 dd (15.5, 3.7)
H-14β ...	2.30 m	2.71 dt (15.0, 8.7)	2.19 dt (14.7, 8.5)	1.65 s	1.65 s
H-16	1.17 s	1.69 s	1.39 s	1.24 s	1.08 s
H-17	1.26 s	1.09 s	0.78 s	2.31 br s	2.03 br s
H-18	1.82 br s	2.24 d (1.3)	1.62 s	1.03 s	1.45 s
H-19	1.66 s	1.20 s	0.82 s	2.90 d (4.4)	4.41 d (7.7)
H-20a(α) .	4.28 d (8.6)	3.47 d (5.3)	5.04 s	2.57 d (4.4)	4.36 d (7.7)
H-20b(β) .	4.20 d (8.6)	2.30 d (5.3)	4.74 s	2.14 s, 2.11 s, 2.07 s	2.12 s, 2.10 s, 2.10 s, 2.08 s, 2.01 s
Ac	2.35 s, 2.26 s	2.09 s, 2.04 s, 2.03 s, 1.97 s, 1.94 s	—		

[a]Assignments were made by comparison with related compounds whose spectra have been fully assigned [taxol C (7) for **1** and triacetylcinnamoyltaxicin I (14) for **6b**] or by inspection of the COSY and NOESY spectra (10) (**2a** , **5b**, and **7a**).

[b]Signals of the phenylisoserine moiety: H-2′, 4.68 br s; H-3′, 5.58 dd (9.0, 2.5); N-H, 6.25 d (9.0); H-2″, 2.18 t (7.3); H-3″, 1.61 m; H-4″, 0.90 t (6.7); phenyl, ca. 7.40 m. Signals of the benzoate moiety: 8.10 d (7.8); 7.50 t (7.8); 7.63 t (7.8). Exchangeable signals: 1-OH, 1.86 s; 7-OH, 2.43 d (4.0); 2′-OH, 3.60 d (5.0).

[c]Signals of the Winterstein acid moiety: H-2′, 3.95 t (7.8); H-3′a, 3.03 dd (13.6, 8.0); H-3′b, 2.86 dd (13.6, 7.6); $N(Me)_2$, 2.13 s; phenyl, 7.35–7.20 m.

[d]DMSO-d_6.

[e]Could not be assigned owing to overlapping.

[f]Signals of the cinnamate moiety: H-2′, 6.52 d (16.1); H-3′, 7.67 d (16.1); phenyl, 7.75 br d (8.5), 7.40 m.

polarimeter. Uv and ir spectra were taken on Beckman DB-GT and Perkin-Elmer model 237 spectrophotometers, respectively. ^{1}H-Nmr (300 MHz) and ^{13}C-nmr (75.4 MHz) spectra were recorded on a Varian VXR 300 spectrometer at 25°. Cims were taken on a VG EQ 70/70 apparatus. Cc was carried out on Si gel (Merck, 70–230 mesh). A Waters microPorasil column (0.8×30 cm) was used for prep. hplc, with detection by a Waters differential refractometer 3401.

PLANT MATERIAL.—Commercially available roots of *T.*×*media* cv. Hicksii were used. A voucher specimen is kept at the Indena laboratories.

ISOLATION.—The mother liquors from the crystallization of taxol C (20 g) (7) were chromatographed on Si gel [150 g, $CHCl_3$-EtOH (95:5) as eluent] to give 1.60 g of a mixture of **8**, **9**, and **2a** (ca. 4:1:1, hplc),

and 610 mg of a fraction containing **1**, **7a**, *N*-methyltaxol C (7), and cephalomannine (ca. 2:1:1:1, hplc). Compound **2a** crystallized from the mixture upon treatment with cyclohexane-EtOAc (7:3); in the other cases, pure products were obtained after hplc [hexane-EtOAc (3:7)] and crystallization ($CHCl_3$/MeOAc for **8** and **9**, Et_2O/diisopropyl ether for **1** and **7a**).

Taxol D [**1**].—White powder, mp 206–208°; $[\alpha]D^{25}$ −16° ($CHCl_3$, *c*=0.45); uv (EtOH) λ max 285, 275, 232, 220 nm; ir ν max (KBr) 3420, 3310, 1735, 1640, 1380, 1240, 1110, 1100, 1070, 980 cm^{-1}; cims (NH_3) $[M+NH_4]^+$ 837 ($C_{44}H_{53}NO_{14}+NH_4)^+$ (75), 586 $(M+NH_4-251)^+$ (75), 269 (100); ^1H and ^{13}C nmr, see Tables 1 and 2.

7β-Acetoxy-9-acetylspicataxine [**2a**].—White powder, mp 212–213°; $[\alpha]D^{25}$ +56° ($CHCl_3$, *c*=1.1); cims (NH_3) $[M+H]^+$ 770 ($C_{41}H_{55}NO_{13}+H)^+$ (80); ^1H and ^{13}C nmr, see Tables 1 and 2.

4-Deacetylbaccatin IV [**7a**].—White powder, mp 179° (dec); $[\alpha]D^{25}$ +60° ($CHCl_3$, *c*=0.40); ir ν max (KBr) 3460, 1745, 1370, 1230, 1015, 960 cm^{-1}; cims (NH_3) $[M+NH_4]^+$ 628 ($C_{30}H_{42}O_{13}+NH_4)^+$ (100); ^1H and ^{13}C nmr, see Tables 1 and 2.

Epinortrachelogenin [**9**].—White powder, mp 166–168°; $[\alpha]D^{25}$ −21.1° (MeOH, *c*=0.45); uv (EtOH) λ max 280, 232, 218 nm; ir ν max (KBr) 3460, 3300, 1790, 1605, 1270, 1240, 1225, 1130, 1090 cm^{-1}; cims (NH_3) $[M+NH_4]^+$ 392 ($C_{20}H_{22}O_7+NH_4)^+$ (100); ^1H nmr δ 6.88 and 6.85 (2H, d, *J*=7.8 Hz, H-5 and H-5′), 6.74 and 6.65 (2H, dd, *J*=7.8 and 2.0 Hz, H-6 and H-6′), 6.71 and 6.68 (2H, d, *J*=2.0 Hz, H-2 and H-2′), 5.61 and 5.45 (2H, s, OH), 4.19 (1H, dd, *J*=9.5 and 8.0 Hz, H-9′a), 3.87 (1H, t, *J*=9.5 Hz, H-9′b), 3.88 and 3.87 (6H, s, OCH_3), 3.13 (1H, dd, *J*=14.0 and 4.0 Hz, H-7′a), 2.98 (1H, d, *J*=14.0 Hz, H-7a), 2.94 (1H, d, *J*=14.0 Hz, H-7b), 2.93 (1H, m, H-8′), 2.74 (1H, br s, OH), 2.65 (1H, dd, *J*=14.0 and 11.5 Hz, H-7′b).

TABLE 2. ^{13}C-Nmr Data (67.5 MHz, TMS as Reference, $CDCl_3$) for Compounds **1**, **2a**, **5b**, **6b**, and **7a**.[a]

Carbon	Compound				
	1[b]	**2a**[c]	**5b**[d]	**6b**[e]	**7a**
C-1	78.90 s	47.86 d	41.96 d	76.79 s	77.36 s
C-2	74.96 d	69.92 d	25.91 t	71.82 d	72.54 d
C-3	45.60 d	39.10 d	34.77 d	40.65 d	50.50 d
C-4	81.13 s	58.61 s	152.98 s	60.11 s	74.96 s
C-5	84.38 d	76.98 d	72.25 d	78.26 d	86.31 d
C-6	35.62 t	31.33 t	39.00 t	26.29 t	33.91 t
C-7	72.13 d[f,*]	69.02 d	69.41 d	24.93 t	70.97 d
C-8	58.56 s	46.55 s	44.85 s	44.38 s	45.15 s
C-9	203.65 s	75.59 d	80.76 d	75.37 d	74.81 d
C-10	75.58 d	71.31 d	73.62 d	72.99 d	70.71 d
C-11	138.06 s	134.35 s	67.10 s	152.87 s	136.44 s
C-12	142.00 s	137.03 s	65.99 s	141.11 s	139.74 s
C-13	72.39 d[f,*]	70.17 d	66.40 d	199.22 s	71.00 d
C-14	35.62 t	28.83 t	39.50 t	44.82 t	35.85 t
C-15	43.21 s	38.33 s	33.87 s	43.57 s	42.12 s
C-16	21.88 q	26.98 q	27.26 q	19.47 q	20.31 q
C-17	26.80 q	31.28 q	31.31 q	33.90 q	29.81 q
C-18	14.79 q	15.37 q	16.49 q	14.03 q	16.40 q
C-19	9.56 q	13.76 q	13.38 q	17.28 q	13.16 q
C-20	76.48 t	49.60 t	111.01 t	50.89 t	79.74 t
Ac	171.25 s, 170.23 s	170.25 s, 169.71 s, 169.46 s, 169.15 s, 168.29 s		171.49 s, 169.79 s, 169.61 s	170.97 s, 169.99 s, 169.99 s, 169.99 s, 169.09 s
	22.57 q, 20.84 q	21.40 q, 21.35 q, 21.08 q, 20.90 q, 20.68 q		21.10 q, 20.84 q, 20.64 q	21.25 s, 21.25 s, 21.07 s, 20.90 s, 20.63 s

[a]Assignments were made by comparison with related compounds whose spectra have been fully assigned [taxol C (7) for **1** and triacetylcinnamoyltaxicin I (14) for **6b**], or by inspection of the C-H correlation, FLOCK and ROESY spectra (10) (**2a**, **5b**, and **7a**).

[b]Signals of the phenylisoserine moiety: C-1′, 172.85 s†; C-2′, 73.10 d; C-3′, 54.58 d; phenyl, 133.18 s, 126.96 d, 128.26 d[§], 128.67 d; C-1″, 172.94 s†; C-2″, 38.47 t; C-3″, 19.11 t; C-4″, 13.64 q. Signals of the benzoate moiety 166.90 s, 129.18 s, 130.19 d, 128.95 d[§], 133.67 d.

[c]Signals of the Winterstein acid moiety: C-1′, 170.32 s; C-2′, 39.35 t; C-3′, 66.82 d; phenyl, 138.00 s, 128.36 d, 128.32 d, 127.58 d; $N(Me)_2$, 41.79 q.

[d]DMSO-d_6.

[e]Signals of the cinnamate moiety, C-1′, 166.37 s; C-2′, 117.47 d; C-3′, 146.08 d; phenyl: 134.43 s, 130.46 d, 128.96 d, 128.44 d.

[f]Values with the same symbols are interchangeable.

EPOXIDATION OF **3a**.—Compound **3a** (280 mg, 0.5 mmol) was dissolved in CH_2Cl_2 (ca. 5 ml) and *meta*-chloroperbenzoic acid (85%, 203 mg, 1 mmol, 2 mol. equiv.) and NaOAc (280 mg) were added. After being stirred 20 h at room temperature, the reaction was worked up by washing with aqueous Na_2CO_3, and drying (Na_2SO_4). A white powder was obtained, which, when analyzed by ^{1}H nmr, turned out to be a ca. 4:1 mixture of **4** and **5a**. Relevant ^{1}H-nmr data for **4**: δ 6.23 (1H, d, J=10 Hz, H-10), 5.81 (1H, d, J=10 Hz, H-9), 5.80 (1H, br t, J=8.0 Hz, H-13), 5.56 (1H, dd, J=10.3 and 4.2 Hz, H-7), 4.55 (1H, br s, H-5), 2.86 (1H, d, J=4.0 Hz, H-3), 2.64 and 2.59 (2H, d, J=5.0 Hz, H-20a and b). ^{13}C nmr: δ 137.77 and 134.62 (s, C-11 and C-12). Relevant ^{1}H-nmr data for **5a**: δ 6.00 (1H, d, J=10.3 Hz, H-10), 5.90 (1H, d, J=10 Hz, H-9), 5.86 (1H, dd, J=10.4 and 4.2 Hz, H-7), 5.41 and 5.10 (2H, br s, H-20a and b). ^{13}C nmr: δ 145.20 (s, C-4), 117.03 (t, C-20).

EPOXIDATION OF **3b**.—Compound **3b** (300 mg, 0.85 mmol) was dissolved in CH_2Cl_2-THF (4:3, 7 ml), and *meta*-chloroperbenzoic acid (85%, 350 mg, 1.70 mmol, 2 mol. equiv.) and NaOAc (300 mg) were added. The suspension was stirred at room temperature for 3 h, and then worked up as described above. The residue was crystallized from Et_2O to give 155 mg (50%) **5b** as a white powder: mp 182°; $[\alpha]_D^{25}$ +5.5° (MeOH, c=0.54); ir ν max (KBr) 3500–3300 (br), 1250, 1050, 1025, 925 cm^{-1}; cims (NH_3) $[M+NH_4]^+$ 386 $(C_{20}H_{32}O_6+NH_4)^+$ (100).

EPOXIDATION OF **6a**.—Compound **6a** (170 mg, 0.27 mmol) was dissolved in CH_2Cl_2, and *meta*-chloroperbenzoic acid (85%, 100 mg, 0.27 mmol) and NaOAc (170 mg) were added. After stirring 20 h at room temperature, the reaction was worked up as described above. The residue crystallized as flakes that were washed with Et_2O, with 162 mg (94%) of **6b** being obtained, mp 230° (dec); $[\alpha]_D^{25}$ +199° ($CHCl_3$, c=0.64); uv (EtOH) λ max 281, 224, 219 nm; ir ν max (KBr) 3500, 1750, 1710, 1670, 1630, 1225, 1170, 1020, 765 cm^{-1}; cims (NH_3) $[M+NH_4]^+$ 656 $(C_{35}H_{42}O_{11}+NH_4)^+$ (100); ^{1}H- and ^{13}C-nmr data, see Tables 1 and 2.

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