Total Synthesis of Woodrosin I—Part 2: Final Stages Involving RCM and an Orthoester Rearrangement

Alois Fürstner,* Fabien Jeanjean, Patrick Razon, Conny Wirtz, and Richard Mynott[a]

Abstract: The completion of the first total synthesis of the complex resin glycoside woodrosin I (**1**) is outlined using the building blocks described in the preceding paper. Key steps involve the TMSOTf-catalyzed coupling of diol **2** with trichloroacetimidate **3** which leads to the selective formation of orthoester **5** rather than to the expected tetrasaccharide. Diene **5**, on treatment with catalytic amounts of the Grubbs carbene complex **6** or the phenylindenylidene ruthenium complex **7**, undergoes a high yielding ring closing olefin metathesis reaction (RCM) to afford macrolide **8**. Exposure of the latter to the rhamnosyl donor **4** in the presence of TMSOTf under "inverse glycosylation" conditions delivers compound **9** by a process involving glycosylation of the sterically hindered 2′-OH group and concomitant rearrangement of the adjacent orthoester into the desired β-glycoside. This transformation constitutes one of the most advanced applications of the Kochetkov glycosidation method reported to date. Cleavage of the chloroacetate followed by exhaustive hydrogenation completes the total synthesis of the targeted glycolipid **1**.

Keywords: glycosides · metathesis · natural products · oligosaccharides · ruthenium

Introduction

Woodrosin I (**1**), isolated from the stems of *Ipomoea tuberosa* L,[1, 2] is one of the most complex resin glycosides known to date. Glycolipids of this type are generally endowed with a wide range of physiological activities including cytotoxicity against human cancer cell lines, hemolytic, antibacterial, purgative or ionophoretic properties, as well as significant plant growth regulating capacity. Their intriguing structures stimulated the imagination of preparative chemists as witnessed by the increasing number of total syntheses that have been published over the last few years.[3–8]

In the preceding paper we outlined in detail a synthesis plan that should bring compound **1** within reach. Specifically, it envisages that the repeated use of the trichloroacetimidate method[9] provides an entry into its oligosaccharide backbone, while ring closing olefin metathesis (RCM) should enable the formation of the macrolactone entity.[10] High yielding routes to the required building blocks **2**–**4** have been developed starting from simple precursors (Scheme 1).[11] Moreover, a model study has suggested that the consecutive glycosylation of the two vicinal secondary OH groups in **2** with donors **3** and **4** critically depends on the phasing of events and would probably be successful only if the pending rhamnose unit is introduced last. In this article we describe that the main features of this strategy have been successfully put into practice, although the caprice of one of the protecting groups together with the severe steric hindrance in the core region of the molecule enforced an unforeseen detour.[12]

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Results and Discussion

Preparation of the metathesis precursor: The distinctly different reactivity of the vicinal hydroxyl groups in **2** allows consecutive glycosylation reactions to be carried out without recourse to protecting groups. Since the model studies reported in the accompanying paper showed that the 3′-OH function reacts regioselectively with various trichloroacetimidates to afford the corresponding oligosaccharides in high yields,[11] the coupling of **2** with donor **3** was investigated (Scheme 2). Treatment of a mixture of these components in CH_2Cl_2 with a catalytic amount of TMSOTf under carefully controlled conditions[13] affords a single product in 84% isolated yield. Its NMR spectra, however, are inconsistent with the expected tetrasaccharide but correspond to orthoester **5** formed by participation of the chloroacetyl moiety. Most indicative is a signal in the ^{13}C NMR spectrum at $\delta = 118.7$ ppm (s) assigned to the newly formed orthoester linkage.

The chloroacetyl group had originally been chosen because it allows the stereochemical course of glycosidation reactions to be controlled by neighboring group participation while at

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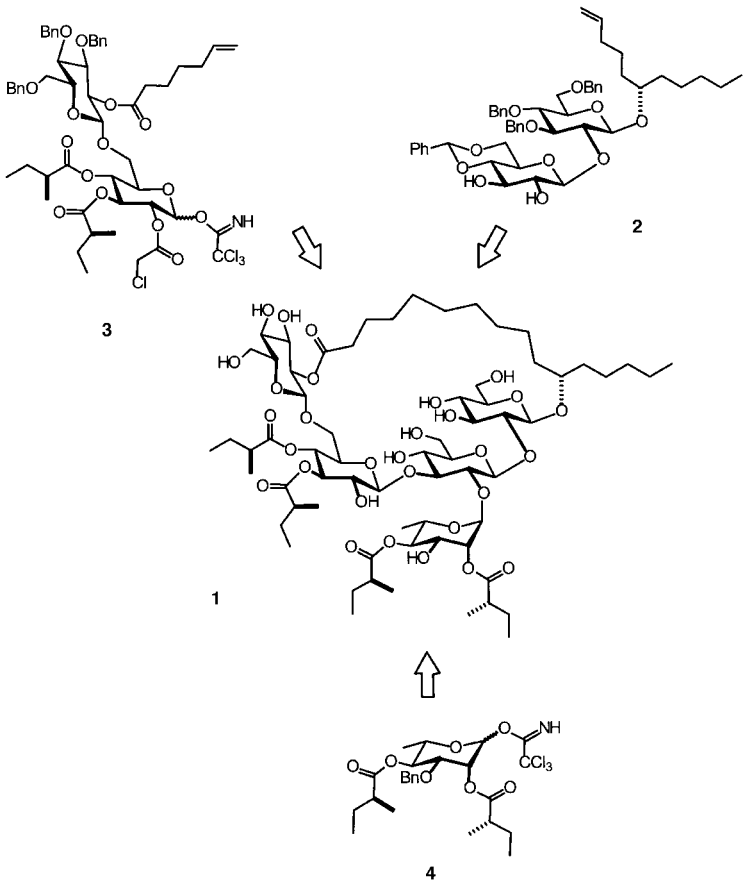
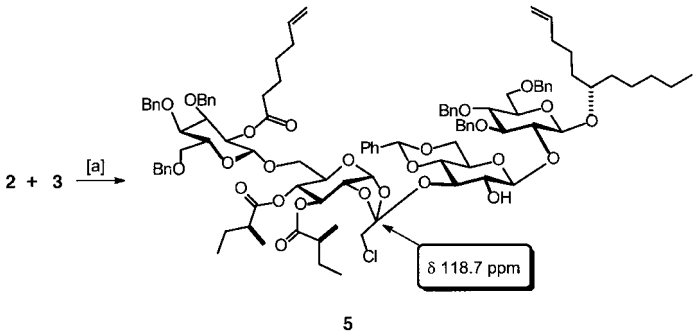


Scheme 1. Retrosynthetic strategy.



Scheme 2. [a] TMSOTf cat., CH_2Cl_2, RT, 84%.

the same time being orthogonal to the residual ester moieties in **1**.

Despite some literature precedence for the engagement of chloroacetates in the formation of orthoesters, the use of strong Lewis acids as promoters in the absence of a buffering base is usually an easy way to obtain the desired β-glycosides with good selectivity.[14, 15] Therefore the exclusive formation of **5** in the TMSOTf-catalyzed coupling of **2** and **3** was rather unexpected.

The total synthesis of woodrosin was pursued further in the hope of rectifying this connectivity pattern at a later stage.[16] Prior to that, however, we were faced with the severe steric hindrance exerted by the orthoester moiety in **5**. Thus, all attempts to attach the missing rhamnosyl unit to the adjacent 2′-OH group were in vain, likely because this site is strongly shielded in this part of the molecule and hence innately unreactive. Only the rapid decomposition of the starting materials **4** and **5** was observed without any indication of the formation of the desired coupling product.

At this stage, it seemed inevitable to redesign the building blocks used for the assembly of **1**. However, prior to taking recourse to this laborious yet uncertain option, a tactically different approach was pursued. Inspection of models suggested that the trajectory of a glycosyl donor towards the hidden 2′-OH group might be less narrow *after* forging the macrocyclic ring. Therefore the completion of the sugar backbone was postponed until after the ring closing olefin metathesis reaction.

Ring closing olefin metathesis: In contrast to the significant problems encountered during the assembly of the oligosaccharide backbone, the formation of the macrocycle by RCM proceeded uneventfully. Previous investigations from this laboratory had shown that RCM is particularly successful if the site of ring closure is far enough away from potential donor sites in the diene substrate to avoid the formation of unreactive metal chelate complexes.[17–19] In accordance with this, a virtually quantitative conversion of compound **5** into cycloalkene **8** was observed on treatment with catalytic amounts of the Grubbs carbene complex **6**[20] in a dilute, refluxing solution in CH_2Cl_2. The newly developed and particularly easily accessible phenylindenylidene complex **7**[21, 22, 29] is equally efficient, affording product **8** in 94% isolated yield (Scheme 3). This result highlights once again the truly remarkable potential of RCM, which is responsible for the breathtaking evolution of this transformation within the last few years into one of the most reliable, efficient and flexible entries into macrocyclic ring systems.[10]

Cycloalkene **8** is obtained as an E:Z mixture (E:$Z \approx 9$:1, HPLC). The detailed analysis of its 600 MHz spectra leaves no doubt about the connectivities and establishes that the major isomer is (E)-configured (cf. Experimental Section). This is deduced from the ^{13}C NMR spectrum; an unambiguous assignment was not possible from the ^{1}H NMR spectrum because the signals of H-6 and H-7 are obscured by severe overcrowding. The shifts of the allylic C-atoms C-5 and C-8 at 33.2 and 33.0 ppm (for the numbering Scheme see the Experimental Section), however, are highly characteristic.[18b] The unusually large J(C-1,H-1) = 185 Hz for the anomeric

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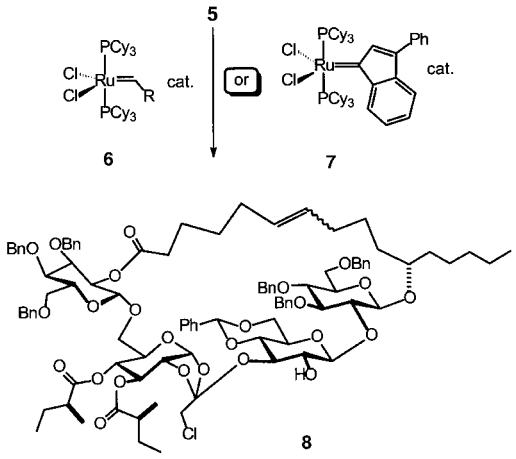
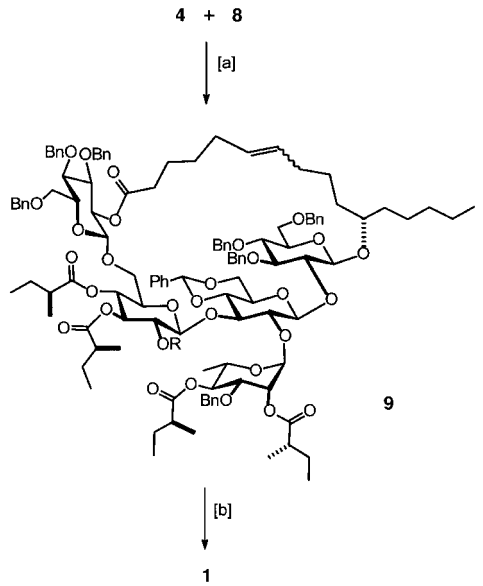


Scheme 3. Complex **6** or **7** cat., CH_2Cl_2, reflux, 24 h, 94%.

position of the C-ring as well as the small ^3J(H-2,H-3) = 3.2 Hz indicate that the annellation to the orthoester moiety forces this glucopyranose out of the usual chair conformation.

Completion of the total synthesis: With product **8** in hand, the introduction of the missing rhamnose moiety was re-investigated. The lability of donor **4** in the presence of a Lewis acid, however, made it necessary to apply the "inverse glycosylation procedure" developed by Schmidt for such purposes.[23] Specifically, alcohol **8** was premixed with catalytic amounts of TMSOTf in rigorously anhydrous Et_2O prior to the slow addition of compound **4** to the resulting solution.

The outcome of this key experiment surpassed our expectations (Scheme 4). Not only was it possible to attach the missing rhamnose unit to the oligosaccharide backbone, but the compromising orthoester junction was found to rearrange concomitantly to the required β-glycosidic linkage.[24] By optimizing the pre-mixing and addition times it was possible to isolate product **9** in 60% yield. In view of the delicacy of this transformation and the lability of the reaction partners this result showcases the power of the trichloroacetimidate method[9] and represents one of the most advanced applications of Kochetkov's orthoester protocol reported to date.[16, 24, 25]



Scheme 4. [a] TMSOTf cat., Et_2O, 0 °C, slow addition of **4** over 20 min, then 30 min, 60%. [b] i) Hydrazinium acetate, DMF, $-10 \rightarrow 0$ °C, 15 min; ii) 1 atm H_2, Pd/C, MeOH, 18 h, 84% (over both steps).

Extensive investigations involving DEPT, COSY, HSQC, and HMBC experiments allowed us to unambiguously assign all signals in the high field (600 MHz) NMR spectra of **9**. On this basis, the connectivities were established beyond doubt, proving that compound **9** constitutes fully protected woodrosin I with the intact oligosaccharide perimeter and the proper macrolide ring in place.

The final deprotection commences with a short treatment of **9** with hydrazinium acetate to remove the chloroacetyl moiety.[26] After washing the crude material with dilute acid, an extensive hydrogenation over palladium on charcoal saturates the olefin and simultaneously cleaves off all remaining protecting groups. Synthetic **1** thus obtained as an amorphous solid is identical to natural woodrosin I in all respects, see Experimental Section.

Conclusions

Despite the substantial methodological advances in glycosylation chemistry that have been achieved in recent decades, the assembly of sophisticated oligosaccharides is still far from routine. This is substantiated by the total synthesis of the complex glycolipid woodrosin I described in this and the accompanying paper. Although we lay no claim to the uniqueness of the trichloroacetimidate method for reaching this particular target, this synthetic endeavor certainly attests to the performance and maturity of this methodology pioneered and perfected by Schmidt.[9]

The ease with which the ruthenium carbene complexes **6** and **7** allowed the 27-membered macrolide spanning the oligosaccharide scaffold in **1** to be formed constitutes an instructive counterpoint to the subtle difficulties encountered in the assembly of the carbohydrate perimeter. Ring closing metathesis has evolved within a few years into a very reliable tool that can now be safely implemented even into complex synthesis plans.[10] Although several issues related to this transformation still remain to be solved,[27] the strategic advantages of metathesis in general[28] together with the truly spectacular application profile of the available catalysts will continue to shape modern organic chemistry. Further studies intended to illustrate this concept are underway in this laboratory and will be reported in the near future.[29, 30]

Experimental Section

General: All reactions were carried out under Ar in carefully dried glassware. The solvents used were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et_2O (Mg/anthracene), CH_2Cl_2 (P_4O_{10}), MeCN, Et_3N (CaH_2), MeOH (Mg), DMF, DMA (Desmodur, dibutyltin dilaurate), hexane, toluene (Na/K). Flash chromatography: Merck silica gel 60 (230–400 mesh). NMR: Spectra were recorded on a Bruker DPX300 or DMX600 spectrometer in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling

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constants (J) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: $\delta_C = 77.0$ ppm; residual $CHCl_3$ in $CDCl_3$: $\delta_H = 7.24$ ppm; CD_2Cl_2: $\delta_C = 53.8$ ppm; residual CH_2Cl_2 in CD_2Cl_2: $\delta_H = 5.32$ ppm). IR: Nicolet FT-7199 spectrometer, wavenumbers in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: Finnigan MAT 95, accurate mass determinations: Bruker APEX III FT-MS (7 T magnet). Melting points: Gallenkamp melting point apparatus (uncorrected). Optical rotation: Perkin–Elmer 343 at $\lambda = 589$ nm (Na D-line). Elemental analyses: H. Kolbe, Mülheim/Ruhr. All commercially available compounds (Lancaster, Aldrich) were used as received.

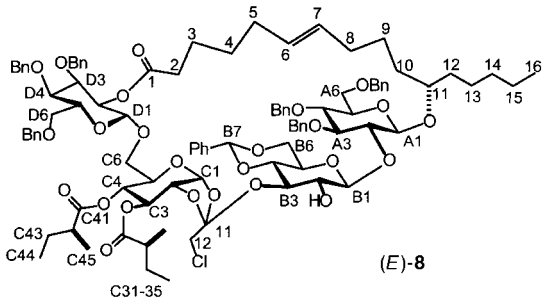
Tetrasaccharide 5: TMSOTf (1.1 mL of a 0.014 M stock solution in CH_2Cl_2) was added to a solution of diol **2** (100 mg, 0.12 mmol) and trichloroacetimidate **3** (169 mg, 0.15 mmol) in CH_2Cl_2 (1.2 mL) and the resulting mixture was stirred at ambient temperature for 3 h. The reaction was quenched with aq. sat. $NaHCO_3$ (5 mL), the aqueous phase was repeatedly extracted with CH_2Cl_2 (30 mL in several portions), the combined organic layers were dried (Na_2SO_4), the solvent was evaporated and the residue was purified by flash chromatography (pentane/EtOAc 84:16) affording product **5** as a colorless syrup (180 mg, 84%). ^{1}H NMR (300 MHz, CD_2Cl_2): $\delta = 7.31-7.15$ (m, 35H), 6.05 (br s, OH), 5.80–5.63 (m, 2H), 5.43 (d, $J = 5.6$ Hz, 1H), 5.35 (s, 1H), 5.21 (m, 1H), 5.06 (m, 1H), 4.96–4.41 (m, 24H), 4.31 (t, $J = 7.7$ Hz, 2H), 4.23 (dd, $J = 3.6$, 8.0 Hz, 1H), 4.18–4.11 (m, 2H), 3.83–3.45 (m, 20H), 3.44–3.26 (m, 4H), 3.12 (m, 1H), 2.34–1.88 (m, 6H), 1.58–1.10 (m, 12H), 0.96 (t, $J = 6.7$ Hz, 6H), 0.83–0.75 (m, 9H); ^{13}C NMR (75 MHz, CD_2Cl_2): $\delta = 175.4$, 175.1, 172.6, 139.2, 139.1, 138.8, 138.7, 138.6, 138.5, 138.4, 137.7, 137.6, 129.7, 129.0, 128.8, 128.7, 128.6, 128.5, 128.3, 128.2, 128.1, 127.9, 126.5, 118.7, 114.8, 114.7, 105.5, 102.4, 101.5, 101.4, 97.9, 84.1, 83.3, 81.7, 80.4, 79.6, 79.2, 78.3, 76.5, 76.1, 75.5, 75.3, 75.2, 75.1, 75.0, 74.5, 74.2, 73.9, 73.8, 72.9, 71.4, 69.1, 68.8, 68.0, 67.8, 67.3, 44.2, 41.2, 40.8, 34.9, 34.4, 34.1, 33.9, 33.6, 32.4, 28.8, 26.8, 26.6, 25.0, 24.6, 24.5, 23.1, 21.1, 16.5, 16.4, 14.4, 14.3, 14.2, 11.7, 11.6; MS (ESI): m/z: 1823 $[M+Na]^+$, 923; elemental analysis calcd (%) for $C_{103}H_{129}ClO_{25}$ (1802.56): C 68.63, H 7.21; found C 68.55, H 7.16.

Ring closing metathesis: A mixture of diene **5** (127 mg, 0.069 mmol) and the ruthenium complex **7** (7 mg, 0.007 mmol) in CH_2Cl_2 (50 mL) was heated under reflux for 24 h. The solvent was removed in vacuo and the residue was purified by flash chromatography (hexane/EtOAc 4:1) affording product **8** as a colorless solid (118 mg, 94%). M.p. 67–72 °C; $[\alpha]_D^{20} = -11.5$ ($c = 0.34$, CH_2Cl_2); IR (KAP): $\tilde{\nu} = 3423$, 3089, 3064, 3031, 2934, 2872, 1747, 1607, 1587, 1497, 1455, 1382, 1362, 1312, 1178, 1146, 1094, 1071, 1028, 915, 751, 736, 698; HR ESI-MS: calcd for $[C_{101}H_{125}ClO_{25}+Na]^+$: 1795.809616; found: 1795.80768 (Δ 1.08 ppm); elemental analysis calcd (%) for $C_{101}H_{125}ClO_{25}$ (1774.54): C 68.4, H 7.1; found: C 68.45, H 7.04. For a compilation of the NMR data of this compound see Table 1.

Pentasaccharide 9: A cooled solution of compound **8** (100 mg, 0.056 mmol) and TMSOTf (113 μL of a 0.01 M stock solution in CH_2Cl_2, 1.12×10^{-6} mol, 2 mol%) in Et_2O (1 mL) was stirred for 2 min at 0 °C. A solution of trichloroacetimidate **4** (57.5 mg, 0.101 mmol) in Et_2O (1 mL) was added dropwise through a syringe pump over a period of 20 min and stirring was continued for 30 min after the addition was completed. The reaction was quenched with sat. aq. $NaHCO_3$ (2 mL), the aqueous layer was extracted with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography (hexane/EtOAc 4:1) delivering product **9** as a colorless syrup (73.7 mg, 60%). $[\alpha]_D^{20} = -14.8$ ($c = 1.5$, CH_2Cl_2); IR (KAP): $\tilde{\nu} = 3089$, 3064, 3031, 2964, 2931, 2875, 1745, 1607, 1587, 1497, 1455, 1383, 1364, 1234, 1178, 1142, 1094, 1072, 1027, 925, 749, 735, 697; HR ESI-MS: calcd for $[C_{124}H_{157}ClO_{31}+Na]^+$: 2200.029505; found: 2200.03346 (Δ 1.79 ppm); elemental analysis calcd (%) for $C_{124}H_{157}ClO_{31}$ (2179.04): C 68.3, H 7.3; found C 68.22, H 7.26. For a compilation of the NMR data of this compound see Table 2.

Woodrosin I (1): Hydrazinium acetate (3.5 mg, 0.038 mmol) was added to a solution of compound **9** (65.4 mg, 0.030 mmol) in DMF (0.5 mL) and the resulting mixture was stirred for 15 min at $-10 \rightarrow 0$ °C. Et_2O (10 mL) was then added, the organic layer was successively washed with aq. HCl (1 N), water and brine (2 mL each), dried over Na_2SO_4 and evaporated. Pd on charcoal (10% w/w, 10 mg) was added to a solution of the residue in MeOH (2 mL) and the resulting suspension was stirred under an atmosphere of H_2 (1 atm) for 18 h. The catalyst was filtered off through a short pad of silica gel and the filtrate was evaporated, thus affording the title compound **1** as a colorless solid (34.9 mg, 84%). M.p. 145–147 °C (ref. [1]: 142–148 °C);

Table 1. NMR data (Bruker DMX-600) of compound (*E*)-**8** in [D_8]toluene at 300 K. The signal assignments are unambiguous, the numbering scheme is arbitrary and shown in the insert. Signals marked * might be mutually interchanged. The multiplicity in the ^{13}C NMR refers to the DEPT spectrum.[a]



No.	δ ^{13}C [ppm]	[b]	δ ^{1}H [ppm]	[b]	J [Hz]
A1	102.81	d	4.30	d	$J = 7.7$
A2	78.91	d	3.83	dd	$J = 7.7$, 9.1
A3	85.03	d	3.55		
A4	78.86	d	3.63		
A5	75.48	d	3.27		
A6	69.34	t	3.64, 3.62		
B1	130.75	d	4.68	d	
B2	74.59	d	3.50		
B3	74.46	d	3.96		
B4	80.47	d	3.19	t	$J = 9.4$
B5	66.85	d	3.15	m	
B6	68.88	t	3.98, 3.36		
B7	102.11	d	5.08	s	
C1	98.01	d	5.94	d	$J = 8.3$
C2	74.94	d	4.58		
C3	72.09	d	5.66	dd	$J = 3.2$, 4.3
C4	69.00	d	4.95	t	$J = 4.1$, 10.3
C5	69.54	d	4.73		
C6	69.88	t	4.10, 3.50	dd	$J = 11.5$, 1.7
D1	102.67	d	4.41	d	
D2	73.34	d	5.36	dd	$J = 9.5$, 8.0
D3	83.59	d	3.64		
D4	78.42	d	3.56		
D5	75.76	d	3.25	ddd	$J = 9.5$, 4.0, 2.3
D6	69.25	t	3.57		
1	171.61	s			
2	34.68	t	2.58	ddd	$J = 16.0$, 10.5, 5.6
			2.45	ddd	$J = 16.0$, 10.4, 5.9
5, 8	33.21, 32.96	t	2.16, 2.10	m	
6	131.60*	d	5.65*	m	
7	139.14*	d	5.57*	m	
10, 12	35.43, 34.22	t	1.80–1.35		
11	81.78	d	3.68	m	
15	23.19	t	1.80–1.35		
16	14.41	q	0.95	t	$J = 7.3$
3,4,9,	32.65, 30.20,25.32	t	1.88	m	
13,14	25.25, 25.13		1.80–1.35		
A3-Bn	76.04	t	4.86, 4.76	d	$J = 10.6$
A4-Bn	74.90	t	4.75, 4.58	d	$J = 11.5$
A6-Bn	73.77	t	4.51, 4.43	d	$J = 12.1$
C11	119.14	s			
C12	44.18	t	4.16, 3.95	d	$J = 12.8$
C31	174.34	s			
C32	40.97	d	2.23		
C33	26.60	t	1.66, 1.31		
C34	11.73	q	0.84	t	$J = 7.3$
C35	16.64	q	1.08	d	$J = 7.1$
C41	175.26	s			
C42	40.95	d	2.13	m	
C43	26.66	t	1.56, 1.23		
C44	11.60	q	0.75	t	$J = 7.4$

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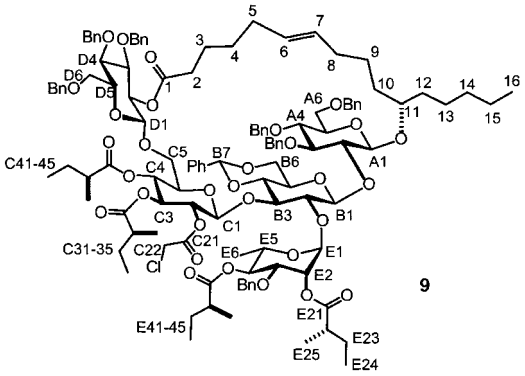
Table 1. (Continued)

No.	δ ^{13}C [ppm]	[b]	δ ^{1}H [ppm]	[b]	J [Hz]
C45	16.35	q	0.99	d	$J = 7.1$
D3-Bn	74.82	t	4.71	d	
D4-Bn	74.86	t	4.68, 4.44	d	
D6-Bn	73.60	t	4.42, 4.37	d	$J = 12.1$

[a] Signals of the phenyl rings: ^{13}C NMR: $\delta = 139.30$, 139.24, 139.04, 138.90, 138.89, 138.51, 137.91 (s each); further signals are obscured by the resonances of the solvent ([D$_8$]toluene); ^{1}H NMR: $\delta = 7.44 - 7.05$ (m). [b] Multiplicity of the signals.

Table 2. NMR data (Bruker DMX-600) of compound **9** in [D$_8$]toluene at 300 K. The signal assignments are unambiguous, the numbering Scheme is arbitrary and shown in the insert. Signals marked * might be mutually interchanged. The multiplicity in the ^{13}C NMR refers to the DEPT spectrum.[a]



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No.	δ ^{13}C [ppm]	[b]	δ ^{1}H [ppm]	[b]	J(C,H) [Hz]
A1	101.97	d	4.57	d	$J = 7.5$
A2	77.98	d	4.16	dd	$J = 7.5$, 8.7
A3	87.12	d	4.01	t	$J = 8.9$
A4	79.18	d	3.76		
A5	75.58	d	3.51		
A6	69.47	t	3.73		
B1	101.12	d	5.33	d	$J = 7.6$
B2	76.49	d	4.06		
B3	82.95	d	4.21		
B4	80.87	d	4.20		
B5	67.33	d	3.31	m	
B6	68.76	t	4.19, 4.09		
B7	101.74	d	6.05	s	
C1	99.22	d	5.33	d	$J = 8.3$
C2	75.21	d	5.07	dd	$J = 8.2$, 9.3
C3	73.34	d	5.25	t	$J = 9.3$
C4	68.91	d	5.05	t	$J = 9.5$
C5	73.97	d	3.57		
C6	68.35	t	3.57		
D1	101.52	d	4.10	d	$J = 8.2$
D2	72.73	d	5.23	dd	$J = 9.5$, 8.2
D3	83.34	d	3.53		
D4	78.11	d	3.49		
D5	75.71	d	3.20	ddd	$J = 9.5$, 4.0, 2.3
D6	69.32	t	3.56		
E1	99.03	d	5.61	d	$J = 1.9$
E2	68.13	d	5.81	dd	$J = 3.0$, 1.9
E3	76.55	d	4.31	dd	$J = 9.8$, 3.2
E4	72.91	d	5.57	t	$J = 10.0$
E5	67.33	d	4.88	dd	$J = 10.1$, 6.2
E6	18.41	q	1.53	d	$J = 6.2$
1	172.19	s			
2	34.26	t	2.38, 2.36		
3	23.89	t	1.86	m	
4, 7	33.16, 31.65	t	2.30, 2.22, 2.15, 2.13		
5	131.48*	d	5.63	m	
6	131.51*	d	5.63	m	
8, 9,	27.95,	t	1.66, 1.54,		
13	25.37, 25.16		1.60, 1.54		
10, 12	35.64, 33.82	t	1.76, 1.68, 1.66, 1.58		
11	80.20	d	3.74		
14	32.63	t	1.35		
15	23.23	t	1.35		
16	14.46	q	0.94	t	$J = 7.0$
A3-Bn	75.25	t	5.08, 5.21	d	$J = 11.5$
A4-Bn	74.81	t	4.70, 4.59	d	$J = 11.5$
A6-Bn	73.87	t	4.57, 4.49	d	$J = 12.1$
C21	166.44	s			
C22	40.31	t	3.74		
C31	175.14	s			
C32	41.01	d	2.17		
C33	26.54	t	1.61, 1.26		
C34	11.60	q	0.75	t	$J = 7.4$
C35	16.29	q	1.00	d	$J = 7.0$
C41	174.90	s			
C42	40.93	d	2.13		
C43	26.72	t	1.62, 1.29		
C44	11.78	q	0.79	t	$J = 7.4$
C45	16.49	q	0.99	d	$J = 7.0$
D3-Bn	75.06	t	4.69, 4.64	d	$J = 11.6$
D4-Bn	74.93	t	4.70, 4.45	d	$J = 11.3$
D6-Bn	73.62	t	4.45, 4.38	d	$J = 12.5$
E21	175.67	s			
E22	41.26	d	2.47	m	
E23	27.39	t	1.78, 1.47		
E24	11.63	q	0.93	t	$J = 7.4$
E25	16.53	q	1.19	d	$J = 7$
E41	174.80	s			
E42	41.85	d	2.38		
E43	27.13	t	1.76, 1.34		
E44	11.98	q	0.82	t	$J = 7.4$
E45	17.25	q	1.12	d	$J = 7$
E3-Bn	71.66	t	4.97, 4.41	d	$J = 11.5$

[a] Signals of the phenyl rings: ^{13}C NMR: $\delta = 139.09$, 139.05, 139.02, 138.99, 138.90, 138.84, 138.74, 138.69 (s each); further signals are obscured by the resonances of the solvent ([D$_8$]toluene); ^{1}H NMR: $\delta = 7.84 - 7.00$ (m). [b] Multiplicity of the signals.

$[\alpha]_D^{20} = -25.2$ ($c = 1.4$, MeOH) [ref. [1]: $[\alpha]_D^{25} = -25.4$ ($c = 2.9$, MeOH)]; IR (KAP): $\tilde{\nu} = 3448$, 2967, 2933, 2877, 1744, 1463, 1384, 1261, 1187, 1150, 1077, 1031, 895; the spectroscopic and analytical data of **1** are in full agreement with those reported in ref. [1]. For a comparison see Tables 3 and 4.

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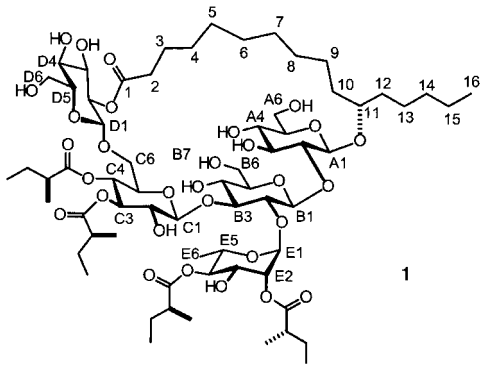
Table 3. Comparison of the published ^{13}C NMR data of woodrosin I with those of the synthetic sample (in both cases in [D_5]pyridine, 150 MHz); n.r. = not reported.



1

No.	δ ^{13}C (ppm)	[a]	Ref. [1]
A1	104.01	d	104.0
A2	78.97	d	79.1
A3	79.88	d	79.9
A4	71.88	d	71.8
A5	78.30	d	78.3
A6	62.76	t	62.7
B1	100.91	d	100.9
B2	75.55	d	75.5
B3	90.03	d	89.8
B4	70.71	d	70.6
B5	77.47	d	77.5
B6	63.00	t	63.0
C1	104.09	d	104.0
C2	72.61	d	72.6
C3	75.97	d	75.8
C4	68.97	d	69.0
C5	73.39	d	73.3
C6	66.43	t	66.2
D1	102.11	d	102.1
D2	75.09	d	75.0
D3	76.10	d	76.1
D4	71.67	d	71.6
D5	79.15	d	78.9
D6	62.30	t	62.3
E1	97.91	d	97.8
E2	73.45	d	73.4
E3	67.65	d	67.6
E4	75.45	d	75.4
E5	66.90	d	66.9
E6	18.74	q	18.7
1	173.23	s	n.r.
2	34.45	t	n.r.
3	25.46	t	n.r.
4	28.79	t	n.r.
5, 6, 7, 8	31.11, 30.71, 30.06, 29.44	t	n.r.
9, 13	25.56, 25.37	t	n.r.
10	35.41	t	n.r.
11	82.94	d	n.r.
12	35.90	t	n.r.
14	32.37	t	n.r.
15	22.92	t	n.r.
16	14.27	q	n.r.

[a] Refers to the multiplicity in the DEPT spectrum.

Table 4. Comparison of the published ^1H NMR data of woodrosin I with those of the synthetic sample (in both cases in [D_5]pyridine, 600 MHz). For the chosen numbering Scheme see the insert in Table 3; n.r. = not reported.

No.	δ (muliplictiy, J [Hz])	Ref. [1]
A1	4.88 (d, J = 7.6)	4.89 (d, J = 7.5)
A2	4.39 (dd, J = 7.6, 9.0)	4.39 (dd, J = 9.1, 7.5)
A3	4.45 (m)	4.45 (dd, J = 9.1, 9.1)
A4	4.11 (t, J = 9.2)	4.11 (dd, J = 9.1, 9.1)
A5	3.90 (m)	ca. 3.88
A6	4.50 (dd, J = 2.5, 11.6)	4.50 (dd, J = 2.2, 11.7)
	4.34 (dd, J = 5.1, 11.6)	4.34 (dd, J = 5.1, 11.7)
B1	5.84 (d, J = 7.7)	5.84 (d, J = 8.1)
B2	4.17 (m)	4.16 (dd, J = 8.1, 8.6)
B3	3.92 (m)	ca. 3.92
B4	3.92 (m)	ca. 3.92
B5	3.70 (m)	3.71 (ddd, J = 2.9, 5.8, 9.3)
B6	4.45, 4.20 (m)	4.20 (dd, J = 5.8, 11.7)
		4.46 (dd, J = 2.9, 11.7)
C1	4.90 (d, J = 7.3)	4.90 (d, J = 7.7)
C2	3.93 (m)	ca. 3.91
C3	5.57 (t, J = 9.4)	5.59 (dd, J = 9.4, 9.4)
C4	5.48 (dd, J = 9.4, 9.9)	5.49 (dd, J = 9.4, 9.4)
C5	3.88 (m)	ca. 3.88
C6	4.09 (dd, J = 2.7, 12.4)	4.10 (dd, J = 2.6, 12.6)
	4.01 (dd, J = 4.2, 12.4)	4.01 (dd, J = 4.0, 12.5)
D1	4.95 (d, J = 8.0)	4.97 (d, J = 8.1)
D2	5.49 (dd, J = 8.0, 9.4)	5.49 (dd, J = 8.1, 9.4)
D3	4.30 (t, J = 9.4)	4.30 (dd, J = 9.4, 9.4)
D4	4.20 (m)	4.19 (dd, J = 9.4, 9.4)
D5	3.85 (m)	ca. 3.86
D6	4.46, 4.31 (m)	4.31 (dd, J = 4.7, 11.7)
		4.44 (dd, J = 2.9, 11.7)
E1	6.25 (d, J = 1.5)	6.24 (d, J = 1.5)
E2	5.87 (dd, J = 1.5, 3.4)	5.86 (dd, J = 1.5, 3.7)
E3	4.92 (dd, J = 3.4, 9.9)	4.93 (dd, J = 3.7, 9.9)
E4	5.69 (t, J = 9.4)	5.70 (dd, J = 9.9, 9.9)
E5	5.19 (dq, J = 6.2, 9.9)	5.19 (dq, J = 9.9, 6.2)
E6	1.67 (d, J = 6.2)	1.67 (d, J = 6.2)
2a	2.57 (dt, J = 7.4, 16.1)	n.r.
2b	2.43 (dt, J = 6.8, 16.1)	n.r.
3	1.82, 1.55 (m)	n.r.
4	1.46, 1.26 (m)	n.r.
5–8	1.46–1.24, 1.31–1.20 (m)	n.r.
9,13	1.96, 1.72, 1.48, 1.44 (m)	n.r.
10	1.73, 1.69 (m)	n.r.
11	3.86 (m)	n.r.
12	1.96, 1.66 (m)	n.r.
14	1.23, 1.20 (m)	n.r.
15	1.23 (m)	n.r.
16	0.81 (t, J = 7.0)	n.r.

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