

Straightforward Synthesis of Aromatic Polycyclic Terpenoids through Biomimetic Cascade Cyclizations Triggered by Photochemical Electron Transfer

Viale Rosales,^[a] Jorge Zambrano,^[b] and Martin Demuth^{*[a]}

Keywords: Biomimetic cascade cyclizations / Biomimetic synthesis / Natural products / Photochemical electron transfer / Terpenoids

Photoinduced biomimetic cascade cyclizations of suitably functionalized terpenoid arylpolyalkenes via radical cationic intermediates represent a powerful route to polycyclic compounds in a single operational step. In all cases examined, the radical cation, created selectively and exclusively at the ω -polyalkene position, is trapped in *anti*-Markovnikov fashion by water, liberating a free radical site, which ultimately initiates cascade-style bond formation to afford the all-chair

polycyclic conformation containing one aromatic moiety. The products, some of which are podocarpic-type structures **17–19**, are beneficially 3 β -hydroxylated. Mechanistically, the reaction is probably initiated by a radical cation trapped by water prior to the cyclization event, which is driven by a pure radical-type process.

(© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2004)

Introduction

Biomimetic polycyclizations of acyclic terpenoid polyalkenes to natural products and their precursors through photochemical electron transfer (PET) have been shown to constitute a powerful synthetic method.^[1–4] This methodology is based on the highly regioselective creation of a radical cation at the ω -alkene site of the starting acyclic polyalkene (**1a–c** $\rightarrow$ **2** in Scheme 1), which is in turn regio- and stereoselectively trapped in an *anti*-Markovnikov sense by a nucleophile (Nu) such as water or methanol along the major reaction path (**2** $\rightarrow$ **3**).^[1] As a mechanistic consequence, the resulting tertiary radical centre in **3** (Scheme 1) gives rise to cascade polycyclizations yielding *trans,anti,trans*-all-chair products which are beneficially 3 β -hydroxylated (**4a–c** and **5a–c**).^[2]

The termination of such processes involves saturation of the radical centres, giving either six-membered ring products or mixed structures containing six-membered rings and/or one terminal five-membered ring, depending on the electron-donating and -withdrawing capacities of the substituents R¹ and R².^[1] There are numerous reports regarding the isolation of^[3–6] and biological data for^[7–9] these

3 β -hydroxylated compounds. However, synthetic work on these structures is scarce.

Our previously developed photoelectron transfer (PET) methodology has emerged as a viable alternative to analogous structures of known polycyclic compounds containing a 3 β -hydroxy group and one terminal aromatic ring.^[10]

Results and Discussion

The starting materials **10–15** (Scheme 2) for the corresponding photochemical transformations en route to the products **16–21** [Equation (1), Table 1], are readily available through an efficient and highly regioselective palladium-catalysed coupling of the allylic halides **6–9** with benzylic Grignard reagents (Scheme 2).^[11]

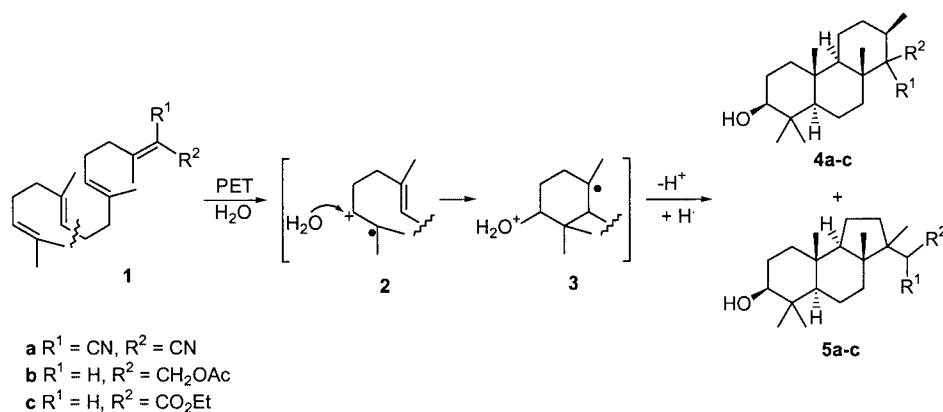
The conditions for the photochemically triggered single-electron transfer have been adopted from earlier work in this field. As a result, the best conditions resulted from irradiation of the samples with light ($\lambda_{\text{max.}} = 300 \text{ nm}$, Rayonet reactor) in CH₃CN/water (4:1) solutions in the presence of an electron-acceptor couple such as 1,4-dicyanotetramethylbenzene (DCTMB, 25 mol %) and 1,1'-biphenyl (BP, 28 mol %) at -10°C .^[2,12,13]

While the spectroscopic data (¹H and ¹³C NMR, IR, elemental analyses and LR/HRMS) for compounds **16–21** were completely consistent with their structures, further confirmation was sought by means of single-crystal X-ray analyses of **20**^[14] and **21**.^[15]

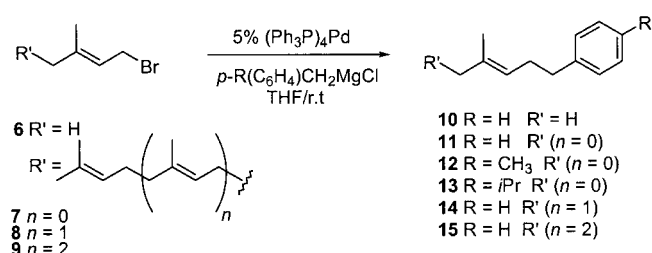
^[a] Max Planck Institute for Bioinorganic Chemistry (former MPI for Radiation Chemistry)
45413 Mülheim an der Ruhr, Germany
E-mail: demuthm@mpi-muelheim.mpg.de

^[b] Universidad Simón Bolívar, Departamento de Química,
Valle de Sartenejas, Baruta, Caracas D.C. 1080-A, Apartado 89000, Venezuela

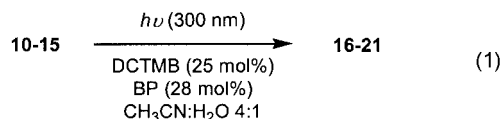
Supporting information for this article is available on the WWW under <http://www.eurjoc.org> or from the author.



Scheme 1. PET-triggered tricyclizations of polyalkenes



Scheme 2. Pd-catalysed allylic alkylation of polyene halides with benzylic Grignard reagents



Mechanistically, the photochemically induced electron-transfer reactions **10–15** $\rightarrow$ **16–21** are assumed to follow the reaction scheme proposed and substantiated for the conversion of non-aromatic acyclic polyterpenoids (Scheme 1),^[2] except for the termination step. Analogously with the generally proposed mechanistic pathway,^[2,16–18] the aromatic polyalkene (i.e., **15**) should, prior to or after electron transfer, adopt the all-*trans*-prechair conformation **A** (Scheme 3), uniformly giving rise to *anti,trans*-fused polycyclic compounds. In the course of these reactions, the electron transfer to the excited acceptor (DCTMB*)^[19] from BP gives rise to a DCTMB^{•–}/BP^{•+} pair.^[1] Subsequently, single-electron transfer from the arylpolyalkene **15** to BP^{•+} regioselectively oxidizes the ω -alkene of the arylpolyalkene **A** (Scheme 3).^[20] The initially formed arylpolyalkene radical cation (Scheme 3, **A**) is regio- (*anti*-Markovnikov)^[21] and stereoselectively (β -face)^[22] trapped by the nucleophile, such as water in the present case (for applications with other nucleophiles, see refs.^[2,21,23]). The resulting β -distonic radical cation^[24] would be expected to undergo rapid deprotonation^[23a,25] to afford neutral β -hydroxy radicals, which would in turn be able to initiate the cyclization, which is ultimately driven by a pure radical-type mechanism.^[1,26] The intramolecular addition of a tertiary radical centre to

an alkene proceeds in a cascade 6-*endo*-trig fashion to form the all-*trans*-fused radical intermediate **B** (Scheme 3). The radical intermediate **B** is finally oxidized to afford the aromatic product **21** (Scheme 3). This mechanistic event is unprecedented in photoelectron transfer chemistry, although in the termination step (**B** $\rightarrow$ **21**, Scheme 3) it parallels analogous transformations of aromatic polyalkene terpenoids through application of radical chemistry.^[27–29] Notably, this finding gives further support in favour of our proposed mechanism (Scheme 3).^[30] The termination of such a cascade cyclization probably involves electron transfer from **B** (Scheme 3) to the oxidizing species (BP^{•+} or DCTMB), followed by loss of a proton.^[31]

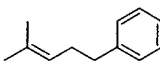
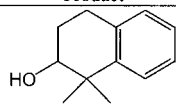
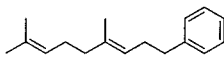
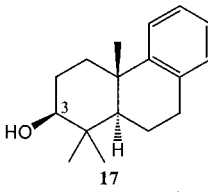
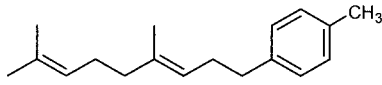
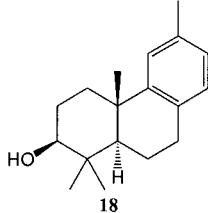
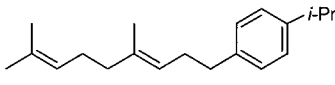
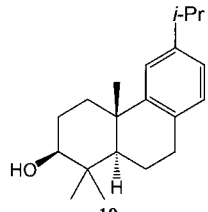
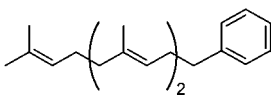
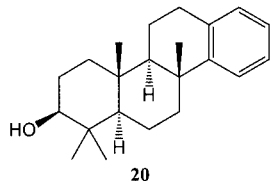
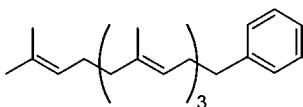
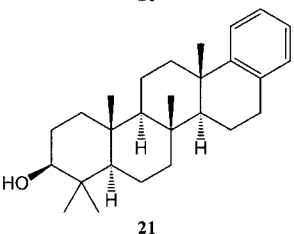
The photochemical transformations summarized in Table 1 represent highly stereo- and regioselective syntheses of all-*trans,anti*-fused polycyclic products, some of which are podocarpa-type structures **17–19**, from readily available arylpolyalkenes. Notably, all products are beneficially and exclusively β -hydroxylated through the addition of water, these results constituting strong evidence for spontaneous folding of the arylpolyalkene chain and supporting the idea of “minimal enzymatic assistance” in non-oxidative biosynthesis.^[32]

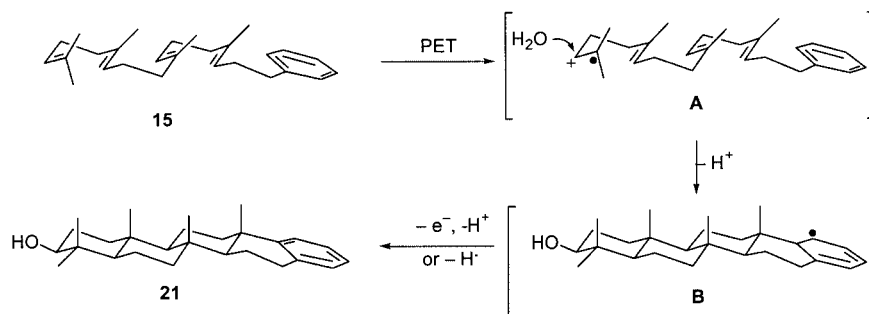
The relative stereochemical configurations (*trans*-fused for **17**, **18**, **19**, *trans,anti,trans*-fused for **20** and *trans,anti,trans,anti,trans*-fused for **21**) assigned to our newly synthesized compounds were determined by detailed 1D and 2D NMR analysis. The known γ -*gauche* effects support the *trans,transoid* stereochemistry.^[33] The bridged methine groups show a low-field ¹³C NMR chemical shift indicating the absence of γ -*gauche* effects with angular methyl groups. The stereochemistry of the 3-OH group (β -face) was assigned from the chemical shifts observed for neighbouring geminal methyl groups.^[34]

Conclusion

The photochemical transformations summarized in Table 1 constitute straightforward stereo- and regioselective syntheses of highly functionalized terpenoids, each in a sin-

Table 1. Synthesis of polycyclic compounds through PET; conditions: 1,4-dicyanotetramethylbenzene (DCTMB, 25 mol %), biphenyl (BP, 28 mol %), CH₃CN/H₂O (4:1), λ_{max} = 300 nm, -10 °C

Starting Olefin	Product	Yield (%)
		40
		22–25
		22–25
		25
		18
		9



Scheme 3. Biomimetic polyalkene cyclization **15** → **21** through PET

gle step from readily available acyclic terpenoid arylpolyalkenes. These photochemical processes triggered by radical cation formation and followed by nucleophile addition (i.e., water in the present case), closely mimic the proposed biosynthetic principle of such cyclizations. This novel methodology has allowed the syntheses of two new (**18** and **19**) and four known compounds (**16**,^[35] **17**,^[36] **20**^[14] and **21**^[15]), the latter class, however, by routes much shorter than known in the literature. The transformations described in this paper represent a powerful synthetic method for a single-step build-up of arrays of up to seven stereogenic centres.

Experimental Section

General: All manipulations of compounds and solvents were carried out by use of standard airless techniques. All glassware was flame-dried and purged with argon prior to use. Solvents: acetonitrile (PA grade) was purchased from Fluka and used directly. Reagents: 1,4-dicyanotetramethylbenzene (DCTMB) was prepared by a known procedure.^[37] All samples were stirred and flushed with argon prior to irradiation. Cylindrical Pyrex vessels equipped with cooling fingers (2-propanol coolant) were used. Rayonet reactors (RPR-100-System, Southern New England Ultraviolet company) with sixteen 300-nm (λ_{max}) lamps (8 Watt/lamp) were employed. Melting points were obtained with a Reichert or a Kofler apparatus and are uncorrected. Spectroscopic measurements were recorded for CDCl₃ solutions with the following Bruker instruments: DRX 500 (500 MHz for ¹H, 125.8 MHz for ¹³C), AM 400 (400 MHz for ¹H, 100.6 MHz for ¹³C), JEOL (400.10 MHz for ¹H, 100.6 MHz for ¹³C) or ARX 250 (250 MHz for ¹H, 62.9 MHz for ¹³C). Chemical shifts are reported in δ units (ppm) relative to tetramethylsilane (Me₄Si), the residual CHCl₃ resonance in ¹H spectra being assigned at δ = 7.24 ppm and the CDCl₃ resonance in ¹³C spectra at δ = 77.0 ppm. All coupling constants (*J*) are reported in Hz. High resolution mass spectra (HRMS) were recorded with a Finnigan MAT 95 instrument at 70 eV ionization energy. Column chromatography was performed on Merck silica gel 60 (0.063–0.20 mm or 0.04–0.063 mm). All reactions were monitored by TLC on Merck silica gel 60 F₂₅₄ precoated aluminium plates and were viewed with the aid of UV light followed by spraying with acidic vanillin solution. Elemental analysis was performed by Dornis and Kolbe, Mülheim an der Ruhr.

General Procedure for the Cyclization of Polyenes through PET: An argon-flushed solution (CH₃CN/H₂O, 4:1, 0.04 M solution of olefin) of the starting arylpolyene **10–15**, biphenyl (28 mol %) and 1,4-dicyanotetramethylbenzene (25 mol %) in a Pyrex vessel was irradiated (λ_{max} = 300 nm) at –10 °C in a Rayonet reactor for 24–30 h. The resulting clear yellowish solution was concentrated at reduced pressure to give a pale yellow solid. Additional water was added, and the resulting aqueous phase was extracted with dichloromethane. The organic phase was dried (MgSO₄) and then concentrated under vacuum. The residue was chromatographed (up to 3 times) on silica gel with pentane/10% ethyl acetate/pentane as eluent to afford the corresponding polycyclic products **16–21**.

1,1-Dimethyl-1,2,3,4-tetrahydronaphthalen-2-ol (16):^[35] Yield: 0.5 g (40%). White solid; m.p. 85–87 °C. IR (KBr): $\tilde{\nu}$ = 3317 (OH, br. s), 2922, 1488, 1059, 758 cm^{–1}. ¹H NMR: δ = 1.32 (s, 3 H), 1.38 (s, 3 H), 1.88–2.12 (m, 2 H), 2.15 (br. s, OH), 2.81–3.06 (m, 2 H), 3.77 (dd, *J* = 8.6, 3.4 Hz, 1 H), 7.09 (dd, *J* = 7.5, 1.5 Hz, 1 H),

7.15 (td, *J* = 7.5, 1.5 Hz, 1 H), 7.21 (td, *J* = 7.5, 0.7 Hz, 1 H), 7.38 (dd, *J* = 7.5, 1.1 Hz, 1 H) ppm. ¹³C NMR: δ = 24.9, 26.7, 27.0, 29.0, 39.0, 75.4, 125.5, 126.1, 126.7, 128.6, 134.4, 144.2 ppm. HRMS (EI): *m/z* calcd. 176.1201 [M⁺]; found 176.1202. C₁₂H₁₆O (176.2): calcd. C 81.77, H 9.15; found C 81.69, H 9.21.

1,1,4a-Trimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-2 β -ol (17):^[22] Yield: 0.2 g (25%). White solid; m.p. 82–85 °C. IR (KBr): $\tilde{\nu}$ = 3355 (br. s, OH), 2962, 2929, 2869, 1488, 1477, 1448, 1375, 1186, 1091, 1029, 759 cm^{–1}. ¹H NMR: δ = 0.90 (s, 3 H), 1.07 (s, 3 H), 1.20 (s, 3 H), 1.33 (dd, *J* = 12.4, 2.3 Hz, 1 H), 1.55 (td, *J* = 12.8, 4.6 Hz, 1 H), 1.57 (br. s, OH), 1.71–1.79 (m, 2 H), 1.83 (dddd, *J* = 13.3, 5.0, 4.6, 3.7 Hz, 1 H), 1.88 (ddt, *J* = 13.3, 7.3, 1.8 Hz, 1 H), 2.32 (dt, *J* = 12.8, 3.7 Hz, 1 H), 2.86 (ddd, *J* = 16.9, 11.5, 7.3 Hz, 1 H), 2.97 (dd, *J* = 16.9, 6.4 Hz, 1 H), 3.30 (dd, *J* = 11.0, 5.0 Hz, 1 H), 7.04 (d, *J* = 7.3 Hz, 1 H), 7.07 (td, *J* = 7.3, 1.4 Hz, 1 H), 7.12 (t, *J* = 7.4 Hz, 1 H), 7.23 (d, *J* = 7.3 Hz, 1 H) ppm. ¹³C NMR: δ = 15.4, 18.8, 24.9, 27.9, 28.1, 30.6, 36.9, 37.6, 39.0, 49.7, 78.7, 124.4, 125.4, 125.7, 128.9, 134.9, 149.3 ppm. HRMS (EI): *m/z* calcd. 244.1827 [M⁺]; found 244.1827. C₁₇H₂₄O (244.38): calcd. C 83.55, H 9.90; found C 83.39, H 9.96.

1,1,4a,6-Tetramethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-2 β -ol (18): Yield: 0.15 g (25%). White solid; m.p. 95–96 °C. IR (KBr): $\tilde{\nu}$ = 3354 (br., OH), 2965, 2944, 2870, 1606, 1501, 1455, 1366, 1034, 806 cm^{–1}. ¹H NMR: δ = 0.89 (s, 3 H), 1.06 (s, 3 H), 1.19 (s, 3 H), 1.31 (dd, *J* = 12.4, 2.3 Hz, 1 H), 1.54 (td, *J* = 13.3, 4.6 Hz, 1 H), 1.83–1.74 (m, 3 H), 1.88 (ddt, *J* = 13.3, 7.3, 1.8 Hz, 1 H), 2.28 (s, 3 H), 2.31 (dt, *J* = 13.3, 3.7 Hz, 1 H), 2.81 (ddd, *J* = 16.9, 11.5, 7.3 Hz, 1 H), 2.92 (dd, *J* = 16.9, 6.4 Hz, 1 H), 3.29 (dd, *J* = 11.5, 5.0 Hz, 1 H), 6.89 (d, *J* = 7.8 Hz, 1 H), 6.93 (d, *J* = 7.8 Hz, 1 H), 7.03 (s, 1 H) ppm. ¹³C NMR: δ = 15.4, 18.9, 21.2, 24.8, 28.0, 28.2, 30.2, 36.9, 37.6, 39.0, 49.9, 78.7, 124.9, 126.3, 128.9, 131.8, 134.9, 149.2 ppm. HRMS (EI): *m/z* calcd. 258.1983 [M⁺]; found 258.1984. C₁₈H₂₆O (258.4): calcd. C 83.67, H 10.14; found C 83.76, H 10.08.

6-Isopropyl-1,1,4a-trimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-2 β -ol (19): Yield: 0.14 g (25%). White solid; m.p. 81–83 °C. IR (KBr): $\tilde{\nu}$ = 3312 (br. s, OH), 2963, 2866, 1611, 1458, 1261, 1027, 809 cm^{–1}. ¹H NMR: δ = 0.89 (s, 3 H), 1.06 (s, 3 H), 1.20 (d, *J* = 0.6 Hz, 3 H), 1.22 (dd, *J* = 7.0, 0.5 Hz, 6 H), 1.33 (dd, *J* = 12.2, 2.4 Hz, 1 H), 1.48 (br. s, OH), 1.55 (td, *J* = 12.9, 4.6 Hz, 1 H), 1.74–1.82 (m, 3 H), 1.88 (ddt, *J* = 13.4, 7.5, 2.1 Hz, 1 H), 2.34 (dt, *J* = 13.0, 3.5 Hz, 1 H), 2.79–2.81 (m, 1 H), 2.84 (sept, *J* = 7.0 Hz, 1 H), 2.93 (ddd, *J* = 17.0, 6.8, 1.9 Hz, 1 H), 3.30 (dd, *J* = 11.3, 5.3 Hz, 1 H), 6.96–6.97 (m, 2 H), 7.09 (s, 1 H) ppm. ¹³C NMR: δ = 15.4, 18.9, 24.2, 24.9, 28.0, 28.2, 30.3, 34.0, 36.9, 37.7, 39.0, 49.9, 78.8, 122.5, 123.4, 128.9, 132.4, 146.2, 149.2 ppm. HRMS (EI): *m/z* calcd. 286.2297 [M⁺]; found 286.2298. C₂₀H₃₀O (286.4): calcd. C 83.86, H 10.56; found C 83.74, H 10.50.

1,1,4a,10b-Tetramethyl-1,2,3,4,4a,5,6,6b,11,12,12a,12b-dodecahydrochrysen-2 β -ol (20): Yield: 0.1 g (18%). White solid; m.p. 164–166 °C. IR (KBr): $\tilde{\nu}$ = 3446 (br., OH), 2992, 2965, 2931, 2869, 1774, 1706, 1602, 1488, 1448, 1384, 1377, 1365, 1095, 1042, 1030, 983, 724 cm^{–1}. ¹H NMR: δ = 0.82 (s, 3 H), 0.84 (dd, *J* = 11.9, 2.3 Hz, 1 H), 0.93 (s, 3 H), 0.98 (s, 3 H), 1.01 (td, *J* = 12.8, 5.0 Hz, 1 H), 1.19 (s, 3 H), 1.24 (dd, *J* = 12.4, 2.2 Hz, 1 H), 1.43 (br. s, OH), 1.48 (td, *J* = 12.8, 3.7 Hz, 1 H), 1.59 (qd, *J* = 13.3, 2.8 Hz, 1 H), 1.59–1.70 (m, 3 H), 1.73 (dq, *J* = 13.3, 3.2 Hz, 1 H), 1.83 (ddt, *J* = 14.7, 7.3, 2.2 Hz, 1 H), 1.85 (dt, *J* = 12.8, 3.7 Hz, 1 H), 2.40 (dt, *J* = 12.4, 3.2 Hz, 1 H), 2.81 (ddd, *J* = 17.4, 11.5, 7.3 Hz, 1 H), 2.92 (dd, *J* = 16.9, 5.9 Hz, 1 H), 3.20 (dd, *J* = 11.0, 5.0 Hz, 1 H), 7.00 (d, *J* = 7.3 Hz, 1 H), 7.05 (td, *J* = 7.3, 0.9 Hz, 1 H), 7.11 (t, *J* = 7.3 Hz, 1 H), 7.23 (d, *J* = 7.3 Hz, 1 H) ppm. ¹³C NMR:

δ = 15.3, 16.3, 18.1, 18.8, 26.0, 27.3, 27.9, 30.7, 37.4, 37.9, 38.3, 38.9, 40.6, 55.1, 55.2, 78.9, 124.6, 125.2, 125.7, 128.8, 134.9, 150.0 ppm. HRMS (EI): m/z calcd. 312.2453 [M^+]; found 312.2455. $C_{22}H_{32}O$ (312.5): calcd. C 84.56, H 10.32; found C 84.43, H 10.30.

4,4,6a,12b,14b-Pentamethyl-1,2,3,4,4a,5,6,6a,6b,7,8,12b,13,14,14a,14b-hexadecahydricen-3 β -ol (21):^[15] Yield: 80 mg (9%). White solid; m.p. 150–154 °C. IR (KBr): $\tilde{\nu}$ = 3421 (br, OH), 2962, 2962, 2932, 2870, 1488, 1447, 1384, 1262, 1094, 1027, 907, 803, 731 cm^{-1} . 1H NMR: δ = 0.74 (dd, J = 12.6, 2.7 Hz, 1 H), 0.77 (s, 3 H), 0.78 (dd, J = 11.8, 2.2 Hz, 1 H), 0.85 (s, 3 H), 0.92 (s, 3 H), 0.92 (td, J = 12.4, 4.6 Hz, 1 H), 0.93–0.94 (m, 1 H), 0.95 (s, 3 H), 1.17 (s, 3 H), 1.23 (br. s, OH), 1.25 (dd, J = 12.1, 2.2 Hz, 1 H), 1.45 (td, J = 12.7, 3.3 Hz, 1 H), 1.51–1.69 (m, 2 H), 1.40–1.70 (m, 5 H), 1.74 (dt, J = 12.9, 3.6 Hz, 1 H), 1.81 (ddt, J = 13.3, 7.5, 2.2 Hz, 1 H), 1.91 (dt, J = 12.9, 3.3 Hz, 1 H), 2.36 (dt, J = 12.4, 3.0 Hz, 1 H), 2.80 (ddd, J = 17.1, 11.3, 7.2 Hz, 1 H), 2.90 (ddd, J = 16.9, 5.5, 1.4 Hz, 1 H), 3.17 (dd, J = 10.5, 5.3 Hz, 1 H), 6.99 (dd, J = 7.5, 0.8 Hz, 1 H), 7.03 (td, J = 7.5, 1.1 Hz, 1 H), 7.09 (tt, J = 7.7, 0.8 Hz, 1 H), 7.21 (dd, J = 8.0, 1.1 Hz, 1 H) ppm. ^{13}C NMR: δ = 15.2, 16.3, 17.4, 18.0, 18.0, 18.1, 26.1, 27.4, 27.9, 30.9, 37.2, 37.8, 38.1, 38.3, 38.9, 40.6, 41.8, 55.5, 55.6, 60.7, 78.9, 124.6, 125.1, 125.7, 128.8, 135.1, 150.2 ppm. HRMS (EI): m/z calcd. 380.3079 [M^+]; found 380.3077. $C_{27}H_{40}O$ (380.6): calcd. C 85.20, H 10.59; found C 84.75, H 11.34.

Acknowledgments

We thank the Ministerium für Wissenschaft und Forschung des Landes Nordrhein Westfalen (Germany) for research grants partly supporting this work.

- [1] K.-D. Warzecha, X. Xing, M. Demuth, *Pure Appl. Chem.* **1997**, 69, 109–112.
- [2] K.-D. Warzecha, X. Xing, M. Demuth, R. Goddard, M. Kessler, C. Krüger, *Helv. Chim. Acta* **1995**, 78, 2065–2076.
- [3] Y. Orihara, J.-W. Yang, N. Komiya, K. Koge, T. Yoshikawa, *Phytochemistry* **2002**, 59, 385–389.
- [4] I. Ara, B. S. Siddiqui, S. Faizi, S. Siddiqui, *J. Nat. Prod.* **1990**, 53, 816–820.
- [5] Y. Takaishi, N. Wariishi, H. Tateishi, K. Kawazoe, K. Miyagi, K. Li, H. Duan, *Phytochemistry* **1997**, 45, 979–984.
- [6] R. Fujita, H. Duan, Y. Takaishi, *Phytochemistry* **2000**, 53, 715–722.
- [7] Antioxidant: H. Haragushi, H. Ishikawa, I. Kubo, *Planta Med.* **1997**, 63, 213–215.
- [8] Cathartic and emetic: G. Appendino, E. Belloro, G. C. Tron, J. Jakupovic, M. Ballero, *Fitoterapia* **2000**, 71, 134–142.
- [9] Anti-tumoral: Y. Takaishi, N. Wariishi, H. Tateishi, K. Kawazoe, K. Nakano, Y. Ono, H. Tokuda, H. Nishino, A. Iwashima, *Phytochemistry* **1997**, 45, 969–974.
- [10] Abietatrien-3 β -ol: J. G. Urones, I. S. Marcos, J. F. Ferreras, P. B. Barcala, *Phytochemistry* **1988**, 27, 523–526. Micrandrol: M. A. De Alvarenga, J. J. Da Silva, H. E. Gottlieb, O. R. Gottlieb, *Phytochemistry* **1981**, 20, 1159–1161. Totaradiol: H. Haraguchi, H. Ishikawa, I. Kubo, *Planta Med.* **1997**, 213–215.
- [11] V. Rosales, J. L. Zambrano, M. Demuth, *J. Org. Chem.* **2002**, 67, 1167–1170.
- [12] P. G. Gassman, K. J. Bottorf, *J. Am. Chem. Soc.* **1987**, 109, 7547–7548.
- [13] K.-D. Warzecha, H. Görner, M. Demuth, *J. Chem. Soc., Faraday Trans.* **1998**, 94, 1701–1706.
- [14] Previously reported X-ray data for **20**: J. Y. Lallemand, M. Julia, D. Mansuy, *Tetrahedron Lett.* **1973**, 45, 4461–4464.
- [15] Published separately in: J. L. Zambrano, V. Rosales, H. Schucht, T. Weyhermüller, M. Demuth, *J. Chem. Crystallogr.* **2002**, 32, 391–394.
- [16] C. Heinemann, X. Xing, K.-D. Warzecha, P. Ritterskamp, H. Görner, M. Demuth, *Pure Appl. Chem.* **1998**, 70, 2167–2176.
- [17] S. Handa, G. Pattenden, *J. Chem. Soc., Perkin Trans. 1* **1999**, 843–845.
- [18] G. Stork, A. W. Burgstahler, *J. Am. Chem. Soc.* **1955**, 5068–5077. A. Eschenmoser, L. Ruzicka, O. Jeger, D. Arigoni, *Helv. Chim. Acta* **1955**, 38, 1890–1904.
- [19] H. Weng, C. Scarlata, H. D. Roth, *J. Am. Chem. Soc.* **1996**, 118, 10947–10953.
- [20] C. Heinemann, K.-D. Warzecha, X. Xing, M. Demuth, *Indian J. Chem., Sect. A* **1997**, 36, 494–497.
- [21] P. G. Gassman, K. J. Bottorff, *Tetrahedron Lett.* **1987**, 28, 5449–5452.
- [22] C. Heinemann, M. Demuth, *J. Am. Chem. Soc.* **1999**, 121, 4894–4895.
- [23] [23a] S. L. Mattes, S. Farid, *J. Am. Chem. Soc.* **1986**, 108, 7356–7361. [23b] A. J. Moroulis, D. R. Arnold, *Synthesis* **1979**, 819–820. [23c] M. Demuth, H. Icil, M. Ozser, manuscript in preparation.
- [24] D. A. Connor, D. R. Arnold, P. K. Bakshi, T. S. Cameron, *Can. J. Chem.* **1995**, 73, 762–771.
- [25] H. Zipse, *J. Am. Chem. Soc.* **1995**, 117, 11798–11806.
- [26] B. B. Snider, *Chem. Rev.* **1996**, 96, 339–363.
- [27] B. B. Snider, R. Nohan, S. A. Kates, *J. Org. Chem.* **1985**, 50, 3659–3661.
- [28] P. D. Curran, *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), Pergamon, New York, **1991**, vol. 4.
- [29] D. Mansuy, M. Julia, *Bull. Soc. Chim. Fr.* **1972**, 2689–2695.
- [30] X. Xing, M. Demuth, *Synlett* **1999**, 987–990.
- [31] J. Den Heijer, O. B. Shadid, J. Cornelisse, E. Havinga, *Tetrahedron* **1977**, 33, 779–786.
- [32] I. Abe, M. Rohmer, G. D. Prestwich, *Chem. Rev.* **1993**, 93, 2189–2206.
- [33] H. Beierbeck, J. K. Saunders, J. W. ApSimon, *Can. J. Chem.* **1977**, 55, 2813–2828. P. E. Hamman, H. Kluge, G. G. Habermehl, *Magn. Reson. Chem.* **1991**, 29, 133–136.
- [34] J. M. Miguel Del Corral, M. Gordaliza, M. A. Salinero, A. San Feliciano, *Magn. Reson. Chem.* **1994**, 32, 774–781.
- [35] J. A. Elings, R. S. Downing, R. A. Sheldon, *Eur. J. Org. Chem.* **1999**, 837–846.
- [36] S. Ghosh, A. K. Ghosh, U. R. Ghatak, *Synth. Commun.* **1992**, 22, 553–564.
- [37] H. Suzuki, T. Hanafusa, *Synthesis* **1974**, 53–55. H. Suzuki, K. Nakamura, R. Goto, *Bull. Chem. Soc. Jpn.* **1966**, 39, 128–131.

Received September 17, 2003