

Lipophilic Phenolic Constituents from *Helichrysum* Species Endemic to Madagascar

Michel Randriamahy^a, Peter Proksch^a, Ludger Witte^b, and Victor Wray^c

^a Institut für Botanik und Pharmazeutische Biologie, Universität Würzburg, Mittlerer Dallenbergweg 64, D-8700 Würzburg, Bundesrepublik Deutschland

^b Institut für Pharmazeutische Biologie, TU Braunschweig, Mendelssohnstraße 1, D-3300 Braunschweig, Bundesrepublik Deutschland

^c Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, D-3300 Braunschweig, Bundesrepublik Deutschland

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Helichrysum, Asteraceae, Flavonoids, Benzophenones, Phloroglucinols

Eight species of the genus *Helichrysum*, all of them endemic to Madagascar, were analyzed for lipophilic phenolic constituents deposited on the surfaces of leaves and stems. A total of 35 compounds was isolated and identified by spectroscopic means. Chalcones (**10**) comprised the largest group of compounds encountered, followed by flavonols (**8**), flavanones (**7**), flavones (**4**), benzophenones (**3**) and phloroglucinol derivatives (**3**). Many of the flavonoids were characterized by unsubstituted B-rings and/or C- or O-bound prenyl or neryl substituents. The *Helichrysum* species analyzed in this study are very similar to African species of this genus with regard to their lipophilic phenolic constituents. The phenolic compounds studied thus appear to be conservative chemical characters of *Helichrysum* that were retained more or less unchanged during the origin of endemic taxa in Madagascar.

Introduction

Madagascar, the fourth largest island in the world, is known for its immense wealth of endemic plant species [1]. Approximately 80% of the more than 10,000 plant taxa found in Madagascar today are endemic as a consequence of the early geographic isolation of this island some 270 million years ago [1, 2]. The wealth in endemic plant taxa, however, is contrasted with the threat of extinction caused by man made changes in the natural environment which have drastically accelerated during the last decades [1]. There is worldwide concern that many potentially useful plants and plant products especially from the tropics may be lost before they are uncovered and studied [3]. This holds especially true for the native flora of Madagascar.

Phytogeographically Madagascar and Africa share a relatively large number of plant families and genera but have only very few species in common [1]. An example is provided by the genus *Helichrysum* Miller corr. Pers. (Asteraceae, tribe Inuleae) comprising more than 500 known species with a major centre of distribution in South Africa

[4]. More than 100 *Helichrysum* taxa, however, are endemic to Madagascar [5]. Phytochemical studies of *Helichrysum*, especially from species of South and East Africa (e.g. 6–8, 10–12 and references listed herein), established the presence of characteristic flavonoids many of them distinguished by an unsubstituted B-ring and by prenyl substituents, as well as of phloroglucinol derivatives. In comparison no phytochemical studies have so far been conducted with any of the *Helichrysum* species found in Madagascar.

As part of a larger phytochemical screening of indigenous plants from Madagascar we have now studied 8 endemic *Helichrysum* species and report on the lipophilic phenolic constituents isolated.

Materials and Methods

H. aphelexioides DC, *H. benthami* R. Vig. et H. Humb. and *H. bracteiferum* (DC) H. Humb. were collected in the neighbourhood of Arivonimamo, *H. triplinerve* DC was collected at Ambatolampy and *H. hirtum* H. Humb., *H. achyroclinoides* Bak. *H. lecomtei* Vig. et Humb. and *H. retrorsum* DC were collected along Route d' Antsirabe (30 km from Tananarive). All were collected in March 1986. Exact localities can be obtained from the authors (M.R. and P.P.). Voucher specimens

Reprint requests to Prof. Proksch.

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were deposited with Dr. A. Rakotozafy (Centre National de Recherches de Tananarive).

Leaves and stems were dipped into MeOH for 2 min to remove the external resin exudates which included the lipophilic phenolics (**1–35**). The extracts were taken to dryness, redissolved in $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (95:5 or 99.5:0.5 v/v) and chromatographed on a silica gel column using the same solvent as eluent. Fractions of 10 ml were collected and monitored by TLC on silica gel (same eluent) under $\text{UV}_{366\text{ nm}}$. Similar fractions were combined and subjected to column chromatography on Sephadex LH-20 with MeOH as eluent. If necessary further purification was achieved by prep. TLC on silica gel.

^1H NMR and ^{13}C NMR spectra were recorded on Bruker AM-300 or WM-400 spectrometers, respectively. All 1D- or 2D-spectra were obtained using the standard Bruker software. Mass spectra (direct probe, EI, 70 eV) were measured on a Finnigan MAT 8430 mass spectrometer. The GC-MS system consisted of a Carlo Erba 5160 GC (equipped with a $30\text{ m} \times 0.32\text{ mm}$ i.d. fused silica glass capillary column coated with a methyl silicone stationary phase; conditions: temperature program $100\text{--}300\text{ }^\circ\text{C}$, $6\text{ }^\circ\text{C}/\text{min}$) that was coupled with the quadrupole mass spectrometer Finnigan MAT 4515. Spectra (EI) were recorded at 40 eV in combination with the Incos data system. Retention indices (RI) were calculated using co-chromatographed standard hydrocarbons.

2: RI: 2775; MS (GC-MS) (m/z , rel. int.): 324 (M^+ , 85), 309 (35), 281 (29), 269 (52), 205 (68), 192 (17), 177 (27), 165 (100), 123 (31), 103 (22).

3: RI: 3150; MS (GC-MS) (m/z , rel. int.): 392 (M^+ , 23), 269 (42), 231 (22), 219 (100), 205 (25), 203 (12), 177 (23), 165 (62), 121 (17).

4: RI: 2975; MS (GC-MS) (m/z , rel. int.): 338 (M^+ , 94), 323 (60), 295 (38), 283 (59), 219 (90), 191 (27), 179 (100), 131 (16), 103 (29).

5: RI: 2715; MS (GC-MS) (m/z , rel. int.): 324 (29, M^+), 256 (74), 255 (79), 238 (18), 179 (100), 178 (13), 153 (23), 152 (87), 124 (28), 123 (29), 104 (33), 103 (24), 69 (92).

9: MS (m/z , rel. int.): 354 (M^+ , 83), 353 (25), 283 (26), 281 (27), 277 (50), 267 (15), 250 (50), 217 (16), 205 (42), 180 (18), 179 (100).

10: ^{13}C NMR (CD_3OD): 200.78, 197.99, 194.05, 186.34 (C-6', C-3', C-2', C-; $4 \times \text{s}$); 143.50 (C-1; s); 135.46 (C-3''; s); 129.47, 129.22 (C-2, C-6, C-3,

C-5; $2 \times \text{d}$); 126.71 (C-4; d); 118.50 (C-2''; d); 106.15 (C-1'; s); 95.53 (C-4'; d); 88.99 (C-5'; s); 53.60 (OMe; q); 43.86 (C- β ; t); 41.31 (C-; t); 33.05 (C-1''; t); 25.98 (C-4''; q); 17.97 (C-5''; q). MS (m/z , rel. int.): 356 (M^+ , 12), 288 (100), 255 (15), 183 (58), 165 (17), 156 (30), 105 (30).

13: MS (m/z , rel. int.): 324 (M^+ , 54), 256 (88), 255 (81), 238 (17), 179 (100), 153 (15), 152 (51), 124 (17), 104 (16).

14: MS (m/z , rel. int.): 392 (36), 324 (27), 323 (17), 269 (19), 257 (98), 256 (100), 255 (85), 238 (16), 179 (92), 153 (28), 152 (38), 137 (29), 136 (31), 123 (18), 104 (58), 69 (88).

21: $\text{UV}_{(\text{max, MeOH})}$ 278, 326, 370; (+ NaOMe) 296, 324, 424; (+ NaOAc) 284, 308, 323, 394). MS (GC-MS) (m/z , rel. int.): 330 (M^+ , 89), 315 (100), 287 (29), 272 (17), 165 (10), 105 (29).

22: $\text{UV}_{(\text{max, MeOH})}$ 278, 324, 352; (+ NaOMe) 272, 284, 378; (+ NaOAc) 272, 282, 362). RI: 2810; MS (GC-MS) (m/z , rel. int.): 344 (M^+ , 86), 329 (100), 315 (11), 311 (10), 301 (11), 105 (17).

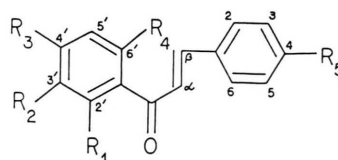
26: MS (m/z , rel. int.): 344 (M^+ , 63), 329 (100), 211 (18), 183 (16).

29: MS (m/z , rel. int.): 360 (M^+ , 64), 345 (100), 330 (20), 211 (20), 183 (18).

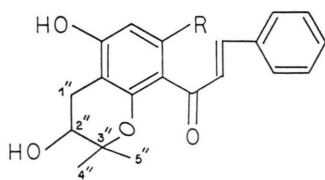
32: MS (m/z , rel. int.): 380 (M^+ , 8), 245 (34), 244 (46), 243 (100), 167 (20), 136 (12), 105 (18).

Results and Discussion

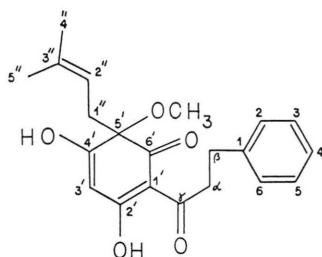
The phenolic compounds studied were isolated by a brief solvent wash of intact leaves and stems. A total of 35 compounds was identified (Fig. 1). Chalcones (**1–10**) including the unusual dihydrochalcone derivative **10** were the largest group of compounds encountered followed by flavanols (**18–25**), flavanones (**11–17**), flavones (**26–29**),



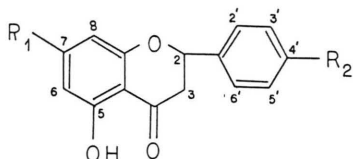
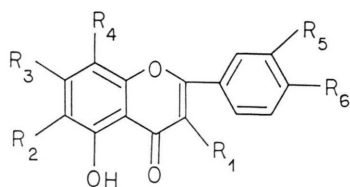
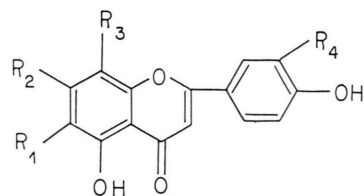
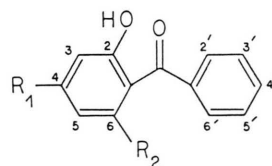
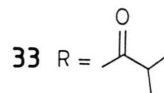
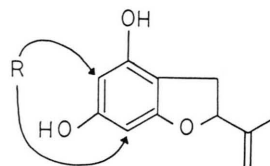
- 1** $\text{R}_1 = \text{OH}$; $\text{R}_2 = \text{H}$; $\text{R}_3 = \text{OH}$; $\text{R}_4 = \text{OCH}_3$; $\text{R}_5 = \text{H}$.
- 2** $\text{R}_{1,3,4} = \text{OH}$; $\text{R}_2 = \text{prenyl}$; $\text{R}_5 = \text{H}$.
- 3** $\text{R}_{1,3,4} = \text{OH}$; $\text{R}_2 = \text{neryl}$; $\text{R}_5 = \text{H}$.
- 4** $\text{R}_{1,3} = \text{OH}$; $\text{R}_2 = \text{prenyl}$; $\text{R}_4 = \text{OCH}_3$; $\text{R}_5 = \text{H}$.
- 5** $\text{R}_{1,4} = \text{OH}$; $\text{R}_2 = \text{H}$; $\text{R}_3 = \text{O-prenyl}$; $\text{R}_5 = \text{H}$.
- 6** $\text{R}_1 = \text{OH}$; $\text{R}_2 = \text{H}$; $\text{R}_3 = \text{O-prenyl}$; $\text{R}_4 = \text{OCH}_3$; $\text{R}_5 = \text{H}$.
- 7** $\text{R}_1 = \text{OH}$; $\text{R}_2 = \text{H}$; $\text{R}_3 = \text{OCH}_3$; $\text{R}_{4,5} = \text{OH}$.



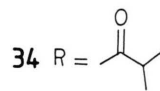
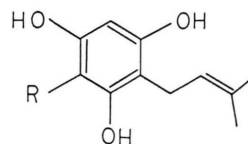
8 R=OH

9 R=OCH₃

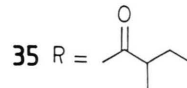
10

11 R₁ = OH; R₂ = H.12 R₁ = OCH₃; R₂ = H.13 R₁ = O-prenyl; R₂ = H.14 R₁ = O-neryl; R₂ = H.15 R₁ = OCH₃; R₂ = OH.16 R_{1,2} = OCH₃.17 R₁ = O-prenyl; R₂ = OH.18 R₁ = OH; R₂ = H; R₃ = OH; R₄₋₆ = H.19 R_{1,2} = OCH₃; R₃ = OH; R₄₋₆ = H.20 R₁ = OCH₃; R₂ = H; R₃ = OH; R₄ = OCH₃; R_{5,6} = H.21 R₁ = OH; R₂ = OCH₃; R₃ = OH; R₄ = OCH₃; R_{5,6} = H.22 R_{1,2} = OCH₃; R₃ = OH; R₄ = OCH₃; R_{5,6} = H.23 R₁ = OH; R₂ = H; R₃ = OH; R₄ = H; R_{5,6} = OH.24 R_{1,2} = OCH₃; R₃ = OH; R₄ = H; R_{5,6} = OH.25 R₁₋₄ = OCH₃; R_{5,6} = OH.26 R₁₋₃ = OCH₃; R₄ = H.27 R₁ = OCH₃; R₂ = OH; R₃ = H; R₄ = OH.28 R₁ = OCH₃; R₂ = OH; R₃ = OCH₃; R₄ = OH.29 R₁₋₃ = OCH₃; R₄ = OH.30 R_{1,2} = OH.31 R₁ = OH; R₂ = OCH₃.32 R₁ = O-geranyl; R₂ = OCH₃.

33 R =



34 R =



35 R =

benzophenones (**30–32**) and phloroglucinol derivatives (**33–35**). The structural assignments of the various compounds, many of them isomers, were mainly based on ¹H NMR studies. For an overview, the ¹H NMR data of the rare and unusual compounds isolated are summarized in Table I.

Table I. ¹H NMR data of selected lipophilic phenolics from *Helichrysum* species endemic to Madagascar.

	2		3		4		5		9		10 ^b
H-2	m	7.65	m	7.65	m	7.65	m	7.63	m	7.68	
H-3											
H-4	m	7.39	m	7.40	m	7.38	m	7.37	m	7.41	m 7.13
H-5		-7.48		-7.47		-7.45		-7.45		-7.50	-7.29
H-6	m	7.65	m	7.65	m	7.65	m	7.63	m	7.68	
H-3'		—		—		—	s	5.97		—	s 4.65
H-5'	s	5.98	s	5.98	s	5.94	s	5.97	s	6.16	—
H-α	d	7.74	d	7.74	d	7.64	d	7.75	d	7.71	m 2.65–3.15
H-β	d	8.25	d	8.26	d	8.02	d	8.23	d	8.11	m 2.65–3.15
H-1''	d	3.24	d	3.25	d	3.32	d	4.54		—	d 2.27
H-2''	t	5.23	m	5.24	t	5.25	t	5.45		—	t 4.99
H-4''	s	1.74	m	2.16–2.26	s	1.81	s	1.81		—	s 1.51
H-5''	s	1.69	m	2.16–2.26	s	1.68	s	1.77		—	s 1.40
H-6''		—	m	5.24		—		—		—	—
H-8''		—	s	1.73		—		—		—	—
H-9''		—	s	1.69 ^a		—		—		—	—
H-10''		—	s	1.68 ^a		—		—		—	—
H-1 a'''		—		—		—		—	dd	2.87	—
H-1 b'''		—		—		—		—	dd	2.54	—
H-2'''		—		—		—		—	dd	3.85	—
H-4'''		—		—		—		—	s	1.47 ^a	—
H-5'''		—		—		—		—	s	1.42 ^a	—
OMe-5'		—		—		—		—		—	s 2.88
OMe-6'		—		—	s	3.99		—	s	3.91	—

Table I (continued).

	13		14		21		22		26 ^b		29 ^b
H-2	m	5.46	dd	5.51		—		—		—	—
H-3a	dd	3.11	dd	3.15		—		—	s	6.81	s 6.78
H-3b	dd	2.80	dd	2.83		—		—		—	—
H-6	d	6.05	d	6.05		—		—		—	—
H-8	d	6.05	d	6.05		—		—		—	—
H-2'	m	7.52	m	7.53	m	8.30	m	8.15	“d”	7.92	d 7.47
H-3'	m	7.44	m	7.45		—		—	“d”	6.91	—
H-4'	m	7.39	m	7.40	m	7.50–7.58	m	7.58–7.60		—	—
H-5'	m	7.44	m	7.45		—		—	“d”	6.91	d 6.90
H-6'	m	7.52	m	7.53	m	8.30	m	8.15	“d”	7.92	dd 7.46
H-1''	d	4.57	d	4.57		—		—		—	—
H-2''	m	5.46	t	5.48		—		—		—	—
H-4''	s	1.81	m	2.18		—		—		—	—
H-5''	s	1.77	m	2.18		—		—		—	—
H-6''		—	t	5.16		—		—		—	—
H-8''		—	s	1.69		—		—		—	—
H-9''		—	s	1.63		—		—		—	—
H-10''		—	s	1.82		—		—		—	—
OMe-3		—		—		—	s	3.85		—	—
OMe-6		—		—	s	3.97 ^a	s	3.95 ^a	s	3.81	s 3.81
OMe-7		—		—		—		—	s	4.01	s 4.02
OMe-8		—		—	s	3.93 ^a	s	3.93 ^a	s	3.91	s 3.93
OH-5		—		—		—		—	s	12.84	s 12.81
OH-3'		—		—		—		—		—	brs 3.17
OH-4'		—		—		—		—	brs	3.45	brs 3.17

Table I (continued).

32		
H-3	d	6.13
H-5	d	6.17
H-2'	m	7.66
H-3'	m	7.48
H-4'	m	7.56
H-5'	m	7.48
H-6'	m	7.66
H-1''	d	4.65
H-2''	t	5.50
H-4''	m	2.14–2.20
H-5''	m	2.14–2.20
H-6''	t	5.15
H-8''	s	1.65
H-9''	s	1.70
H-10''	s	1.81
OMe-6	s	3.57

^a Assignments may be interchanged.^b Spectra were recorded in DMSO-d₆, all other spectra in CD₃OD.

- 2: $J_{(\alpha-\beta)}$: 15.6; $J_{(1''-2'')}$: 7.1.
3: $J_{(\alpha-\beta)}$: 15.6; $J_{(1''-2'')}$: 8.1; irradiation at H-1'' gave nOe's at H-2'' and H-4'', at H-8'' gave H-6'' and at H-9''/10'' gave H-5'', H-4'' and H-2''.
4: $J_{(\alpha-\beta)}$: 15.6; $J_{(1''-2'')}$: 6.5; irradiation at OMe-6' gave nOe's at H-5' and H-β, at H-1'' gave H-2'' and H-4''.
5: $J_{(\alpha-\beta)}$: 15.6; $J_{(1''-2'')}$: 6.5; irradiation at H-1'' gave nOe's at H-3', H-5' and H-2''.
9: $J_{(\alpha-\beta)}$: 15.6; $J_{(1a''-1b'')}$: 16.5; $J_{(1a''-2'')}$: 5.0; $J_{(1b''-2'')}$: 7.0; irradiation at OMe-6' gave a nOe at H-5' but no nOe's at H-1 a'' or H-1 b''; when the spectrum was recorded in DMSO-d₆ no signal indicative for OH-2' was observed.
10: $J_{(1''-2'')}$: 6.9; irradiation at H-2'' gave a nOe at H-1'' and H-4'', at OMe-5' gave nOe's at H-1'' and H-2'' and at H-1'' gave nOe's at H-2'', H-5'' and a small nOe to H-3'.
13: $J_{(2-3a)}$: 13.0; $J_{(2-3b)}$: 3.1; $J_{(3a-3b)}$: 17.1; $J_{(1''-2'')}$: 6.7; when the spectrum was recorded in DMSO-d₆ the signal of OH-5 was observed at 12.06 ppm.
14: $J_{(2-3a)}$: 13.0; $J_{(2-3b)}$: 3.1; $J_{(3a-3b)}$: 17.1; $J_{(1''-2'')}$: 7.5; $J_{(5''-6'')}$: 7.5; irradiation at H-1'' gave nOe's at H-6, H-8, H-2'' and H-4'', and at H-10'' gave H-2'' and H-4''.
21: When the spectrum was recorded in DMSO-d₆ the signal of OH-5 was observed at 12.14 ppm and that of OH-7 at 9.75 ppm. Irradiation of the residual HDO signal at 3.45 ppm caused saturation transfer to all of the OH signals which in turn gave transferred nOe's to OMe-6 and OMe-8 from OH-7 and H-2'/H-6' from OH-3.
22: When the spectrum was recorded in DMSO-d₆ the signal of OH-5 was observed at 12.40 ppm and that of OH-7 at 10.55 ppm. Irradiation at OMe-3 gave nOe's at H-2'/H-6'.
26: "dd": $J_{(2'-3')} + (2'-5')$: 8.8; irradiation at H-3 gave nOe's at H-2' and H-6', and at OMe-6 gave a nOe at OMe-7 and vice-versa.
29: $J_{(2'-6')}$: 2.1; $J_{(5'-6')}$: 8.1; irradiation at OMe-6 gave a nOe at OMe-7 and vice-versa, and at H-3 gave nOe's at H-2' and H-6'.
32: $J_{(3-5)}$: 2.1; $J_{(1''-2'')}$: 6.5; $J_{(5''-6'')}$: 6.5; irradiation at H-9'' gave a nOe at H-5'', at H-8'' gave H-6'', at H-10'' gave H-1'', at OMe-6 gave H-5, at H-2'' gave H-4'' and at H-1'' gave H-3, H-5 and H-10''.

H. aphelexioides yielded a complex pattern of lipophilic phenolics including a number of prenylated chalcones (Table II). The chalcones were further characterized by unsubstituted B-rings. Both chemical features are rare in flavonoids (especially from the Asteraceae) [9] but have frequently been reported from species of *Helichrysum* (e.g. [6–8]). The prenyl substituents were either C-bound (as in 2) or O-bound (as in 5). In O-prenylated chalcones the chemical shift of H-1'' was downfield (4.54 ppm) of that of H-1'' in C-prenylated compounds (3.24–3.32 ppm). O-Prenylated chalcones

Table II. Phenolic compounds of *Helichrysum* species endemic to Madagascar.

Species	Compounds
<i>H. achyroclinoides</i>	2, 7, 33–35
<i>H. aphelexioides</i>	1, 4, 5, 6, 8, 9, 10, 11
<i>H. benthami</i>	26, 27, 28, 29
<i>H. bracteiferum</i>	1, 12, 18, 19, 20, 21, 22
<i>H. hirtum</i>	13, 15, 16
<i>H. lecomtei</i>	23, 24, 25
<i>H. retrorsum</i>	2, 3, 5, 14, 17
<i>H. triplinerve</i>	1, 7, 30, 31, 32

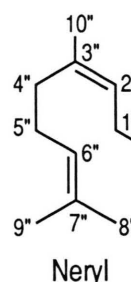
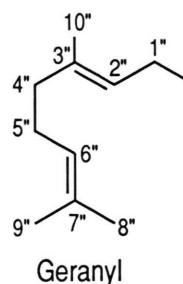
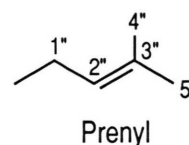
Numbers of compounds follow Fig. 1.

were further characterized by a pair of fragments in the mass spectrum corresponding to $(M-C_5H_8)^+$ and $(M-C_5H_9)^+$ respectively that are not present in the mass spectra of C-prenylated chalcones. The chromanol substituted chalcone **9** was similar to a compound previously reported from the African species, *H. cymosum* ssp. *calvum* [10] except that the hydroxyl and methoxyl groups were interchanged. The position of the OMe-group in **9** followed unambiguously from nOe experiments (Table I). The 1H NMR analysis of several chalcones (*e.g.* **5**) indicated the presence of small amounts of the corresponding flavanone derivatives. The proportions of the flavanones compared to the chalcones increased upon storage of the isolated chalcones indicating that these flavanones were artefacts.

The structure of the highly unusual prenylated phenolic **10** was difficult to determine unambiguously. The presence of the aromatic side chain, a hydrogen bonded OH group, an aliphatic OMe group and a C-prenyl group were evident from the 1H and ^{13}C NMR data. Comparison of these data with data for similar compounds [11] suggested the ring structure shown (**10**). The observation of four ^{13}C signals in the region 185–205 ppm would be compatible with such a tautomeric system and the symmetrical distribution of oxygen substituents indicates a biogenetic relationship to the flavonoids. A similar compound differing from **10** by the presence of an additional prenyl substituent has recently been described from *H. forskahlii* from East Africa [12].

Chalcones as well as flavanones constituted the predominating lipophilic phenolic constituents in the resin of *H. retrorsum*. Chalcone **3** was characterized by the presence of a C-neryl substituent at C-3' as demonstrated by nOe studies. In general neryl substituents seem to occur less frequently in flavonoids than their geranyl isomers [9]. The flavanones **14** and **17** isolated in addition to the chalcones were not artefacts arising from chalcones as indicated by their presence in the crude solvent wash of leaves and stems as well as by their A-ring substitution patterns which differed from those of the chalcones isolated (Table II).

H. bracteiferum yielded a number of highly methylated flavanol derivatives including **21** and **22** characterized by completely substituted A-rings and unsubstituted B-rings (Fig. 1). Compound **21**



showed a yellowish colour under $UV_{366\text{ nm}}$ indicating the presence of a OH group at C-3. The 1H NMR spectrum showed only signals for the B-ring protons as well as signals corresponding to two OMe groups. The $(M-15)^+$ fragment was the base peak in the mass spectrum of **21** indicating that one OMe group had to reside at C-8. When the spectrum was recorded in DMSO- d_6 irradiation of the residual HDO signal at 3.45 ppm caused saturation transfer to all the OH-signals which in turn gave transferred nOe's to OMe-6 and OMe-8 from OH-7 and to H-2'/H-6' from the OH-3 group thus establishing the presence of the second OMe group at C-6 rather than C-7.

The phenolic resin of *H. achyroclinoides* yielded in addition to the chalcones **2** and **7** several phloroglucinol derivatives (**33–35**). The structures of **34** and **35** which differed only by the presence of an isobutyryl or 2-methyl-butyryl substituent respectively followed directly from the respective 1H NMR spectra. The same compounds, as well as several structural isomers, have recently been reported from South African *Helichrysum* species

[8]. An unequivocal assignment of the isobutyryl substituent of the benzofuran **33** by nOe experiments was not possible, however.

The flavonoids isolated from *H. benthami* (**26–29**) and *H. lecomtei* (**23–25**) differed from those of the other species analyzed with regard to their B-rings which showed 3',4'-oxygenation patterns. As far as we are aware none of the flavones (**26–29**) have so far been described for *Helichrysum* species.

Benzophenone derivatives (**30–32**) were the major lipophilic constituents isolated from *H. triplinerve*. Compound **32** showed the most complex structure when compared to the other two derivatives. The position of the OMe and O-geranyl substituents was elucidated from the ¹H NMR spectra and from ¹H nOe studies. Assignment of the OMe group of **32** to C-6 rather than to C-4 was corroborated by irradiation at 3.57 ppm (OMe group) which caused a nOe only for the signal of H-5. The nature and position of the O-geranyl substituent followed from the ¹H NMR spectrum as well as from decoupling and further nOe experiments (Table I). The benzophenones **30–32** have so far not been reported from *Helichrysum* species even though structurally similar compounds (*e.g.* 2, 6-OH-4-O-geranyl-benzophenone) were isolated from the systematically related genus *Leontonyx* [11].

In conclusion, the *Helichrysum* species endemic to Madagascar investigated in this study closely resemble species of this genus from East and South Africa with regard to their lipophilic phenolic constituents. Shared chemical characters include for example the frequent occurrence of flavonoids (especially chalcones) with unsubstituted B-rings and/or C- or O-bound prenyl or neryl substituents which are rare elsewhere in the Asteraceae [9]. Other common features include the occurrence of phloroglucinol derivatives such as **33–35** or [8] of biogenetically unusual compounds such as the dihydrochalcone derivative **10**. The phenolic compounds studied thus appear to be ancestral, conservative chemical characters of *Helichrysum* that were retained largely unchanged during the origin of endemic species of this genus in Madagascar.

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