http://dx.doi.org/10.21577/0103-5053.20190165

J. Braz. Chem. Soc., Vol. 30, No. 11, 2464-2476, 2019
Printed in Brazil - ©2019 Sociedade Brasileira de Química

Article

New Limonoids from *Dictyoloma vandellianum* and *Sohnreyia excelsa*: Chemosystematic Considerations

Claudenice F. P. Sartor,[a] Maria da Paz Lima,[a,b] Maria Fátima G. F. da Silva,[a,*] João B. Fernandes,[a] Moacir R. Forim[a] and José R. Pirani[c]

[a]*Departamento de Química, Universidade Federal de São Carlos, CP 676, 13565-905 São Carlos-SP, Brazil*

[b]*Coordenação de Pesquisas em Produtos Naturais, Instituto Nacional de Pesquisas da Amazônia, CP 478, 69011-970 Manaus-AM, Brazil*

[c]*Instituto de Biociências, Departamento de Botânica, Universidade de São Paulo, 05508-900 São Paulo-SP, Brazil*

Molecular phylogenetic studies separated and united a group of genera that constituted the *Spathelia-Ptaeroxylon* clade, in which *Dictyoloma* and *Sohnreyia* have been included. Our taxonomic interest in the *Dictyoloma vandellianum* and *Sohnreyia excelsa* stimulated an investigation of both species searching for limonoids. Leaves from *D. vandellianum* afforded the new limonoid 1,2-dihydro-1α-hydroxy-8,30-epoxy-cneorin R, and heartwood yielded the new rearranged limonoid dictyolomin. Leaves from *S. excelsa* afforded the new protolimonoid 3β-angeloyloxy-7α,24,25-trihydroxy-21,23-oxide-14,18-cycloapotirucall-21-methoxycetal and the new cycloheptanyl ring C limonoid with carbonate substituent and named as sohnreyolide. The new limonoids from *Sohnreyia* and *Dictyoloma* show similarities with those from Rutaceae and Meliaceae, providing support for moving *Spathelia-Ptaeroxylon* clade near to these associated large families.

Keywords: *Spathelia-Ptaeroxylon* clade, *Dictyoloma*, *Sohnreyia*, Rutaceae, limonoids

Introduction

Molecular phylogenetic studies separated and united a group of genera that constituted the *Spathelia-Ptaeroxylon* clade, which has been included in Rutaceae.[1] This clade comprises seven genera: *Bottegoa*, *Cedrelopsis*, *Cneorum*, *Dictyoloma*, *Spathelia*, *Harrisonia* and *Ptaeroxylon*. However, most of these genera have been associated with other families. *Spathelia* L. and *Dictyoloma* Juss. have been assigned to both Simaroubaceae and Rutaceae.[2,3] The other five genera have been traditionally placed in the Simaroubaceae (*Harrisonia*), Meliaceae (*Ptaeroxylon*, *Cedrelopsis*), Sapindaceae (*Bottegoa*), Cneoraceae (*Cneorum*) and Ptaeroxylaceae (*Ptaeroxylon*, *Cedrelopsis*, *Bottegoa*).[4-8]

Relevant data are available on the anatomical characters and five plastid deoxyribonucleic acid (DNA) regions, which show that with the exception of *Spathelia*, all other genera are monophyletic.[1] These data also show that this clade is well placed in Rutaceae, and they also suggest uniting them in a subfamily, Spathelioideae. The results led to a new circumscription of *Spathelia* species, and Caribbean species were regarded as *Spathelia*, *S. bahamensis*, *S. brittonii*, *S. coccinea*, *S. cubensis*, *S. glabrescens*, *S. sorbifolia*, *S. splendens*, *S. vernicosa* and *S. wrightii*. The South American species of *Spathelia* were distinct from all other Caribbean; thereby they were separated into a *Sohnreyia* genus.

Spathelia excelsa from Brazil and *S. ulei* from Venezuela were originally described as *Sohnreyia excelsa* Krause (1914)[9] and *Diomma* ulei Engl. ex Harms (1931),[10] respectively. Due to the law of priority in botanical nomenclature *Sohnreyia* has priority over *Diomma*. Therefore, *Sohnreyia* comprises four species: *S. excelsa*, *S. giraldiana* (Colombia), *S. terminalioides* (Peru) and *S. ulei*.[1]

Dictyoloma contains one species, *D. vandellianum* Adr. Juss. (syn. *D. incanescens* DC) which occurs in Brazil, and according to above revision includes *D. peruvianum* from Peru.[3,11]

*e-mail: dmfs@ufscar.br

A simple indole (**1**) occurs in *Dictyoloma*, but it is very rare in Rutaceae. *Dictyoloma*, *Spathelia* and *Sohnreyia* are characterized by 2-quinolinone (**2**-**8**), 2-alkyl-4(1*H*)-quinolone (**9**-**21**) alkaloids, simple and prenylated chromones (**22**-**42**), protolimonoids (**43**, **44**) and limonoids (**45**-**54**) (Figures 1-3).

Dictyoloma vandellianum is known to contain indole (**1**), 2-quinolinone (**3**, **4**, **6**, **7**), 2-alkyl-4(1*H*)-quinolone (**12**-**15**, **20**) alkaloids, prenylated chromones (**25**-**27**, **31**-**33**, **42**) and limonoids (**45**, **47**, **49**, **51**, **52**).[12-17] The only known metabolites from *D. vandellianum* ex *D. peruvianum* are two 2-alkyl-4(1*H*)-quinolone alkaloids (**19** and **21**).[18]

The known compounds from *Spathelia* and *Sohnreyia* are typical of *D. vandellianum*. Little is known about the chemistry of the Caribbean species, data are available for *Spathelia glabrescens*, *S. sorbifolia* and *S. wrightii*. In *S. glabrescens* were found prenylated chromones (**23**, **25**, **27**, **42**) and the unusual squalene derivatives glabrescol (**55**) and epoxy tri-tetrahydrofuran (THF) diol (**56**) (Figure 3).[19-21] Ethereal squalene derivatives were also isolated from *Quassia multiflora*,[22] confirming the chemical affinity of *Spathelia* with Simaroubaceae. Chemical data on *S. wrightii* are very scarce; only one prenylated chromone (**35**) was found.[23] *S. sorbifolia* contains 2-quinolinone (**3**, **5**), prenylated chromones (**23**-**25**, **27**-**31**, **33**, **34**, **37**, **39**-**42**) and limonoids (**46**, **48**, **50**).[24-28]

Sohnreyia excelsa has been the more widely investigated (however, it appears in all original literature as *Spathelia excelsa*), and it produces 2-quinolinone (**2**-**4**, **8**), 2-alkyl-4(1*H*)-quinolone (**9**-**11**, **13**, **16**-**18**) alkaloids, prenylated chromones (**22**, **36**, **38**), protolimonoids (**43**, **44**) and limonoids (**45**, **51**, **53**, **54**).[29-32]

As part of our continuous investigation into the chemical composition of Brazilian *S. excelsa* and *D. vandellianum*, we reported the isolation of thirteen 2-alkyl-4(1*H*)-quinolone alkaloids from leaves of both species.[16,29] The isolation of these interesting new alkaloids combined with our taxonomic interest in the *Spathelia-Ptaeroxylon* clade stimulated an investigation of other organs of *D. vandellianum*. The phytochemical studies of *S. excelsa* leaves were undertaken in our laboratory, and we used the same experimental procedures applied in the present work and in others similar, and these allowed to isolate coumarins and limonoids. In order to look

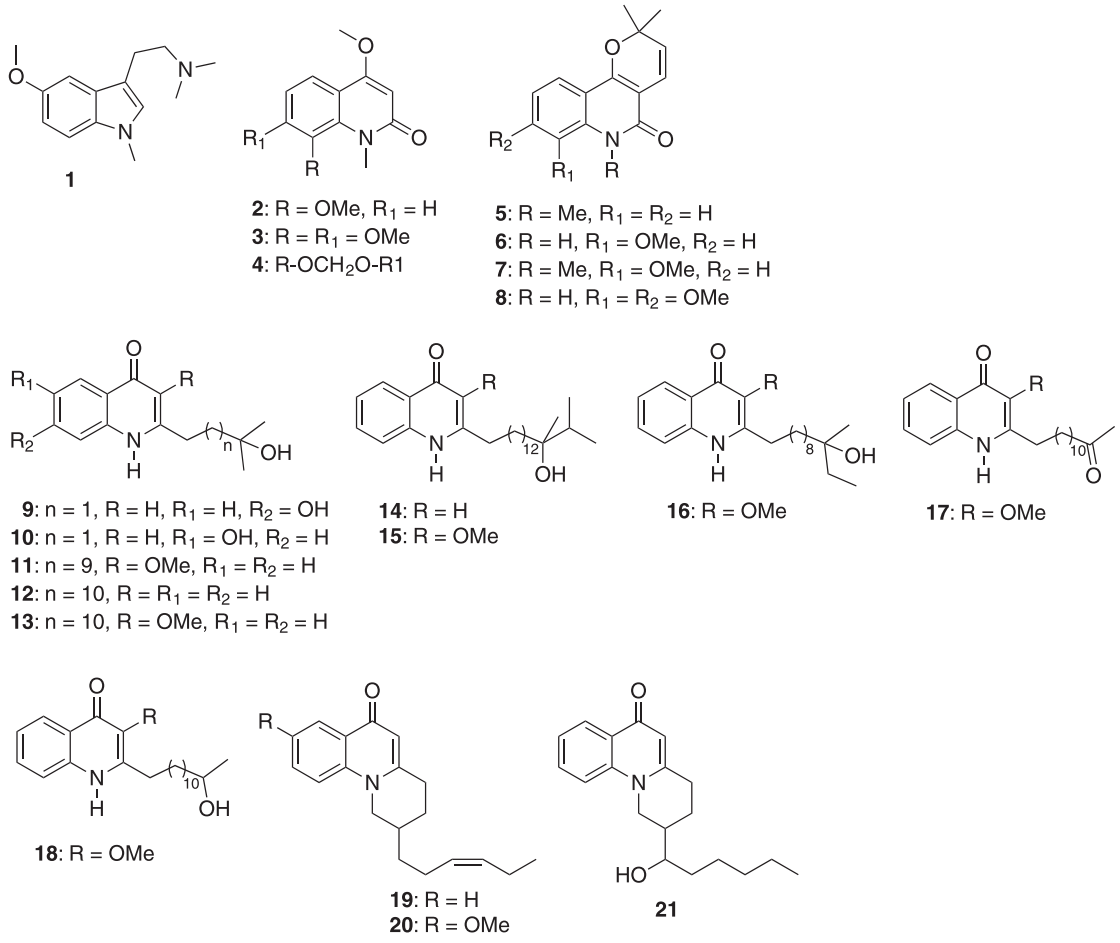


Figure 1. Indole (**1**), 2-quinolinone (**2**-**8**) and 2-alkyl-4(1*H*)-quinolone (**9**-**21**) alkaloids from *Spathelia-Ptaeroxylon* clade.

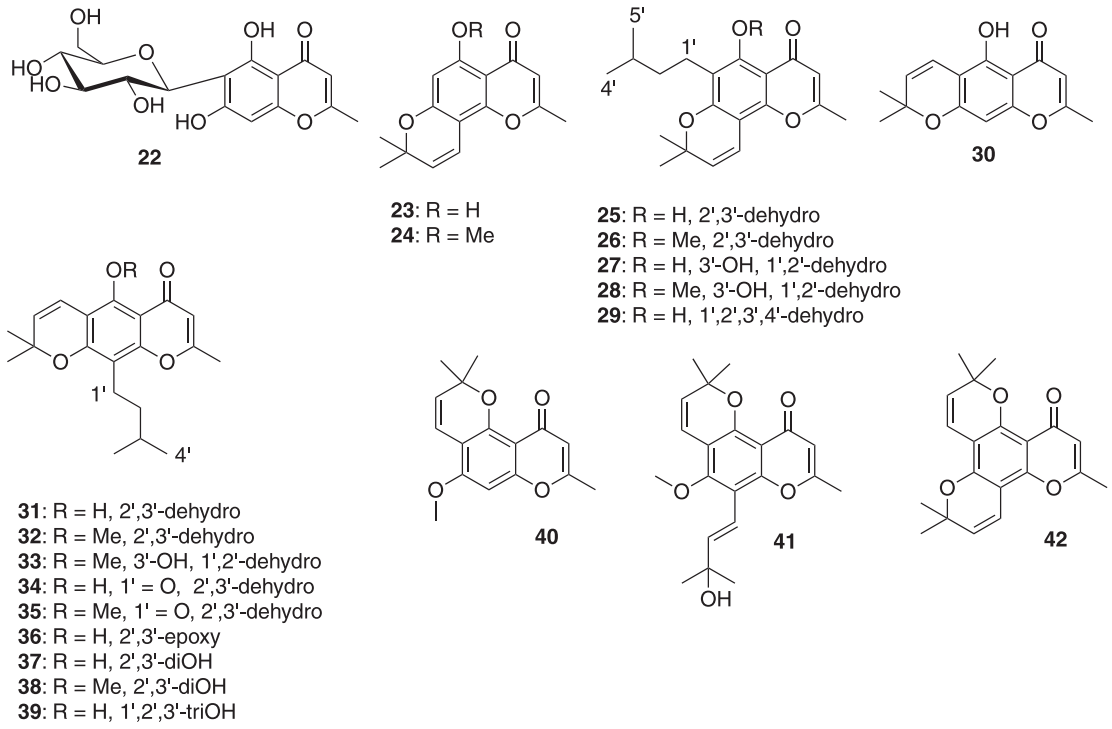


Figure 2. Simple and prenylated chromones (**22**-**42**) from *Spathelia-Ptaeroxylon* clade.

for these compounds we have now undertaken a further investigation of *S. excelsa* leaves. Now we report in this work four new limonoids **57**-**60** (Figure 4).

Limonoids are found in three families, Rutaceae, Meliaceae and Cneoraceae, which help to confirm the close ties between them. However, there are fairly consistent differences between the limonoids of Rutaceae and those of the Meliaceae and Cneoraceae.[33] In a recent paper[34] on limonoids the authors highlights the advances of this class regarding a wide spectrum of biological properties mainly as insecticidal activities. The tetracyclic ring system of limonoid suffers degradation by several routes, by opening of rings A, B, C and D, as the new rearranged limonoids obtained in the present work.[33] Calodendrolide and fraxinellone compounds appear to arise biogenetically by extensive degradation of the limonoid system. Both co-occur with limonoids and represent metabolic fragments containing only the limonoid C- and D-rings. The relative and absolute configurations in both are consistent with their limonoid origin.[35] Fraxinellone containing only C- and D-rings shows insecticidal activities.[36]

Experimental

General

Nuclear magnetic resonance (NMR), heteronuclear single quantum correlation (HSQC), heteronuclear multiple bond correlation (HMBC) and nuclear overhauser effect spectroscopy (NOESY) spectra were acquired on a Bruker DRX 400 spectrometer, with tetramethylsilane (TMS) as internal standard; electrospray ionization mass spectra (ESI-MS) were obtained at low resolution on a triple quadrupole Micromass Quattro LC instrument, equipped with a "'Z-spray"' ion source; high resolution mass spectra (HRMS) were obtained on a Fisons VG Autospec; infrared (IR) spectra were obtained with a Bomem Fourier transform (FT) / IR spectrometer; ultraviolet (UV) spectra were obtained with a PerkinElmer model 8452A spectrophotometer.

Plant material

Dictyoloma vandellianum was collected in Campinas, SP, Brazil, and identified by J. R. Pirani (Universidade de São Paulo (USP)). A voucher (SPF 81-317) is deposited in the Herbarium of Instituto de Biociências, USP, São Paulo. *S. excelsa* was collected in the Adolpho Ducke Forest Reserve, Manaus, AM, Brazil, and identified by J. R. Pirani. A voucher specimen (4227) is deposited in the Herbarium of the Instituto Nacional de Pesquisa da Amazônia (INPA), Manaus, AM, Brazil.

Isolation of compounds

Ground leaves (300 g) and heartwood (1 kg) of *D. vandellianum* were extracted with hexane, then CH_2Cl_2

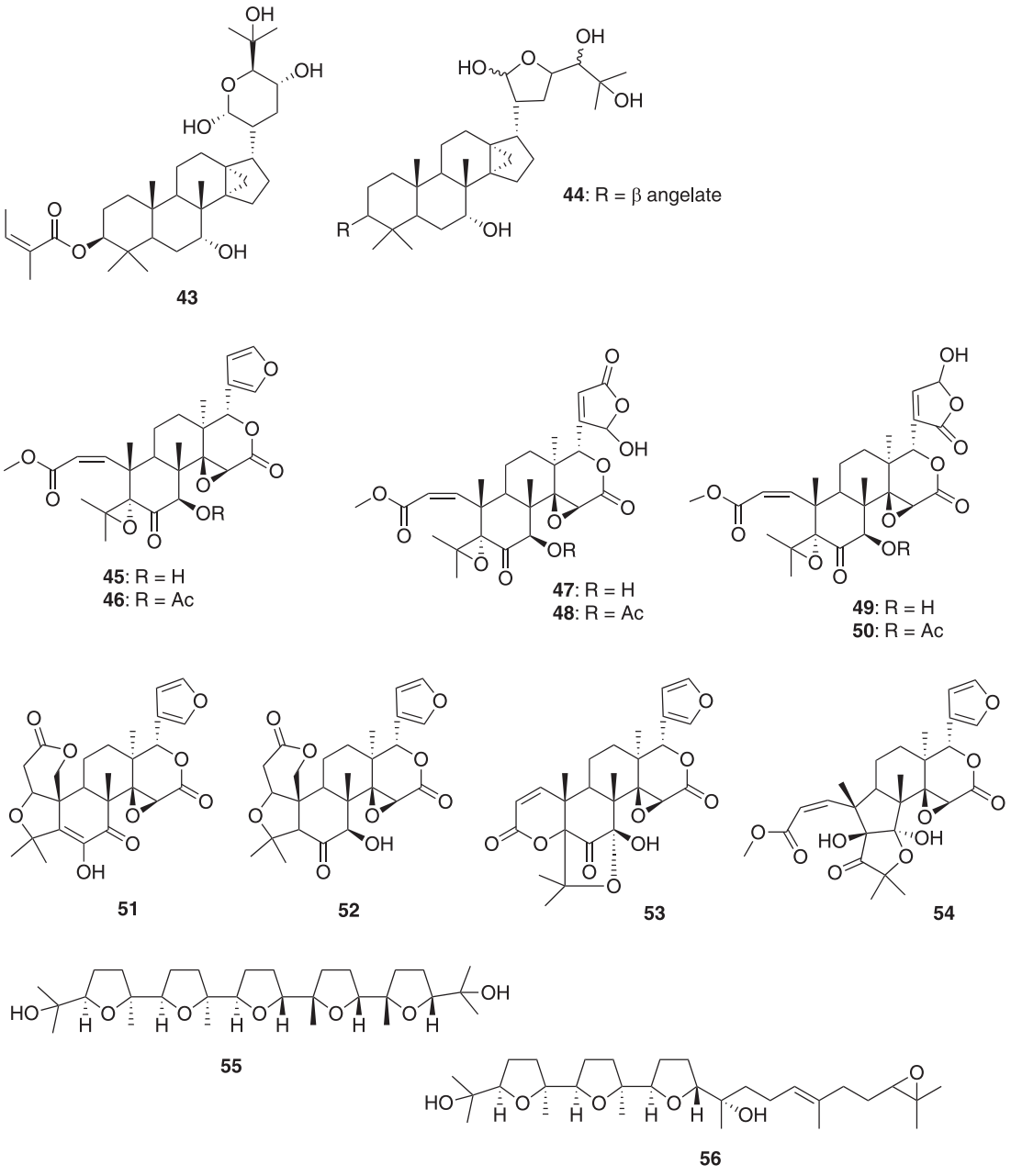


Figure 3. Protolimonoids (**43**, **44**), limonoids (**45**-**54**) and the unusual squalene derivatives (**55**, **56**) from *Spathelia-Ptaeroxylon* clade.

and finally with MeOH. The concentrated CH_2Cl_2 extract from leaves was subjected to column chromatography (CC) over silica gel. Elution with hexane, followed by a CH_2Cl_2-EtOAc-Me_2CO-MeOH gradient yielded eight fractions (frs). Fraction (Fr.) 2 was chromatographed on cellulose, eluting with a hexane-CH_2Cl_2-EtOAc gradient to afford **6** (3 mg) and additional frs. Fr. 2.1 was applied to Sephadex LH-20 (EtOAc), then on silica gel (hexane-CH_2Cl_2-EtOAc gradient) to give β-sitosterol (13 mg). Fr. 6 was chromatographed on Sephadex LH-20, eluting with MeOH affording a Fr. containing **58**. It was then purified by preparative thin-layer chromatography (TLC) (silica gel; $CHCl_3$-MeOH, 95:5) to give 24 mg of **58**. The concentrated MeOH extract from leaves was subjected to CC over silica gel. Elution with hexane, followed by a CH_2Cl_2-EtOAc-Me_2CO-MeOH gradient yielded four frs. Fr. 2 was applied to Sephadex LH-20, eluting with MeOH afforded a Fr. containing **45**. It was then purified by preparative TLC (silica gel; hexane-EtOAc, 20:80) to give 14 mg of **45**. The concentrated CH_2Cl_2 extract from heartwood was subjected to CC over silica gel. Elution with hexane, followed by a CH_2Cl_2-EtOAc-Me_2CO-MeOH gradient yielded sixteen frs. Fr. 7 was applied three times to Sephadex LH-20 ($CHCl_3$-MeOH, 1:1; MeOH;

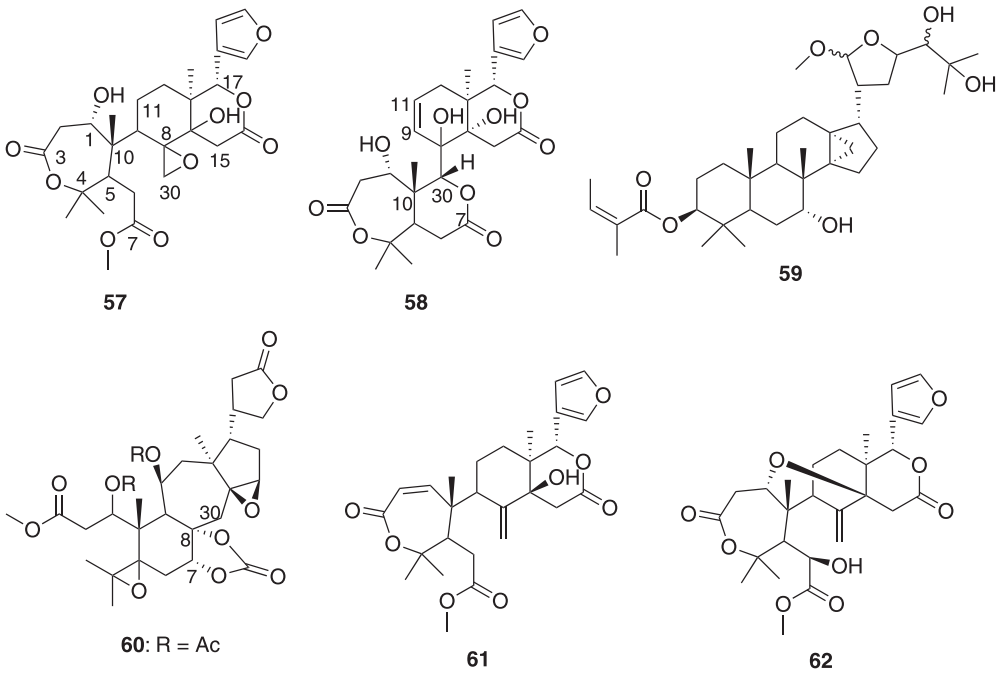


Figure 4. New limonoids isolated from *Dictyoloma vandellianum* and *Sohnreyia excelsa* and model compounds cneorin R (**61**) and khayseneganin D (**62**).

then EtOAc) to give **7** (2.5 mg) and **47** (8 mg). Fr. 8 was chromatographed five times on Sephadex LH-20 ($CHCl_3$-MeOH, 1:1; MeOH; MeOH; MeOH; then EtOAc) to give **45** (14.2 mg) and additional frs. Fr. 8.1 was then rechromatographed as above to yield **26** (5.3 mg). Fr. 10 was applied twice to Sephadex LH-20 ($CHCl_3$-MeOH, 1:1; MeOH) to give 70 mg of **6**. Fr. 11 and Fr. 13 were applied to Sephadex LH-20 as above to yield **3** (2.7 mg) and **8** (5 mg), respectively. The concentrated MeOH extract was subjected to CC over cellulose. Elution with hexane, followed by a CH_2Cl_2-EtOAc-MeOH gradient yielded five frs. Fr. 2 was then rechromatographed as above to yield additional frs. Fr. 2.1 was subjected to CC over silica gel, and elution with hexane, followed by a CH_2Cl_2-EtOAc-Me_2CO-MeOH gradient yielded additional frs. Fr. 2.1.1 was applied to Sephadex LH-20, eluting with MeOH afforded a Fr. containing four compounds. It was then purified by preparative TLC (silica gel; hexane-EtOAc, 40:60) to give **6** (4.7 mg), **8** (3.6 mg), **51** (8 mg) and **57** (3 mg). Fr. 3 was chromatographed twice on Sephadex LH-20 ($CHCl_3$-MeOH, 1:1) to give 74.5 mg of 3β-*O*-β-D-glucopyranosylsitosterol.

Ground leaves (2.9 kg) from *S. excelsa* were extracted with hexane, then CH_2Cl_2 and finally with MeOH. Fractions were monitored by ^{1}H NMR (200 MHz) and only those which showed features of limonoids, absent in the previously investigated leaves, were examined. The concentrated MeOH extract was subjected to CC over silica gel. Elution with hexane, followed by a CH_2Cl_2-MeOH gradient, yielded 16 frs. Fr. 11 was applied to CC over Florisil, eluted with a hexane-CH_2Cl_2 (1:1), CH_2Cl_2-MeOH gradient, affording additional frs. Fr. 11.1 was then rechromatographed on silica gel, eluting with a CH_2Cl_2-MeOH (95:5), and then to Sephadex LH-20 (MeOH) to give the coumarin xanthyletin (7.4 mg). Fr. 11.2 was applied to CC over Florisil, eluting with hexane-EtOAc (5-50%), and then to Sephadex LH-20 (MeOH), and then on silica gel, eluting with hexane-EtOAc (5-50%) to give **45** (3.4 mg) and two additional frs. Fr. 11.2.1 and Fr. 11.2.2 were rechromatographed on cellulose eluting with hexane-CH_2Cl_2 (2%-30%) to yield **51** (6 mg) and **53** (12 mg). Fr. 11.3 was applied to CC over Florisil, eluted with a hexane CH_2Cl_2-MeOH gradient, and then twice on silica gel, eluted with hexane-EtOAc (5-50%), EtOAc-MeOH and then EtOAc (5-50%) to give **53** (80 mg) and two additional frs. Fr. 11.3.1 and Fr. 11.3.2 were rechromatographed on Sephadex LH-20 (EtOAc) to give **59** (21.4 mg) and **60** (9 mg), respectively. Fr. 14 was applied to column chromatography over Florisil, eluted with a CH_2Cl_2-MeOH (9:1), and then twice on silica gel, eluting with CH_2Cl_2-EtOAc-MeOH (8:2 + 0.5) to yield the flavan epicatechin and 3β-*O*-β-D-glucopyranosylsitosterol.

1,2-Dihydro-1α-hydroxy-8,30-epoxy-cneorin R (**57**)

Amorphous solid; IR (film) ν_{max} / cm^{-1} 3340 (hydroxyl group), 1737 (this absorption indicated the presence of ester and / or lactone groups); ^{1}H NMR (300 MHz, $CDCl_3$) see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$) see Table 2; HSQC, HMBC (400 MHz, $CDCl_3$) see text; MS / MS

(ESI) *m/z*, found for $[C_{27}H_{36}O_{10} + K - H_2O]^+$: 541 (40), $[C_{27}H_{36}O_{10} + Na - H_2O]^+$: 525 (100), 283 (15); HRMS *m/z*, calcd. for $C_{27}H_{37}O_{10}$ $[M + H]^+$: 521.23867, found: 521.22837.

Dictyolomin (**58**)

Amorphous solid; IR (film) ν_{max} / cm^{-1} 3335 (hydroxyl group), 1739 (this absorption indicated the presence of lactone groups); ^1H NMR (400 MHz, $CDCl_3$) see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$) see Table 2; HSQC, HMBC, NOESY (400 MHz, $CDCl_3$) see text; MS / MS (ESI) *m/z*, found for $C_{26}H_{32}O_{10}$ $[M + K - H_2O]$: 525 (100), 243 (20), 227 (65), 261 (40); HRMS *m/z*, calcd. for $C_{26}H_{31}O_9$ $[C_{26}H_{32}O_{10} + H - H_2O]$: 487.19680, found: 487.30253.

3β-Angeloyloxy-7α,24,25-trihydroxy-21,23-oxide-14,18-cycloapotirucall-21-methoxycetal (**59**)

Amorphous solid; IR (film) ν_{max} / cm^{-1} 3330 (hydroxyl group), 1704 (this absorption indicated the presence of ester group); ^1H NMR (400 MHz, $CDCl_3$) δ 4.60 (dd, *J* 11.4, 4.7 Hz, H-3), 3.75 (bd, *J* 1.9 Hz, H-7), 4.84 (d, *J* 3.1 Hz, H-21), 4.06 (m, H-23), 3.52 (d, *J* 5.3 Hz, H-24), 0.73 (d, *J* 4.8 Hz, H-18a), 0.49 (d, *J* 4.8 Hz, H-18b), 0.91 (s, Me-19), 1.29 (s, Me-26), 1.20 (s, Me-27), 0.89 (s, Me-28), 0.88 (s, Me-29), 1.02 (s, Me-30), 3.36 (s, OMe), 6.02 (qq, *J* 7.2, 1.4 Hz, H-3'), 1.88 (brd, *J* 1.4 Hz, H-4'), 1.98 (brdq, *J* 7.2, 1.4 Hz, H-5'); ^{13}C NMR (100 MHz, $CDCl_3$) see Table 2; HSQC, HMBC (400 MHz, $CDCl_3$) see text.

Table 1. ^1H NMR spectroscopic data for **57**, **58**, **60** and model **62**

H	δ_H / ppm (*J* / Hz)			
	57	**62**	**58**	**60**
1	4.12 dd (6.0, 2.0)	3.38 dd (5.6, 2.2)	3.80 t (4.0)	5.54 dd (10.7, 1.7)
2a	3.24 dd (15.2, 2.0)	3.25 dd (15.2, 2.2)	3.14 d (4.0)	3.27 dd (15.8, 10.7)
2b	2.97 dd (15.2, 6.0)	2.84 dd (15.2, 5.6)	–	2.80 m
5	3.03 dd (8.4, 2.4)	3.18 s	3.32 dd (13.0, 6.0)	–
6a	2.28 m	4.25 s	2.36 dd (19.0, 13.0)	1.95 dd (13.5, 3.9)
6b	–	–	2.75 dd (19.0, 6.0)	2.21 t (13.5)
7	–	–	–	4.25 dd (13.5, 3.9)
9	1.44 m	2.32 d (3.0)	5.64 dd (10.0, 1,7)	3.05 d (8.0)
11a	2.40 m	2.25 ddd (15.1, 4.6, 3.0)	6.00 ddd (10.0, 6.4, 1.9)	5.14 dd (10.4, 8.0)
11b	1.70 m	1.54 tt (15.1, 3.5)	–	–
12a	1.98 m	1.91 dt (13.5, 4.6)	1.70 m	1.66 brd (14.1)
12b	1.17 m	1.04 dd (13.5, 3.5)	2.30 m	2.80 m
15a	2.63 d (19.0)	2.93 d (18.2)	3.42 d (19.0)	3.38 brs
15b	2.17 d (19.0)	2.56 d (18.2)	3.10 d (19.0)	–
16a	–	–	–	1.81 m
16b	–	–	–	2.45 m
17	5.76 s	5.67 s	5.73 s	2.45 m
21a	7.52 brs	7.46 s	7.43 m	4.43 t (9.0)
20	–	–	–	2.80 m
21b	–	–	–	3.82 t (9.0)
22	6.44 brs	6.40 d (1.5)	6.38 brs	2.45 m
23	7.40 t (1.8)	7.38 t (1.5)	7.41 m	–
18	0.93 s	0.88 s	1.12 s	1.18 s
19	1.19 s	1.29 s	1.30 s	1.17 s
28	1.36 s	1.38 s	1.52 s	1.43 s
29	1.62 s	1.79 s	1.32 s	1.70 s
30a	2.74 s	4.92 s	4.21 s	1.84 d (16.1)
30b	–	5.20 s	–	2.87 d (16.1)
OMe	3.71 s	3.85 s	–	3.65 s
14-OH	–	–	2.86 s	–
OAc / C-1	–	–	–	2.08 s
OAc / C-11	–	–	–	1.98 s

δ_H: hydrogen chemical shift; *J*: coupling constant; dd: doublet of doublet; t: triplet; d: doublet; m: multiplet; s: singlet; tt: triplet of triplet; dt: doublet of triplet; brd: broad doublet; brs: broad singlet. ^1H NMR spectra were acquired in $CDCl_3$ at 300 MHz (**57**), 400 MHz (**58**, **60**) and 500 MHz (**62**). TMS was used as internal standard. Assignments are based on COSY, HSQC and HMBC experiments.

Table 2. ^{13}C NMR spectroscopic data for **57**-**60** and model **62**

C	δ_C / ppm				
	57	**62**	**58**	**60**	**59**
1	71.7	74.3	69.6	72.3	38.2
2	37.6	38.4	37.3	35.1	24.2
3	170.0	171.0	169.2	171.1	80.6
4	83.7	84.2	82.3	64.8	37.4
5	43.9	49.2	37.8	66.2	43.9
6	35.9	71.0	30.6	32.2	26.3
7	173.5	176.3	169.0	80.2	74.2
8	60.5	146.2	70.0	84.6	38.9
9	48.0	56.2	124.3	50.4	46.1
10	47.1	48.6	41.1	43.9	36.2
11	22.3	24.5	129.5	69.5	16.3
12	28.0	28.6	31.1	45.5	23.6
13	42.7	42.1	39.4	43.4	28.5
14	78.6	81.4	78.9	67.5	37.2
15	31.6	34.4	30.1	68.7	25.5
16	169.3	170.1	169.2	29.7	25.8
17	79.0	79.6	79.0	52.9	48.6
18	13.5	14.2	15.7	19.6	13.6
19	24.1	24.1	19.7	18.8	15.8
20	120.4	121.1	120.3	38.6	49.5
21	141.0	141.4	141.2	73.1	108.6
22	110.0	110.4	110.0	32.8	32.4
23	142.7	143.1	142.9	176.7	77.6
24	–	–	–	–	77.9
25	–	–	–	–	72.1
26	–	–	–	–	26.8
27	–	–	–	–	25.0
28	31.6	31.9	22.4	22.9	17.0
29	22.4	27.0	32.1	24.2	27.8
30	48.9	112.5	90.7	42.2	19.4
OMe	52.2	54.0		51.9	55.6
OAc	–	–	–	C-1, 170.4 / 21.5	–
OAc	–	–	–	C-11, 170.8 / 20.2	–
OCOO	–	–	–	151.9	–
1’	–	–	–	–	167.8
2’	–	–	–	–	128.5
3’	–	–	–	–	137.1
4’	–	–	–	–	20.7
5’	–	–	–	–	15.8

δ_C: carbon chemical shift. ^{13}C NMR spectrum was acquired in $CDCl_3$ at 100 MHz (**57**-**60**) and 125 MHz (**62**). Assignments are based on HSQC and HMBC experiments.

Sohnreyolide (**60**)

Amorphous solid; IR (film) ν_{max} / cm^{-1} 1808, 1770, 1745 (these absorptions indicated the presence of carbonate substituent, ester and lactone groups); ^1H NMR (400 MHz, $CDCl_3$) see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$) see Table 2; HSQC, HMBC, NOESY (400 MHz, $CDCl_3$) see text; MS / MS (ESI) *m/z*, found for $C_{32}H_{42}O_{13}$ [M + H]: 635 (100), [M + H – CO_3]: 575 (10); HRMS *m/z*, calcd. for $C_{32}H_{43}O_{13}$ [$C_{32}H_{42}O_{13}$ + H]: 635.27036, found: 635.28010.

Unfortunately the mass error for the HRMS spectra of all compounds were high, but the obtained low resolution ESI-MS / MS, 1D and 2D NMR (HSQC, HMBC) data confirmed the structures.

Results and Discussion

Isolated compounds

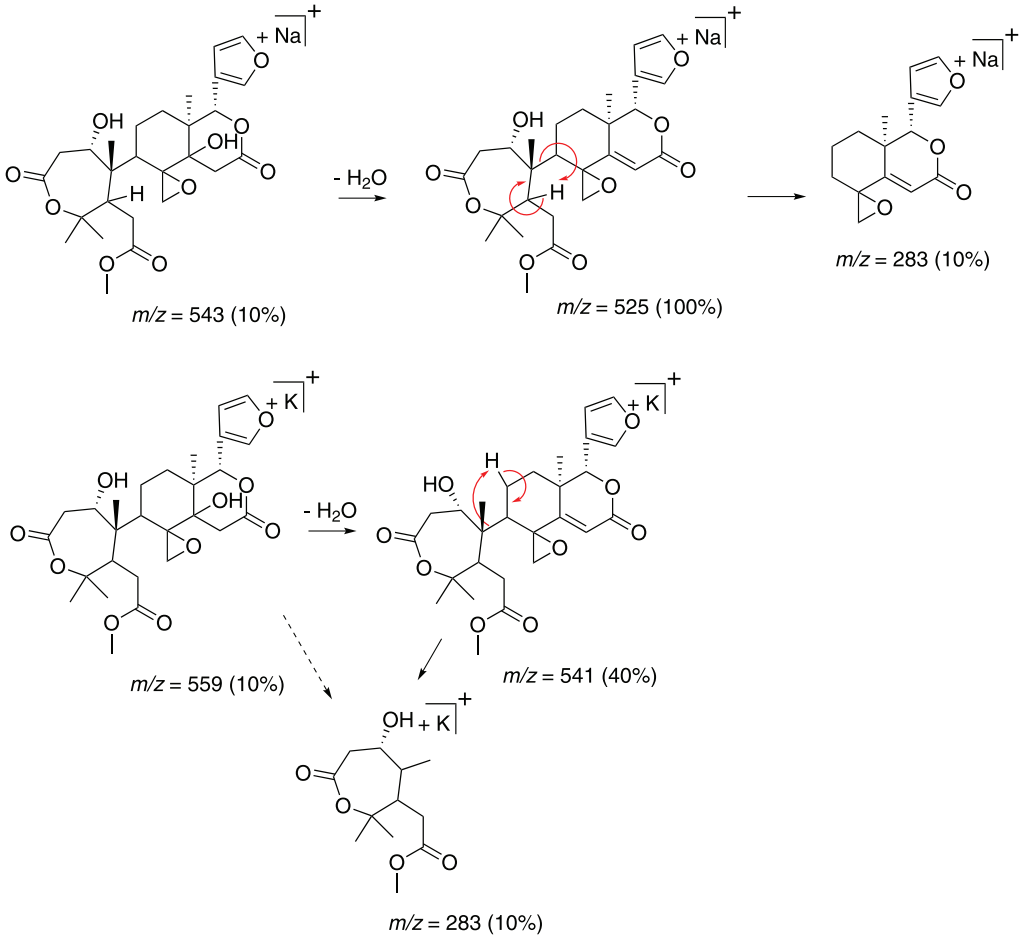
In a continuation of our investigation of the leaves of *D. vandellianum*, we have isolated from the dichloromethane extract the known sitosterol, 2-quinolinone alkaloid 8-methoxyflindersine (**6**), and a new limonoid (**58**) (Figure 4). The methanol extract afforded the limonoid deacetylspathelin (**45**).

The dichloromethane extract from heartwood yielded 2-quinolinone alkaloids 4,7,8-trimethoxy-1-methyl-2-quinolinone (**3**), **6**, 8-methoxy-*N*-methylflindersine (**7**), 7,8-dimethoxyflindersine (**8**), prenylated chromone 6-(3-methylbut-2-enyl)allopeteroxylin methyl ether (**26**) and limonoids deacetylspathelin (**45**), 21,23-dihydro-21-hydroxy-23-oxo-deacetylspathelin (**47**). The methanol extract gave 3β-*O*-β-D-glucopyranosylsitosterol, 2-quinolinone alkaloids **6** and **8**, limonoids limonin diosphenol (**51**), and **57** which is an unpublished limonoid.

The new limonoids were identified as **57** and **58** on the basis of the following data. The ^1H NMR spectra of both limonoids indicated the presence of three downfield shifted signals attributable to a β-substituted furan ring (δ 7.52, 6.44, 7.40 for **57**, and δ 7.43, 6.38, 7.41 for **58**), one signal characteristic of protons attached to a carbon adjacent to an oxygen atom of a carboxyl group (δ 5.76 for **57**, δ 5.73 for **58**), and two isolated methylenes (δ 2.63, 2.17, d, *J* 19 Hz for **57**; δ 3.42, 3.10, d, *J* 19 Hz for **58**) (Table 1). The large geminal coupling constant of these methylene protons was consistent with their situation α to a carboxyl group and with C-14 fully substituted. From HMBC spectra the observed correlation between the ^1H signal at δ 5.76 for **57** and δ 5.73 for **58**, assigned to H-17, and the ^{13}C signal at δ 141.0 for **57** and δ 141.2 for **58** (C-21) determined the position of furan ring at C-17. The correlation of the methylene signals to the C-16 signal at δ_C 169.3 for **57** and δ 169.2 for **58**, as well as of the C-18 signal at δ 0.93 for **57** and δ 1.12 for **58** to the oxygen-bearing C-14 signal at δ_C 78.6 for **57** and δ_C 78.9 for **58**, suggesting the presence of a D 14-hydroxylactone. The signals at δ 2.63, 2.17, d, *J* 19 Hz for **57**; δ 3.42, 3.10, d, *J* 19 Hz for **58** were then assigned to H-15a and H-15b, respectively.

The principal change observed in the ^{13}C NMR spectrum of limonoid isolated from heartwood (**57**) was the resonance for an epoxy methylene δ_H 2.74, brs, δ_C 48.9. The signal for H-15b at δ 2.17 and the methylene signal at δ_H 2.74 showed correlation with the ^{13}C signal at δ 60.5, suggesting the presence of an epoxy formed by C-30 and C-8, and requiring the ring B cleaved. The C-18 signal at δ 0.93 showed cross peaks with the ^{13}C signal at δ 28.0, which correlated in the HSQC with the ^{1}H signals at δ 1.98, m (H-12a) and 1.17, m (H-12b), and the last two were coupled to the ^{1}H signals at δ 2.40, m (H-11a) and 1.70, m (H-11b) (by correlation spectroscopy (COSY)), confirming the intact ring C. Comparison of the NMR data of **57** with those of cneorin R (**61**; H-17, δ 5.65 (s), 78.0; C-7 δ 173.9, OMe, 3.70, 51.8)[37] indicated that **57** has a similar ring A. The differences were the presence of a secondary hydroxyl (δ_H 4.12, dd, *J* 6.0, 2.0 Hz; δ_C 71.7) and the absence of a double-bond at C-1. This was supported by the ESI-MS / MS low resolution which indicated the molecular formula to be $C_{27}H_{36}O_{10}$, and provides fragments by loss of a neutral H_2O at *m/z* 525 $[C_{27}H_{36}O_{10} + Na - H_2O]^+$ (100%) and *m/z* 541 $[C_{27}H_{36}O_{10} + K - H_2O]^+$ (40%), by cleavage at C–C bond between ring A and C at *m/z* 283, giving a good indication of the substitution patterns of A–B (*m/z* 244 + K = 283) and C–D rings (*m/z* 260 + Na = 283) (Scheme 1). In the NOESY experiments the H-1 signal did not influence any group with a spatial proximity such as Me-19, and the hydroxyl hydrogen at C-14 was not detected. Thus, this experiment did not facilitate elucidation of the relative configuration of C-1 and C-14, thus the stereochemistry suggested for **57** was based on the biosynthesis of limonoids. However, for C-1 the coupling constants between H-1 and H-2a and H-2b were characteristic of 1α-oxygenated derivative as in khayseneganin D (**62**) (Table 1).[38] The new limonoid was therefore identified as 1,2-dihydro-1α-hydroxy-8,30-epoxy-cneorin R (**57**). The structural assignment was also supported by comparison of the NMR data with those of khayseneganin D (**62**).[38]

In limonoid **58** the Me-18 signal at δ 1.12 showed cross peaks with the ^{13}C signal at δ 31.0, which correlated in the HSQC with the ^{1}H signals at δ 2.30, m (H-12b) and 1.70, m (H-12a), and the latter two were coupled to the ^{1}H signals at δ 6.00 (ddd, *J* 10.0, 6.4, 1.9 Hz), and this was coupled to another olefinic hydrogen at δ 5.64 (dd, *J* 10.0, 1.7 Hz),



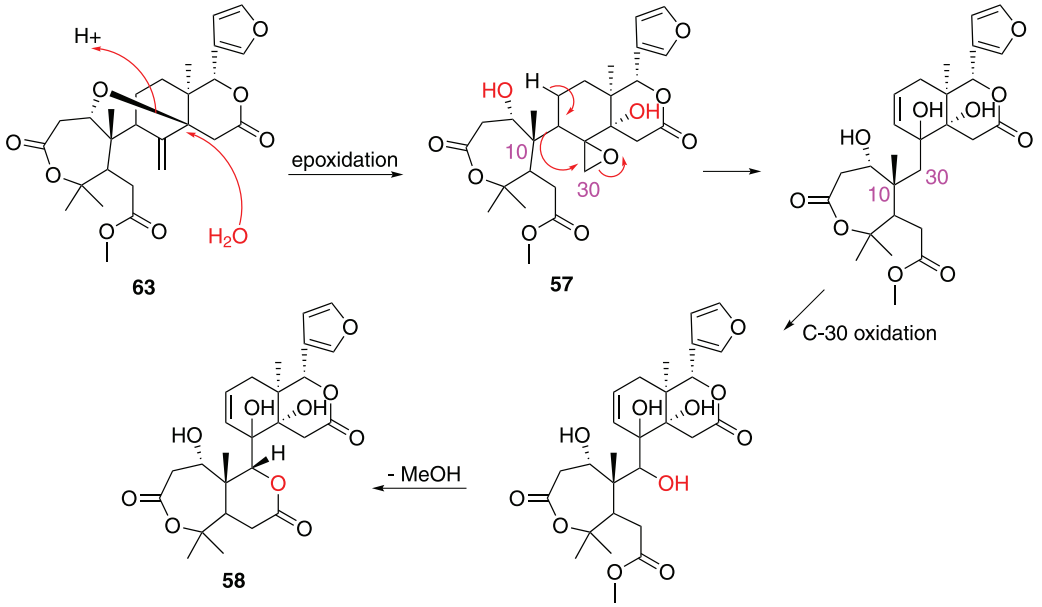
Scheme 1. ESI-MS fragmentation patterns for limonoid **57**.

ascribed to H-11 and H-9, respectively. These observations could not be explained by the presence of ring C as in **57**. Indicating that we were not dealing with a normal B-seco limonoid. The strained three membered ring of epoxide makes it highly susceptible to ring opening reactions, and this may have occurred. Acid can catalyze the ring opening by cleavage of the carbon-oxygen bond (C-30–O–C-8) in **57**. However, the processes may be a concerted reaction, and the molecular fragment ring A by C-10 acting as a nucleophile attacks the protonated epoxide at C-30, with concomitant abstraction of hydrogen from C-11 to form a double bond between C-11 and C-9, and yielding an alcohol at C-8 (see biosynthesis proposal later, and Scheme 2).

The chemical shift of C-8 was established as δ 70.0 via correlation in HMBC between H-11 (δ 6.00) and C-8 (quaternary). In the same way, C-30 emerged from the correlation between H-9 (δ 5.64) and the carbon at δ 90.7 (CH by HSQC, δ 4.21, s). The deshielded resonance for C-30 and H-30 indicated the presence of a lactone involving an intramolecular esterification by secondary hydroxyl at C-30 and C-7 carboxylic ester. This was supported by the correlations of the H-30 signal at δ 4.21, and the ^{1}H signals at δ 2.36 and 2.75 (attributed to H_2-6) to δ 169.0, which confirm ring B lactone with C-30–O–, and permitting the assignment of the signal at δ 169.0 to C-7. These data suggest that ring A via a carbanion at C-10 migrated to C-30 and subsequent oxidation of C-30 to an alcohol occurred (Scheme 2).

Moreover, the H_3-28 and H_3-29 at δ 1.52 and 1.32 showed cross peaks with the ^{13}C signal at δ 82.3 (quaternary), thus indicating ring A as a lactone. Hydroxyl must be connected at C-1 due to the observed correlation between H-1 at δ 3.80 and the carbon at δ 169.2, attributed to C-3. Finally, the cross peak of H-30 (δ 4.21) with the ^{13}C signal of C-1 at δ 69.6 (^3J H-30 → C-10 → C-1) confirms the new bond between C-10 and C-30.

Considering that the rearrangement process in terms of orbitals leads to the prediction that the configuration of the migrating group will be retained in the transition,[39] and based on the biosynthesis of limonoids, the methyl group bonded to carbon 10 remains on face β at the junction of rings A and B. Recall that by definition, the Me-19 is on face β and Me-18 and furan ring on face α of a limonoid, allowing to propose the relative stereochemistry of a limonoid using the nuclear Overhauser effects (NOE). Thereat, the NOESY experiments showed correlations between H-1 and H-30 with H_3-19, implying that H-1 and H-30 were on the β-side of the rings A–B. In nuclear Overhauser effect difference (NOEDIFF) experiments the NOE of the hydroxyl proton at δ 2.86 (C14–OH), coming from H_3-18 showed that the hydroxyl group at C-14 is thus in the α-configuration. The hydroxyl hydrogen at C-8 was not detected, thus the NOESY experiments did not facilitate elucidation of the relative configuration of C-8. A possible pathway leading to the formation of 1,2-dihydro-1α-hydroxy-8,30-epoxy-cneorin R (**57**) and dictyolomin (**58**) cannot be prosed from the more usual 14,15β-epoxide limonoids, since in both compounds the hydroxyl at C-14 appear to be on face α of limonoids. Thus we suggest as precursor methyl ivorensate (**63**), which has a 1α,14β ether



Scheme 2. Probable biogenetic route to limonoids **57** and **58** from methyl ivorensate. The NOESY experiment did not allow determining the relative configuration of C-14 in **57**, based on biogenesis this was proposed as being C14α-OH.

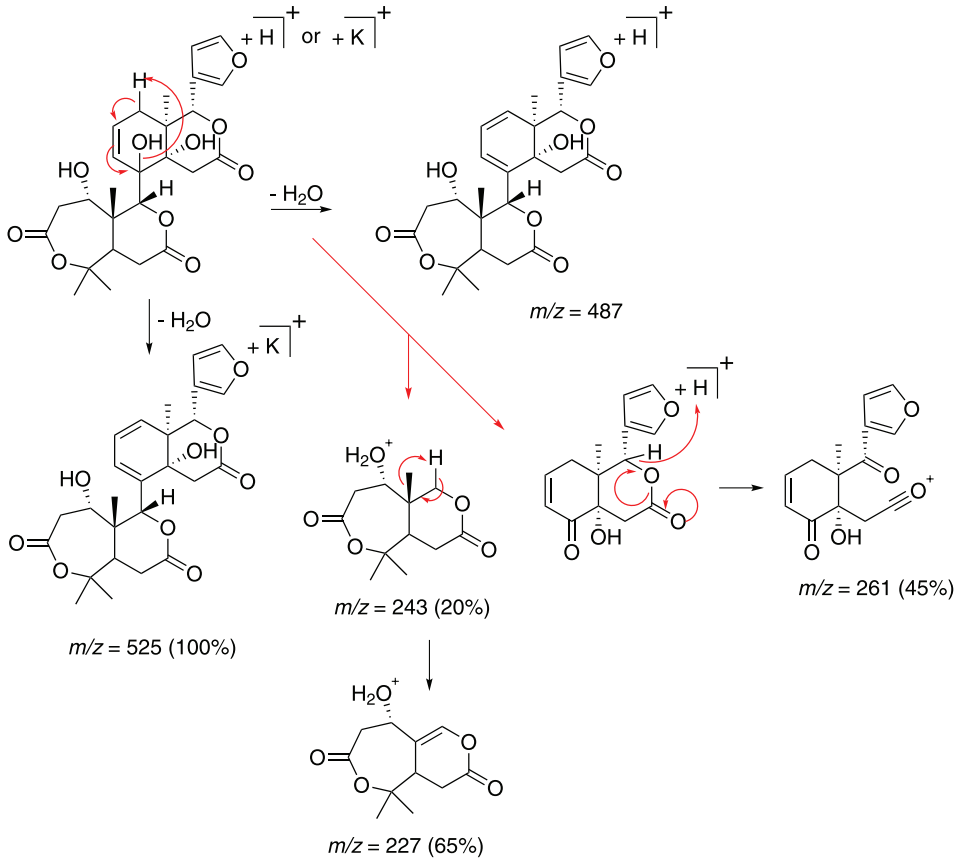
ring, and opening this ether group by water nucleophile attack at C-14 leads to the invariable α-hydroxyl functions at C-1 and C-14. Epoxidation of 8,30 double bond affords **57**, and this leading to **58** is illustrated in Scheme 2.

Limonoid **58** failed to give an $[M]^+$ in the HRMS and in the ESI-MS / MS, the largest fragment observed being *m/z* 487.30253 [$C_{26}H_{32}O_{10}$ + H – H_2O], and *m/z* 525 [$C_{26}H_{32}O_{10}$, M + K – H_2O], respectively. The ESI-MS / MS also showed ions at *m/z* 243, 227 and 261, confirming the substituents at rings AB and CD (Scheme 3). Thus, the structure of the new limonoid was characterized as 1α,8,14α-trihydroxy-8-(30-oxa-10,5,6,7-cyclohexan-7-one-9,11-en-3,4-lactone)-limonoid, and named dictyolomin (**58**).

We have also undertaken a further investigation of *S. excelsa*, and the methanol extract from leaves afforded the known 3β-*O*-β-D-glucopyranosylsitosterol, the coumarin xanthyletin,[26] the flavan epicatechin,[40] limonoids deacetylspathelin (**45**), limonin diosphenol (**51**), perforatin (**53**), the new protolimonoid **59** and the new limonoid **60**.

Protolimonoid **59** exhibited similar NMR spectra to 3β-angeloyloxy-7α,24,25-trihydroxy-21,23-oxide-14,18-cycloapotirucall-21-hemiacetal (**44**), except for the presence of a methoxyl group (δ_H 3.36, δ_C 55.6) (Table 2). The HMBC spectrum showed correlation from methoxyl signal (δ_H 3.36) to the C-21 signal at δ_C 108.6, so placing the methoxyl substituent at C-21. The deshielded resonance observed for C-21 is typical of a ketal function and identifies this compound as 3β-angeloyloxy-7α,24,25-trihydroxy-21,23-oxide-14,18-cycloapotirucall-21-methoxycetal (**59**).

Limonoid **60** instead of showing signals for a furan ring, it showed signals for a γ-lactone (H-20, δ 2.80 (m); C-20, δ 38.6; H-21a, δ 4.43 (brt, *J* 9.0 Hz); H-21b, δ 3.82 (brt, *J* 9.0 Hz); C-21, δ 73.1; H-22, δ 2.45, m; C-22, δ 32.8; C-23, δ 176.7; assignments based on HSQC and HMBC). γ-Lactones and γ-hydroxybutenolides appear to represent stages between the intact side-chain and furan ring (protolimonoid to limonoid), however literature has shown that they also arise by oxidation of the furan ring.[14] Compound **60** showed the spectroscopic characteristics of a ring A cleaved limonoid, thus we consider it a member of this class. In HMBC the cross peak of H-21b (δ 3.82) with the ^{13}C signal at δ 52.9 of C-17 confirms the γ-lactone at C-17. The signal of H-17 (δ_H 2.45, m) showed correlation with ^{13}C signal at δ 68.7 (H-15, δ 3.38, brs) and with Me-18 signal at δ 19.6, whose hydrogen signal at δ 1.80 was correlated to the ^{13}C signal at δ 67.5 (quaternary, C-14),



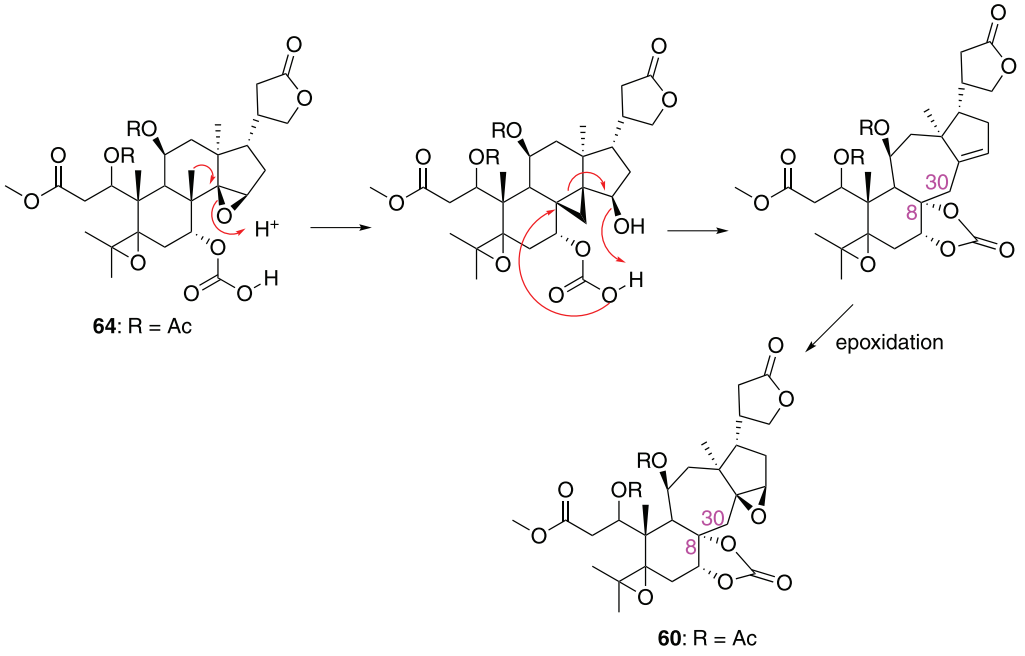
Scheme 3. ESI-MS fragmentation patterns for limonoid **58**.

confirming the presence of a D-five-membered ring with a 14,15-epoxide group.

The identification of the ring A cleaved was supported by comparison of the NMR data with those of deacetylspathelin (**45**). The ^{1}H NMR spectrum instead of signals for a 1-en-3-carbometoxy, showed a signal for an oxymethine proton at δ 5.54 (dd, J 10.7 and 1.7 Hz) and for an acetoxyl group (Me δ_H 2.08, s; Me–COO– δ_C 21.5 and 170.4). This signal showed correlations with Me-19 signal at δ_C 18.8, determining the position of the acetoxyl at C-1. A second oxymethine proton at δ 5.14 (dd, J 10.4 and 8.0 Hz) was coupled to the ^{1}H signals at δ 3.05 (H-9, d, J 8.0 Hz), which showed correlation with Me-19 signal (δ_C 18.8), indicating an acetoxyl group (Me δ_H 1.98, s; Me–COO– δ_C 20.2 and 170.8) to be located at C-11. In addition, the signal for H-7 (δ 4.25, dd, J 13.5 and 3.9 Hz; δ_C 80.2) was coupled to H-6a (δ 1.95, dd, J 13.5 and 3.9 Hz) and H-6b (δ 2.21, t, J 13.5 Hz), which were correlated with the signal for C-5 (δ 66.2), confirming oxygen substituents at C-5 and C-7. The signal for H-7 also showed correlation with a ^{13}C signal at δ 151.9 suggesting a carbon-carbon double bond; however the NMR data did not indicate the presence of the second olefinic carbon, thus suggesting a carbonate substituent, whose chemical shift is normally around δ 149.[41] Moreover, the ^{1}H NMR spectrum suggested the presence of isolated methylene protons (δ 1.18 and 2.87, d, J 16.1 Hz; δ_C 42.3) in ring C, since it was the only location left in the skeleton. These signals showed correlation with the signals for C-14 (δ 67.5) and C-15 (δ 68.7). The ^{1}H signal of H-7 was correlated to ^{13}C signal for this methylene δ_C 42.3. Only an expansion of the C ring could explain these data, and it included C-30, since the HMBC did not indicate Me-30 at C-8. Similar expansion occurred for the delevoyin C limonoid isolated from *Entandrophragma delevoyi*, Meliaceae.[42] The expansion of the C ring of a 7-carbonate-seco-ringA-tetranorapotirucallane precursor (**64**) may have occurred, resulting in structure **60**, whose spectroscopic properties are in accordance with the above data and with one more ^{13}C signal at δ 84.6, attributed to C-8 (Scheme 4). The cross peak from H-30 at δ 2.87 to C-8 confirm this attribution. The ESI-MS indicated the molecular formula to be $C_{32}H_{42}O_{13}$ (*m/z* 635, M + H), and the fragment at *m/z* 575 [M + H – CO_3] confirms the presence of a carbonate substituent. The configuration suggested for **60** was based on the biosynthesis of limonoids, however, these were supported by NOESY experiments. The correlation between the signals H-7 → Me-19 indicates that H-7 is on the face β of the molecule, whereas those between H-15 → Me-18, and H-11 → H-9 and → Me-18 indicate that H-15 and H-11 are on the face α of the structure. Limonoid **60** was then established as 1,11β-diacetoxy-4,5,14β,15β-diepoxy-7α,8α-carbonate-17α-(21,24-γ-lactone)-8,9,11,12,13,14,30-cycloheptanyl-3,4-secotirucalla-3-methylester, and named as sohnreyolide (**60**).

Chemosystematic considerations

The finding of 2-alkyl-4(1*H*)-quinolones in *Dictyoloma vandellianum* and *Sohnreyia excelsa* (synonym



Scheme 4. Probable biogenetic route to limonoid **60**.

Spathelia excelsa) shows strong similarities of both with Zanthoxyleae [*Platydesma* and *Tetradium* (*T. ruticarpum* = *Euodia rutaecarpa*)], Ruteae (*Haplophyllum* and *Ruta*), Boronieae (*Boronia*), Cusparieae (*Raulinoa*), Toddalieae (*Acronychia*, *Vepris* and *Ptelea*), which contain several 2-alkyl-4-quinolones.[16,25,29,43]

The limonoid constituents from both genera suggest a strong affinity with rutaceous genera, but also could be taken as indicative of an affinity to the Meliaceae genera, where the precursor of the new limonoids **57** and **58** occurs, methyl ivorensate (**63**). The latter and its derivative khayseneganin D (**62**) were found in *Khaya senegalensis*.[38] In addition, several limonoids with carbonate as substituent have been reported from *Chukrasia* genus of Meliaceae,[41] and cycloheptanyl ring C limonoid similar to **60** occurs in *Entandrophragma delevoyi*, also Meliaceae.[42] Thus, the co-occurrence of carbonate substituent and cycloheptanyl ring C in *S. excelsa* limonoid **60**, despite having a different skeleton, can also be an indicative of affinity to Meliaceae.

Only one genus, *Harrisonia*, presently classified in Simaroubaceae, is known to contain limonoids, among which perforatin (**53**) and harrisonin (**54**) are also produced by *S. excelsa*.[32] Limonoids occur mainly in Rutaceae, Meliaceae and Cneoraceae, and quassinoids, biosynthetically related compounds, in Simaroubaceae.[34] However, quassinoids had remained undiscovered in *Harrisonia* for many years, but the isolation of perfaraquassin A in *H. abyssinica* was taken as strong evidence in favor of its retention in the Simaroubaceae.[44]

Prenylated chromones have only been reported from the genera *Spathelia*,[19,23,26,27] *Sohnreyia*,[31,32] *Dictyoloma* and *Harrisonia*,[13-15,17,26] as well as from the Cneoraceae, and Ptaeroxylaceae.[26] Chromones have not been found in other Simaroubaceae or Rutaceae. Thus, the co-occurrence of chromones in these taxa is phylogenetically significant by segregating them into a distinct group, according to Appelhans *et al.*[1] in *Spathelia-Ptaeroxylon* clade.[1]

Conclusions

The new limonoids from *Sohnreyia* and *Dictyoloma* show similarities with those from Rutaceae and Meliaceae, providing support for moving *Spathelia-Ptaeroxylon* clade near to these associated large families. As pointed out above, *Sohnreyia* and *Dictyoloma* are well placed in Rutaceae, and then these genera can be regarded as a potential source of coumarins. Thus, it would not be surprising if coumarins had remained undiscovered in both genera because of their low concentration. The most common type of linear furocoumarin, among which xanthyletin is of widespread occurrence, was obtained here from *S. excelsa* in substantial amounts (7.4 mg), which stimulated undertaking a further investigation of *Sohnreyia*, *Spathelia* and *Dictyoloma* species searching for coumarins.

Supplementary Information

Supplementary information (NMR spectra) is available free of charge at http://jbcs.sbq.org.br as PDF file.

Acknowledgments

The authors thank the Brazilian agencies National Council for Scientific and Technological Development (CNPq-INCT, 465357 / 2014-8), São Paulo Research Foundation (FAPESP-INCT, 2014 / 509187; Temático 2012 / 25299-6, APR 2016 / 16117-2), FAPESP-GlaxoSmithKline (2014 / 50249-8) and Coordination for the Improvement of Higher Education Personnel (CAPES, 88887.136357 / 2017-00).

References

1. Appelhans, M. S.; Smets, E.; Razafimandimbison, S. G.; Haevermans, T.; van Marle, E. J.; Couloux, A.; Rabarison, H.; Randrianarivelojosia, M.; Kessler, P. J. A.; *Ann. Bot.* **2011**, *107*, 1259.
2. Bentham, G.; Hooker, J. D.; *Genera Plantarum*, vol. 1; L. Reeve: London, 1862.
3. Engler, A. In *Flora Brasiliensis*, vol. 2; Martius, C. F. P.; Eichler, A. G., eds.; R. Oldenbourg: Munich, 1874, p. 76.
4. Chiovenda E.; *Resultati Scientifici della Missione Stefanini-Paoli nella Somalia italiana*; Tipografia Galletti e Cocci: Firenze, 1916.
5. Engler, A. In *Die Natürlichen Pflanzenfamilien*, vol. 19a, 2nd ed.; Engler, A.; Prantl, K., eds.; Engelmann: Leipzig, 1931, p. 187.
6. Nooteboom H. P.; In *Flora Malesiana*, vol. 6; Van Steenis, C. G. G. J., ed.; Wolters-Noordhoff Publishing: Groningen, 1962, series 1, p. 193.
7. Leroy, J. F.; Lescot, M. In *Flore de Madagascar et des Comores*; Morat, Ph., ed.; Muséum National d'Histoire Naturelle: Paris, 1991, p. 87.
8. Ham, R. W. J. M.; Baas, P.; Bakker, M. E.; *Kew Bull.* **1995**, *50*, 243.
9. Krause, K.; *Notizbl. Königl. Bot. Gartens Mus. Berlin* **1914**, *55*, 143.
10. Harms, H. In *Die Natürlichen Pflanzenfamilien*; Engler, A.; Harms, H., eds.; Verlag von Wilhelm Engelmann: Leipzig, 1931, p. 457.
11. Macbride, J. F.; *Field Mus. Nat. Hist. Publ., Bot. Ser.* **1949**, *3*, 511.
12. Patcher, I. J.; Zacharias, D. E.; Riberio, O.; *J. Org. Chem.* **1959**, *24*, 1285.

13. Campos, A. M.; Dokhac, D.; Fetizon, M.; *Phytochemistry* **1987**, *26*, 2819.
14. Vieira, P. C.; Lázaro, A. R.; Fernandes, J. B.; Silva, M. F. G. F.; *Biochem. Syst. Ecol.* **1988**, *16*, 541.
15. Vieira, P. C.; Lázaro; A. R.; Fernandes, J. B.; Silva, M. F. G. F.; *Quim. Nova* **1990**, *13*, 287.
16. Sartor, C. F.; Silva, M. F. G. F.; Fernandes, J. B.; Vieira, P. C.; Rodrigues Fo, E.; Cortez, D. A. G.; *Phytochemistry* **2003**, *63*, 185.
17. Alves, I. M.; Abreu, L. S.; Costa, C. O. S.; Hyaric, M. L.; Guedes, M. L. S.; Soares, M. B. P.; Bezerra, D. P.; Velozo, E. S.; *Chem. Biodiversity* **2017**, *14*, e1600276.
18. Lavaud, C.; Massiot, G.; Vasquez, C.; Moretti, C.; Sauvain, M.; Balderrama, L.; *Phytochemistry* **1995**, *40*, 317.
19. Box, V. G.; Taylor, D. R.; *Phytochemistry* **1973**, *12*, 956.
20. Harding, W. W.; Lewis, P. A.; Jacobs, H.; McLean, S.; Reynolds, W. F.; Tay, L.-L.; Yang, J.-P.; *Tetrahedron Lett*. **1995**, *36*, 9137.
21. Morimoto, Y.; Takaishi, M.; Iwai, T.; Kinoshita, T.; Jacobs, H.; *Tetrahedron Lett.* **2002**, *43*, 5849.
22. Tinto, W. F.; McLean, S.; Reynolds, W. F.; Carter, C. A. G.; *Tetrahedron Lett.* **1993**, *34*, 1705.
23. Diaz, M.; Preiss, A.; Meyer, H.; Ripperger, H.; *Phytochemistry* **1983**, *22*, 2090.
24. Burke, B. A.; Chan, W. R.; Taylor, D. R.; *Tetrahedron* **1972**, *28*, 425.
25. Mester, I. In *Chemistry and Chemical Taxonomy of the Rutales*; Waterman, P. G.; Grundon, M. F., eds.; Academic Press: London, 1983, p. 31.
26. Gray, A. I. In *Chemistry and Chemical Taxonomy of the Rutales*; Waterman, P. G.; Grundon, M. F., eds.; Academic Press: London, 1983, p. 97.
27. Suwanborirux, K.; Chang, C.-J.; Cassady, J. M; *J. Nat. Prod*. **1987**, *50*, 102.
28. Simpson, D. S.; McLean, S.; Reynolds, W. F.; Jacobs, H.; *Nat. Prod. Commun*. **2010**, *5*, 859.
29. Lima, M. P.; Rosas, L. V.; Silva, M. F. G. F.; Ferreira, A. G.; Fernandes, J. B.; Vieira, P. C.; *Phytochemistry* **2005**, *66*, 1560.
30. Freitas, A. C.; Lima, M. P.; Ferreira, A. G.; Tadei, W. P.; Pinto, A. C. S.; *Quim. Nova* **2009**, *32*, 2068.
31. Moreira, W. A. S.; Lima, M. P.; Ferreira, A. G.; Ferreira, I. C. P.; Nakamura, C. V.; *J. Braz. Chem. Soc.* **2009**, *20*, 1089.
32. Carvalho, L. E.; Lima, M. P.; Máximo, A. C.; Pereira, E. C. S.; Moreira, W. A. S.; Ferreira, A. G.; Véras, S. M.; Souza, M. G.; *Quim. Nova* **2012**, *35*, 2237.
33. Silva, M. F. G. F.; Gottlieb, O. R.; *Biochem. Syst. Ecol.* **1987**, *15*, 85.
34. Zhang, Y.; Xu, H.; *RSC Adv*. **2017**, *7*, 35191.
35. Dreyer, D. L. In *Chemistry and Chemical Taxonomy of the Rutales*; Waterman, P. G.; Grundon, M. F., eds.; Academic Press: London, 1983, p. 215.
36. Li, Q.; Huang, X.; Li, S.; Ma, J.; Lv, M.; Xu, H.; *J. Agric. Food Chem.* **2016**, *64*, 5472.
37. Epe, B.; Mondon, A.; *Tetrahedron Lett*. **1979**, *22*, 2015.
38. Yuan, C.-M.; Zhang, Y.; Tang, G.-H.; Di, Y.-T.; Cao, M.-M.; Wang, X.-Y.; Zuo, G.-Y.; Li, S.-L.; Hua, H.-M.; He, H.-P.; Hao, X.-J.; *J. Nat. Prod.* **2013**, *76*, 327.
39. Carey, F. A.; Sundberg, R. J.; *Advanced Organic Chemistry. Part A: Structure and Mechanisms*, 3rd ed.; Plenum Press: New York, 1990, ch. 11.
40. Agrawal, P. K.; *Carbon-13 NMR of Flavonoids*; Elsevier: New York, 1989.
41. Zhang, H; Liu, H.-B.; Yue, J.-M.; *Chem. Rev.* **2014**, *114*, 883.
42. Mulholland, D. A.; Schwikkard, S. F.; Sandor, P.; Nuzillard, J. M.; *Phytochemistry* **2000**, *53*, 465.
43. Biavatti, M. W.; Vieira, P. C.; Silva, M. F. G. F.; Fernandes, J. B.; Albuquerque, S.; *Z. Naturforsch.* **2001**, *56*, 570.
44. Rajab, M. S.; Fronczek, F. R.; Mulholland, D. A.; Rugutt, J. K.; *Phytochemistry* **1999**, *52*, 127.

Submitted: February 12, 2019
Published online: July 18, 2019