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# APORPHINOID ALKALOIDS AND TERPENOIDS FROM *PIPTOSTIGMA FUGAX**

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**Key Word Index**—*Piptostigma fugax*; Annonaceae; roots; stem bark; aporphinoids; 5α-cycloart-24-ene-3β,16β,21-triol; 4-hydroxy-4,7-dimethyl-1-tetralone; *N*-methylheteropsine; onychines.

**Abstract**—Thirty-eight compounds were isolated from the roots and stem bark of *Piptostigma fugax*, besides three fractions of mixtures of homologues of two 6′-acylated sterol glucosides and fatty acids, respectively. Structures were determined by spectroscopic and chemical methods. Mixtures of homologues were analysed by GC-mass spectrometry after derivatization. 5α-Cycloart-24-ene-3β,16β,21-triol, 4-hydroxy-4,7-dimethyl-1-tetralone and three onychine-type alkaloids (2,7-dihydroxyonychine, 7-hydroxy-2-methoxyonychine and 7-hydroxy-2,8-dimethoxyonychine) represent new compounds. *N*-Methylheteropsine has been isolated as a natural product for the first time.

## INTRODUCTION

The genus *Piptostigma* comprises about 15 species, which are endemic to the West African countries surrounding the Gulf of Guinea between the Ivory Coast and Congo [2]. *Piptostigma fugax* is a small tree of the tropical undergrowth. To our knowledge there exist no phytochemical nor folk medicinal reports on any *Piptostigma* species. Therefore, in the course of our investigations on tropical plants we performed a phytochemical study of the roots and stem bark of *P. fugax* collected in Ghana.

## RESULTS AND DISCUSSION

Air-dried plant material was extracted first with petrol and then with methanol. Chromatographic separation of the petrol extract and work-up of the methanol extract followed by repeated chromatography yielded the individual constituents compiled in Tables 1 and 2, and three mixtures of homologues, which were subjected to chemical derivatization followed by GC-mass-spectral analysis.

The presented structures were determined mainly by spectroscopic investigations and especially by homo- and heteronuclear COSY measurements. As far as possible, known compounds were identified by comparison with authentic substances.

The known 7,7′-bis-6a,7-dehydroaporphines, *N*,*N*′-dimethylurabaine (**5**) [13], heteropsine (**6**) [14], *N*-methylurabaine (**8**) [13], trivalvone (**9**) [15] and urabaine (**10**) [13] were identified on the basis of their physicochemical data (UV, mass spectra, $^1$H, $^{13}$C NMR, mp). It was observed that the $^1$H NMR spectra of these compounds were particularly well resolved when run in benzene-$d_6$ (Table 3). Except for **9** [15], we have measured the $^{13}$C NMR spectra of 7,7′-bis-6a,7-dehydroaporphines for the first time; the assignments of the $^{13}$C resonances were deduced from 2D heteronuclear correlation measurements (Table 4). Comparison of the NMR spectra of **7** with these data led to the structural proposal of a *N*-methylated heteropsine. The decision between the two alternative structures was made by C/H correlation experiments, which gave evidence that the NH is located in the dehydroaporphine moiety carrying the methylenedioxy substituent. These experiments also allowed us to assign the signals of H-8 and H-8′ unambiguously. NOE studies revealed interactions between (a) the proton signals of the *N*-methyl group and H-8′ and (b) the NH and H-8.

The proton resonance data of **11** closely resembled those reported for 5α-cycloart-24-ene-3β,16β-diol [32], except for the signals of Me-18, Me-21 and H-20, but these latter signals were found to be in good agreement with the corresponding data for 5α-cycloart-24-ene-3β,21-diol [33], an observation that suggested the trihydroxylated cycloartene formula **11**. Comparison of the $^{13}$C resonances with those for 5α-cycloart-24-ene-3β,21-diol [33] corroborated the proposed structure. Furthermore, the β-configuration of the 16-hydroxy group was proven by a NOE experiment showing enhancement of H-17 when the frequency of H-16 was irradiated. Since cycloartenol and its 16- or 21-hydroxylated derivatives all exhibit positive optical rotation values in the 20° to 50° range [32–34], we assume the same absolute configuration as depicted in **11**.

*Part 62 in the series 'Constituents of Tropical Medicinal Plants'. For Part 61 see ref. [1].

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Table 1. Constituents isolated from petrol extracts of root and stem bark of *Piptostigma fugax*

| Compound class | Compound | Content [%]* Root | Stem bark | Refs |
|---|---|---|---|---|
| Triterpenes | Lanosta-7,9(11),24-triene-3β,21-diol | 0.06 | | [3] |
| | Polycarpol ( = lanosta-7,9(11),24-triene-3β,15α-diol) | 3.8 | | [4] |
| | Lanosta-8,24-diene-3β,21-diol | 0.12 | | [5] |
| Steroids | 3β-Hydroxystigmasta-5,22-dien-7-one | 0.09 | | [6] |
| | 3β-Hydroxystigmast-5-en-7-one | 0.07 | | [6, 7] |
| | β-Sitosterol | 0.4 | 5.8 | [7] |
| | Stigmasterol | 0.4 | 6.0 | [8] |
| Sesquiterpenes | T-Cadinol (**1**) | 0.6 | | [9] |
| | Cyperenone (**2**) | 0.04 | | [10] |
| | Patchoulenone (**3**) | 0.54 | | [11] |
| | Spathulenol (**4**) | 0.10 | 4.5 | [12] |
| Fatty acids | Mixture of fatty acids (see Table 7) | *ca* 10 | *ca* 10 | |
| Alkaloids | | | | |
| 7,7′-Bis-aporphines | *N*,*N*′-Dimethylurabaine (**5**) | 0.4 | | [13] |
| | Heteropsine (**6**) | 0.2 | | [14] |
| | *N*-Methylheteropsine (**7**) | 0.08 | | |
| | *N*-Methylurabaine (**8**) | 0.7 | | [13] |
| | Trivalvone (**9**) | 0.05 | | [15] |
| | Urabaine (**10**) | 0.5 | | [13] |

*Estimated concentrations in % of total.

Table 2. Constituents isolated from methanol extracts after pre-extraction of root and stem bark of *Piptostigma fugax* with petrol

| Compound class | Compound | Content [%]* Root | Stem bark | Refs |
|---|---|---|---|---|
| Triterpenes | 5α-Cycloart-24-ene-3β,16β,21-triol (**11**) | | 0.5 | |
| | Polycarpol ( = lanosta-7,9(11),24-triene-3β,15α-diol) | 0.4 | | [4] |
| Steroids | Sitosterol-3β-*O*-D-glucoside | 0.7 | | [16, 17] |
| | Stigmasterol-3β-*O*-D-glucoside | 0.7 | | [16, 17] |
| | Mixture of 6′-*O*-acylsitosterol-3β-*O*-D-glucosides (see Table 7) | 0.4 | | [18, 19] |
| | Mixture of 6′-*O*-acylstigmasterol-3β-*O*-D-glucosides (see Table 7) | 0.2 | | [18, 19] |
| Sesquiterpenes | 4-Hydroxy-4,7-dimethyl-1-tetralone (**12**) | | 0.06 | |
| | Patchoulenone (**3**) | 0.9 | | [11] |
| Shikimate pathway | Shikimic acid | | 0.9 | [20] |
| | 3,4,5-Trimethoxyphenyl β-D-apiofuranosyl-(1 → 6)-β-D-glucopyranoside (**13**) | | 0.2 | [21] |
| | Vanillic acid methyl ester | | 0.2 | |
| Alkaloids | | | | |
| Aporphines | *N*-Formylnornuciferine (**14**) | | 0.05 | [22, 23] |
| | Liriodenine (**15**) | 0.04 | 0.09 | [24, 25] |
| | Lysicamine (**16**) | 0.14 | 0.2 | [24, 25] |
| | *O*-Methylmoschatoline (**17**) | | 0.03 | [24, 25] |
| | Nornuciferine (**18**) | 0.2 | 0.7 | [24, 26] |
| 7,7′-Bis-aporphines | *N*-Methylurabaine (**8**) | 0.3 | | [13] |
| | Trivalvone (**9**) | trace | | [15] |
| Onychines | 2,7-Dihydroxyonychine (**19**) | 0.2 | | |
| | 7-Hydroxy-2-methoxyonychine (**20**) | | 0.06 | |
| | 7-Hydroxy-2,8-dimethoxyonychine (**21**) | | 0.04 | |
| Others | *N*-Carbamoyl-2-methoxypyrrolidine | 0.3 | 0.7 | [26] |
| | Dipterine ( = *N*-methyltryptamine) | 2.0 | 1.7 | [27] |
| | *trans*-Feruloyltyramine | 0.3 | | [28] |
| | Indole-3-carbaldehyde | trace | 0.04 | [29] |
| | Stepharanine (**22**) | 0.09 | 0.1 | [30] |

*Estimated concentrations in % of total.

Table 3. $^1$H NMR spectral data of the 7,7′-bis-6a,7-dehydroaporphines **5**–**10** ($C_6D_6$, 360 MHz)

| H | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|
| 1-OMe | 3.92 | 3.93 | 3.91 | 3.92[a] | — | 3.92 |
| 1′-OMe | | | — | 3.91[a] | 3.85 | |
| 2-OMe | 3.58 | 3.53 | 3.58 | 3.57 | 3.31 | 3.52 |
| 2′-OMe | | | — | 3.54 | 3.59 | |
| 1′,2′-$OCH_2O$- | — | 5.59/5.58 *m* | 5.60/5.58 *d* (1.5) | — | — | |
| 3 | 6.89 *br s* | 6.79 | 6.88 | 6.88 | 6.10 | 6.78 |
| 3′ | | 6.78 | 6.81 | 6.79 | 6.90 | |
| 4eq, 4eq′ | 2.57 *ddd* (16.0/3.5/3.5) | | | | 6.70 *d* (4.0) | |
| 4ax, 4ax′ | 3.11 *dddd* (16.0/11.5/4.5/1.0) | 2.55–3.00 *m* | 2.70–3.10 *m* | 2.76–3.09 *m* | 2.52–3.05 *m* | 2.75–2.96 *m* |
| 5eq, 5eq′ | 2.91 *ddd* (12.8/4.5/3.5) | | | | 8.54 *d* (4.0) | |
| 5ax, 5ax′ | 3.35 *ddd* (12.8/11.5/3.5) | | | | | |
| N-H | — | 4.35 *br s* | — | — | — | 4.35 *br s* |
| N′-H | — | 4.31 *br s* | 4.19 *br s* | 4.24 *br s* | — | |
| N-Me | 2.27 | — | 2.47 | 2.48 | — | |
| N′Me | | — | | | 2.13 | — |
| 8 | 7.70 *dd* (8.3/1.5) | 7.58 *br d* (8.0) | 7.75 *dd* (8.3/1.3) | 7.76 *dd* (8.5/1.5) | 8.00 *ddd* (8.7/1.3/0.5) | 760 *dd* (8.0/1.5) |
| 8′ | | 7.52 *br d* (8.0) | 7.44 *dd* (8.3/1.5) | 7.51 *dd* (8.3/1.5) | 7.12 *ddd* (8.3/2.0/0.5) | |
| 9 | 7.20 *ddd* (8.3/6.7/1.3) | 7.22[a] *ddd* (8.0/7.0/1.5) | 7.21 *ddd* (8.3/6.7/1.3) | 7.19 *ddd* (8.5/6.7/1.3) | 7.05 *ddd* (8.7/6.7/1.2) | 7.24 *ddd* (8.0/7.0/1.3) |
| 9′ | | 7.24[a] *ddd* (8.0/7.0/1.5) | 7.24 *ddd* (8.3/7.0/1.3) | 7.25 *ddd* (8.3/6.7/1.5) | 7.09 *ddd* (9.0/6.7/1.3) | |
| 10 | 7.45 *ddd* (8.7/6.7/1.5) | 7.43[b] *ddd* (8.5/7.0/1.5) | 7.47 *ddd* (8.5/6.7/1.3) | 7.47 *ddd* (8.7/6.7/1.5) | 7.52 *ddd* (9.0/6.7/1.3) | 7.43 *ddd* (8.5/7.0/1.5) |
| 10′ | | 7.41[b] *ddd* (8.5/7.0/1.5) | 7.39 *ddd* (8.3/7.0/1.5) | 7.41 *ddd* (8.7/6.7/1.5) | 7.42 *ddd* (8.7/6.3/2.0) | |
| 11 | 10.16 *dd* (8.7/1.3) | 10.14 *br d* (8.5) | 10.17 *dd* (8.5/1.3) | 10.18 *dd* (8.7/1.3) | 10.78 *ddd* (9.0/1.2/0.5) | 10.15 *dd* (8.5/1.3) |
| 11′ | | 9.48 *br d* (8.5) | 9.47 *dd* (8.3/1.3) | 10.13 *dd* (8.7/1.3) | 10.16 *ddd* (8.7/1.2/0.5) | |

[a,b]Assignments interchangeable within a column.

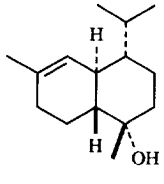
The NMR data of **12** (HREI-mass spectrum: $C_{12}H_{14}O_2$) revealed a hydroxylated 1-tetralone substituted by methyl groups at C-7 and C-4 (or C-2), the latter at a tertiary alcoholic function. NOE between the resonances of the high-field Me-group and the aromatic H-5 established structure **12**. HPLC on Chiralcel® OD provided evidence that **12** was a racemic mixture.

To answer the question whether the tertiary benzylic hydroxy group would enable enantiomeric **12** to an easy racemization we performed stability tests: Enantiomerically pure **12** prepared from synthetic **12** by HPLC on Chiralcel® OD was kept dissolved in (i) petrol + 5% acetic acid, (ii) chloroform in the presence of silica gel and (iii) methanol + 5% acetic acid. After 8 weeks at room

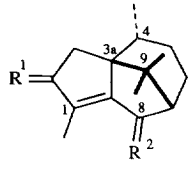
Table 4. $^{13}C$ NMR spectral data of the 7,7'-bis-6a,7-dehydroaporphines **5**–**10** ($C_6D_6$, 90 MHz)

| C | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|
| 1 | 147.0 | 147.0 | 147.0 | 146.7 | 180.4 | 147.0 |
| 2 | 151.4 | 152.2 | 151.8 | 151.8 | 156.9 | 152.2 |
| 3 | 113.7 | 112.8 | 113.4 | 113.4 | 107.1 | 112.8 |
| 3a | 130.9 | 130.2 | 131.0 | 131.0 | 143.1 | 130.3 |
| 3b | 122.6 | 118.8[a] | 122.1 | 122.1 | 123.0 | 119.1 |
| 4 | 26.9 | 31.3[b] | 27.0 | 27.0 | 121.2 | 31.3 |
| 5 | 50.3 | 40.95[c] | 50.5 | 50.5 | 150.6 | 40.9 |
| 6a | 143.7 | 141.1 | 144.9 | 144.9 | 150.4* | 140.7 |
| 7 | 106.8 | 106.7 | 118.7 | 119.3 | 134.1* | 107.1 |
| 7a | 135.8 | 134.6 | 134.2 | 134.3 | 134.8 | 134.7 |
| 8 | 127.1[a] | 124.5[d] | 125.6 | 125.8 | 129.0 | 124.6 |
| 9 | 127.1[a] | 127.3[e] | 127.6[a] | 127.2 | 127.1[a] | 126.1 |
| 10 | 124.5 | 123.2[f] | 124.9[b] | 125.0 | 132.4 | 123.2 |
| 11 | 128.7 | 128.7 | 128.5 | 128.6 | 127.3 | 129.0 |
| 11a | 128.4 | 126.1 | 128.5 | 128.3 | 124.2* | 126.8 |
| 11b | 126.7 | 126.8 | 127.2 | 127.0 | 136.5* | 128.7 |
| 1-OMe | 59.6 | 59.6 | 59.6 | 59.6[b] | | 59.6 |
| 2-OMe | 56.4 | 56.3 | 56.3 | 56.4[c] | 55.2 | 56.2 |
| N-Me | 41.6 | | 41.9 | 41.9 | | |
| 1' | | 142.6 | 142.6 | 146.1 | 147.1 | |
| 2' | | 146.0 | 145.7 | 151.9 | 151.8 | |
| 3' | | 108.1 | 108.1 | 113.0 | 113.8 | |
| 3a' | | 128.9 | 127.3[a] | 130.1 | 130.6 | |
| 3b' | | 118.4[a] | 119.0 | 119.2 | 122.0 | |
| 4' | | 31.0[b] | 31.2 | 31.6 | 25.4 | |
| 5' | | 40.9[c] | 41.1 | 41.0 | 49.8 | |
| 6a' | | 140.7 | 140.0 | 139.5 | 143.9 | |
| 7' | | 106.4 | 111.0 | 111.7 | 122.7* | |
| 7a' | | 134.1 | 134.7 | 135.3 | 135.4 | |
| 8' | | 124.3[d] | 125.0 | 125.4 | 126.8 | |
| 9' | | 127.3[e] | 127.5[a] | 127.4 | 127.1[a] | |
| 10' | | 122.9[f] | 122.5 | 122.9 | 124.9 | |
| 11' | | 127.5 | 127.7 | 128.53 | 127.5 | |
| 11a' | | 124.6 | 124.4 | 125.9 | 130.2* | |
| 11b' | | 119.0 | 118.2 | 126.5 | 127.0* | |
| 1'-OMe | | | | 59.5[b] | 59.5 | |
| 2'-OMe | | | | 56.3[c] | 56.4 | |
| N'-Me | | | | | 41.3 | |
| $-OCH_2O-$ | | 101.0 | 100.8 | | | |

[a–f]Assignments interchangeable within a column.
*Assignments according to refs [15, 31].

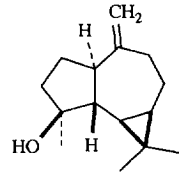



**1**

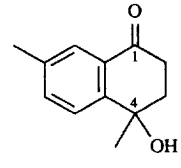



**2** $R^1 = O$, $R^2 = H_2$

**3** $R^1 = H_2$, $R^2 = O$




**4**




**12**

temperature, racemization was measured to have occurred with a rate of less than 4% in petrol and chloroform, respectively, and about 10% in the methanolic solution. Therefore, we regard racemic **12** as a genuine natural product.

The synthesis of **12** was achieved from 6-methyl-2,3-dihydro-1,4-naphthoquinone [35] by reaction with methyl magnesium iodide. Compound **12** was separated from its regioisomer by HPLC after acetylation (Fig. 1).

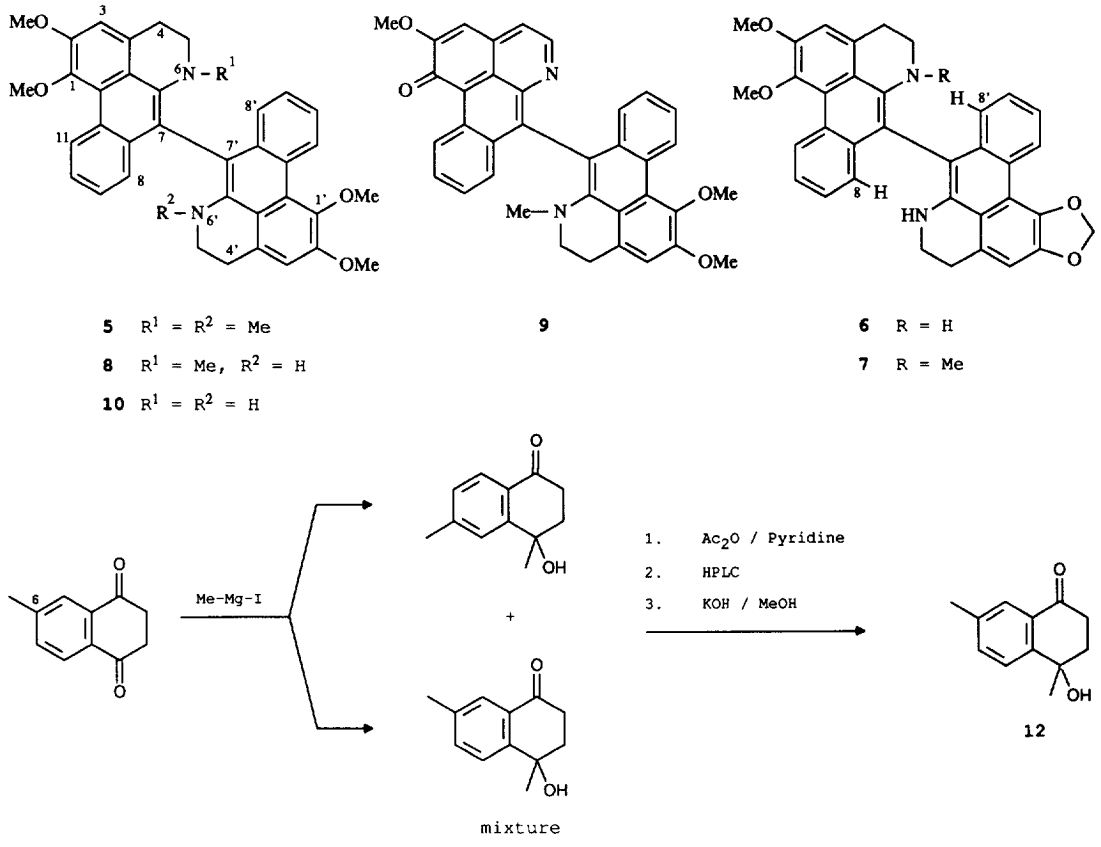



Fig. 1. Synthesis of compound **12** and its regioisomer from 6-methyl-2,3-dihydro-1,4-naphthoquinone.

Table 5. $^1$H NMR data of isolated onychine alkaloids **19**–**21** and the derivatives **23** and **24** ($CDCl_3$, 360 MHz; * in $CDCl_3$–$CD_3OD$, 1:1)

| H | 19* | 20 | 21 | 23 | 24* |
|---|---|---|---|---|---|
| 1-Me | 2.49 *s* | 2.51 *s* | 2.51 *s* | 2.50 *s* | 2.38 *s* |
| 2-OMe | — | 3.93 *s* | 3.93 *s* | 3.91 *s* | 3.91 *s* |
| 3 | 7.86 *s* | 7.98 *s* | 8.0 *s* | 7.96 *s* | 7.90 *s* |
| 5 | 7.51 *d* (8.0) | 7.61 *d* (8.0) | 7.37 *d* (8.0) | 7.62 *d* (8.0) | 7.70 *d* (8.5) |
| 6 | 6.96 *dd* (8.0/2.5) | 6.99 *dd* (8.0/2.5) | 7.07 *d* (8.0) | 7.03 *dd* (8.0/2.5) | 6.93 *dd* (8.5/2.0) |
| 7-OH | — | 5.36 | 6.05 | — | — |
| 7-OMe | — | — | — | 3.85 | 3.84 *s* |
| 8 | 7.05 *d* (2.5) | 7.11 *d* (2.5) | — | 7.17 *d* (2.5) | 7.17 *d* (2.0) |
| 8-OMe | — | — | 4.21 *s* | — | — |
| 9 | — | — | — | — | 5.52 *s* |

The spectroscopic data [mass, UV/VIS, NMR spectra (Tables 5 and 6)] revealed **19**–**21** to belong to the onychine alkaloids ( = 1-methyl-4-azafluoren-9-ones).

UV/VIS studies suggested a hydroxyl group at C-7 [36]. Final structural determination of **19** was achieved by C/H correlation NMR using its dimethyl ether **23** (Fig. 2) and by NOE measurements of the alcohol **24** (Fig. 3), obtained by $NaBH_4$ reduction of **23**. In addition, the $^{13}$C NMR spectrum of **23** was found to be in good agreement with that recently reported for onychines [37].

NOE measurements established the position of a methoxyl group at C-2 in **20** and **21** and methylation of **20** yielded **23**. The final structure of **21** followed from its HMQC and HMBC spectra (Fig. 4).

Furthermore, a new synthetic pathway to 2-oxygenated onychines made **19**–**21** easily accessible and confirmed the determined structures [38].

The mixture of fatty acids isolated as a fraction from the petrol extract did not show any $^1$H NMR signals indicative for branched alkyls. It was converted to the corresponding methyl esters and subjected to GC-mass spectral analysis (Table 7, column a). Identification resulted from the mass spectra and, for most esters, also on co-injection with authentic compounds.

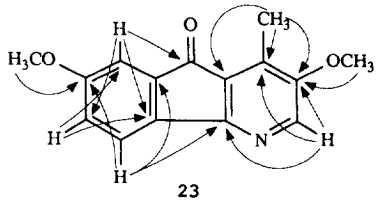
Table 6. $^{13}C$ NMR spectral data of isolated onychine alkaloids **19–21** and the derivatives **23** and **24** (90 MHz in $CDCl_3$; * in $CDCl_3$–$CD_3OD$ (1:1)

| C | 19* | 20* | 21† | 23 | 24* |
|---|---|---|---|---|---|
| 1 | 137.8 | 137.8 | 137 | 137.4 | 136.2 |
| 2 | 153.3 | 154.9 | 154 | 154.4 | 154.6 |
| 3 | 137.1 | 132.3 | 134 | 133.9 | 131.2 |
| 4a | 157.6 | 157.9 | 157.5 | 159.2 | 153.1 |
| 4b | 134.9 | 133.3 | 135 | 135.9 | 139.8 |
| 5 | 121.9[a] | 122.1[a] | 116 | 121.3 | 121.6 |
| 6 | 121.7[a] | 122.2[a] | 120 | 120.8 | 111.3 |
| 7 | 159.8 | 160.1 | 150 | 161.4 | 161.8 |
| 8 | 111.6 | 111.5 | 145 | 108.9 | 115.9 |
| 8a | 137.7 | 139.4 | 125 | 137.6 | 149.8 |
| 9 | 194.4 | 193.4 | –‡ | 193.2 | 72.2 |
| 9a | 127.7 | 127.4 | 126.5 | 126.8 | 132.2 |
| 1-Me | 10.2 | 10.3 | 10 | 10.1 | 11.6 |
| 2-OMe | | 56.9 | 57 | 56.5 | 56.9 |
| 7-OMe | | | | 55.8 | 55.9 |
| 8-OMe | | | 62.5 | | |

[a]Assignments interchangeable within a column.

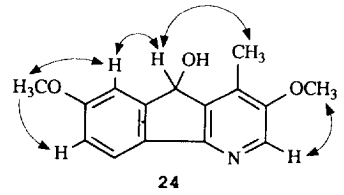
†Values deduced from HMQC and HMBC spectra, respectively.

‡Signal not detected.




23

Fig. 2. Important $^{13}C$–$^1H$ long-range correlations observed in HMBC spectrum of **23**.




24

Fig. 3. NOEs observed in $^1H$ spectrum of **24**.

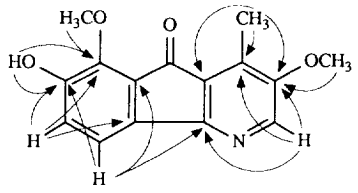



Fig. 4. $^{13}C$–$^1H$ long-range correlations observed in HMBC-spectrum of **21**.

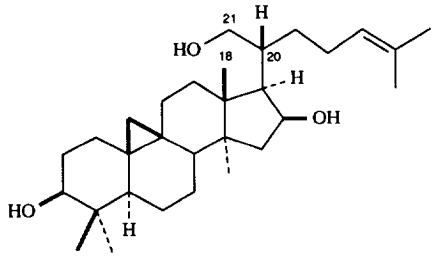
Correspondingly, the mixtures of the 6′-*O*-acylglucosides of β-sitosterol and stigmasterol, respectively, were controlled by $^1H$ NMR spectrometry, treated with sodium methoxide–methanol and were then analysed by GC–mass spectroscopy (Table 7, columns b and c).

The constituents **11**, **12** and **19–21** isolated from *P. fugax* represent new compounds, and **7** also is a new natural product, which hitherto has only been described as a synthetic derivative of **6** [14]. The apioside **13** has to be regarded as a very rare natural product; it was reported once from the bark of *Cinnamomum cassia* (Lauraceae) [21].

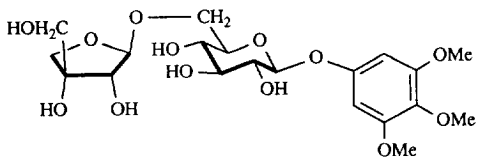
Polycarpol has to be regarded as a typical and frequent constituent of the Annonaceae and up to now has been found exclusively in this family [39]. Aporphinoid alkaloids have also been isolated frequently from the Annonaceae, but they occur in other plant families too. However, the occurrence of 7,7′-bis-aporphines seems to be re-

Table 7. GC-MS analysis of mixtures of fatty acid methyl esters obtained from (a) the corresponding fraction of the petrol extract by methylation, (b) the mixture of 6′-*O*-acylsitosterol-3β-*O*-glucosides by methanolysis, (c) the mixture of 6′-*O*-acyl-stigmasterol-3β-*O*-glucosides by methanolysis (*total esters of a fraction = 100%)

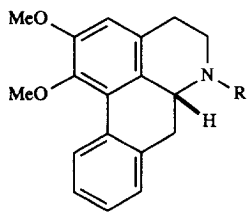
| Methyl ester | Retention time (min) | Content (%) (a) | (b) | (c) |
|---|---|---|---|---|
| Dodecanoic acid | 12.75 | 0.3 | — | — |
| Tetradecanoic acid | 16.03 | 0.6 | 5.8 | 3.0 |
| Pentadecanoic acid | 17.52 | 0.9 | 4.3 | 1.3 |
| Hexadecadienoic acid | 18.55 | 0.5 | — | — |
| Hexadecenoic acid | 18.64 | 1.0 | | — |
| Hexadecanoic acid | 19.15 | 29 | 55 | 70 |
| Heptadecenoic acid | 20.28 | 1.4 | — | — |
| Heptadecanoic acid | 20.68 | 1.4 | 1.9 | 0.8 |
| 9,12-Octadecadienoic acid | 21.98 | 9.0 | — | — |
| 9-Octadecenoic acid | 22.08 | 42 | 13 | 14 |
| Octadecanoic acid | 22.28 | 2.6 | 2.8 | 1.8 |
| Nonadecenoic acid | 23.98 | 1.9 | — | — |
| Eicosanoic acid | 25.71 | | 5.3 | 1.6 |
| Docosanoic acid | 29.83 | 2.2 | 5.4 | 3.2 |
| Tetracosanoic acid | 33.56 | 6.5 | 6.0 | 2.5 |



11

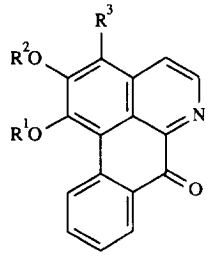


13



**14** R = CHO

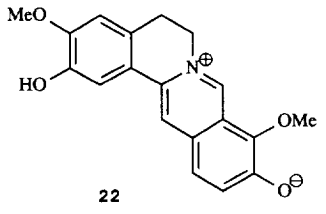
**18** R = H



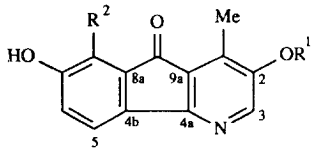
**15** $R^1,R^2$ = $-CH_2-$, $R^3$ = H

**16** $R^1$ = $R^2$ = Me, $R^3$ = H

**17** $R^1$ = $R^2$ = Me, $R^3$ = OMe



22



**19** $R^1$ = $R^2$ = H

**20** $R^1$ = Me, $R^2$ = H

**21** $R^1$ = Me, $R^2$ = OMe

stricted to Annonaceae and up to now, the onychines also have been isolated from the Annonaceae only. Cycloartane-type triterpenes have been reported from the Annonaceae occasionally [33, 40, 41]. T-Cadinol (**1**) might be the biosynthetic precursor of the new tris-nor-sesquiterpene **12**.

Biological tests with the compounds isolated in larger amounts revealed strong antifungal activity for patchoulenone (**3**) against *Rhizoctonia solani* and *Saprolegnia asterophora* in the plate diffusion test, but no antibacterial effect was observed against *Bacillus subtilis*.

Compounds **3** and **12** showed significant, and the 7,7′-bis-aporphine alkaloids **5** and **10** moderate, toxicity in the brine shrimp bioassay [42].

## EXPERIMENTAL

*General.* Mps: uncorr. Analytical TLC were performed on precoated plates (Nano plates Sil-20 UV, Macherey-Nagel) using the solvent systems: S-1 = $CHCl_3$–MeOH (19:1), S-2 = $CHCl_3$–MeOH (9:1), S-3 = $CHCl_3$–MeOH–$H_2O$ (14:16:1), S-4 = $CHCl_3$–$Me_2CO$ (9:1), S-5 = petrol–$Me_2CO$ (9:1), S-6 = cyclohexane–EtOAc (9:1), S-7 = cyclohexane–EtOAc (4:1), S-8 = cyclohexane–EtOAc (3:2); detection: anisaldehyde [43] followed by heating or Dragendorff's reagent [43]. Unless otherwise stated, $[\alpha]_D$ values were measured in $CHCl_3$, UV/VIS and CD in MeOH and IR in $CHCl_3$. EIMS and HR-EIMS were obtained at 70 eV. For GC-MS we used a Permaphase® PVM S/54, 0.3 micron, Perkin-Elmer capillary column (length: 25 m), He gas (pressure: 0.7 bar), temp. prog: 5 min at 50°, then 15° $min^{-1}$ to 300° and 15 min at 300°. Unless indicated otherwise, $^1H$ NMR spectra were measured at 360 MHz and $^{13}C$ NMR spectra at 90 MHz in $CDCl_3$ with TMS as int. standard. For $^1J$-correlation the sequence according to ref. [44] was used, and for long-range correlation the sequence according to ref. [45]; best results were achieved by an evolution delay of 60 msec and a relaxation delay of 2 sec. NOEs were measured by the difference method.

*Plant material.* Roots and stem bark of *P. fugax* were collected in 1988 in the Neung Forest Reserve, Ghana, and identified by Albert Adai Enti (Forestry Enterprises, Legon, Ghana). A voucher specimen is deposited in our institute under No. 88–02.

*Extraction and isolation.* Roots (690 g) were extracted at room temp. with petrol ( = extract A, 3.4 g) and then with MeOH. The MeOH extract was concd to 500 ml and the same vol. of $H_2O$ was added. This suspension was partitioned successively between petrol ( = extract B, 1.2 g), $CH_2Cl_2$ ( = extract C, 2.5 g) and then EtOAc ( = extract D, 3.8 g). The stem bark (480 g) was treated correspondingly, but the original petrol extract was combined with the petrol fr. from the MeOH extract yielding only one combined petrol bark extract ( = extract E, 1.8 g) and, furthermore, a $CH_2Cl_2$ fr. of the MeOH bark extract ( = extract F, 2.8 g) and a EtOAc fr. ( = extract G, 2.5 g). These extracts were subjected to

MPLC on silica gel (Macherey-Nagel, No. 81538), using petrol–$Me_2CO$ or $CHCl_3$–MeOH mixts, and the crude frs were further sepd by repeated MPLC or CC using one or other of the following systems: (a) silica gel: petrol–$Me_2CO$ or cyclohexane–EtOAc or $CHCl_3$–$Me_2CO$ or $CHCl_3$–MeOH–$H_2O$; (b) silica gel RP-18 (LiChroprep): MeOH–$H_2O$ or MeOH–EtOH; (c) Sephadex LH-20: MeOH; (d) Fractogel PVA 500: MeOH. These procedures yielded mostly pure compounds. However, the lanostane-type compounds, except polycarpol, and the phytosterols needed final separation by HPLC. The frs containing mixts of homologues of (a) fatty acids, (b) 6′-*O*-acylsitosterol glucosides and (c) 6′-*O*-acylstigmasterol glucosides were converted to a mixt. of the corresponding fatty acid Me esters and then analysed by GC-MS.

*Extract A*

*Lanosta*-7,9(11),24-*triene*-3β,21-*diol*. Crystals (1.5 mg). Mp 190° (ref. [3] mp 188–190°). TLC: $R_f$ 0.37 (S-8); anisaldehyde reagent: violet. $[\alpha]_D$ + 65° ($CHCl_3$; *c* 0.14) (ref. [3] $[\alpha]_D$ + 65°). UV, IR, $^1$H NMR, MS in agreement with published data [3].

*Lanosta*-7,9(11),24-*triene*-3β-15α-*diol* ( = *polycarpol*). Crystals (95 mg). Mp 172° (ref. [4] mp 171–174°). TLC: $R_f$ 0.16 (S-7); anisaldehyde reagent: violet. $[\alpha]_D$ + 97° ($CHCl_3$; *c* 0.6) (ref. [4] $[\alpha]_D^{25}$ + 100°). UV, IR, $^1$H NMR, MS in agreement with published data [4]. Also isolated from extracts B and E.

*Lanosta*-8,24-*diene*-3β,21-*diol*. Crystals (3 mg). Mp 172° (ref. [5] mp 176–178°; ref. [46] mp 145–147°). TLC: $R_f$ 0.37 (S-8); anisaldehyde reagent: violet. $[\alpha]_D$ + 69° ($CHCl_3$; *c* 0.24). $^1$H, $^{13}$C NMR, MS in agreement with published data [5]. The discrepancies with some data published for uvariol [46] cannot be explained (mp; MS; $^{13}$C resonances for C-17, C-20, C-22).

3β-*Hydroxystigmast*-5,22-*dien*-7-*one*. Crystals (2 mg). Mp 160° (ref. [6] mp 160–162°). TLC: $R_f$ 0.17 (S-8); anisaldehyde reagent: reddish-brown. $[\alpha]_D$ − 82° ($CHCl_3$; *c* 0.21) (ref. [6] $[\alpha]_D$ − 78°). IR, UV, $^1$H NMR, MS in agreement with published data [6].

3β-*Hydroxystigmast*-5-*en*-7-*one*. Prisms (2 mg). Mp 160–162° (ref. [6] mp 128–130°; ref. [7] mp 164–167°). TLC: $R_f$ 0.17 (S-8); anisaldehyde reagent: reddish-brown. $[\alpha]_D$ − 69° ($CHCl_3$; *c* 0.12) (ref. [6] $[\alpha]_D$ − 85°; ref. [7] $[\alpha]_D^{26}$ − 65°). IR, UV, $^1$H NMR, MS in agreement with published data [7].

β-*Sitosterol*. Crystals (90 mg). Mp 135–137° (ref. [7] mp 136°). TLC: $R_f$ 0.34 (petrol–$Me_2CO$, 4:1); anisaldehyde reagent: violet. $[\alpha]_D$ − 40° ($CHCl_3$; *c* 0.5) (ref. [7] $[\alpha]_D^{25}$ − 29.3°). TLC, IR, $^1$H NMR, MS identical with an authentic sample. Also isolated from extract E.

*Stigmasterol*. Crystals (100 mg). Mp 169° (ref. [8] mp 168–169°). $[\alpha]_D$ − 44° ($CHCl_3$; *c* 0.66). TLC: $R_f$ 0.34 (petrol–$Me_2CO$, 4:1); anisaldehyde reagent: violet. TLC, IR, $^1$H, $^{13}$C NMR, MS identical with an authentic sample. Also isolated from extract E.

*T-Cadinol* (**1**). Oil (16 mg). TLC: $R_f$ 0.57 (S-5); anisaldehyde reagent: violet. $[\alpha]_D$ + 3° ($CHCl_3$; *c* 1.0) (ref. [9] $[\alpha]_D$ + 3.4°). IR, $^1$H NMR, MS in agreement with published data [9].

*Cyperenone* ( = *cyperotundone*) (**2**). Oil (0.7 mg). TLC: $R_f$ 0.41 (S-7). $[\alpha]_D$ + 16° ($CHCl_3$; *c* 0.07) (ref. [10] $[\alpha]_D$ + 14.6°). IR, UV, $^1$H NMR, MS in agreement with published data [10].

*Patchoulenone* (**3**). Solid (21 mg). Mp 52° (ref. [11] mp 52.5°). TLC: $R_f$ 0.40 (S-6); anisaldehyde reagent: light-blue. $[\alpha]_D$ − 90° ($CHCl_3$; *c* 0.8) (ref. [11] $[\alpha]_D$ − 97.1°). IR, UV, MS in agreement with published data [11]. $^1$H NMR: δ0.84 (3H, *d*, $J$ = 6.5 Hz, Me-4α), 0.88 (3H, *s*, Me-9$^B$), 1.01 (3H, *s*, Me-9$^A$), 1.14 (1H, *dddd*, $J_1$ = 14 Hz, $J_2$ = 13.5 Hz, $J_3$ = 12 Hz, $J_4$ = 6.5 Hz, H-5α), 1.56 (1H, *dddd*, $J_1$ = 14 Hz, $J_2$ = $J_3$ = 6.5 Hz, $J_4$ = 0.7 Hz, H-5β), 1.64 (1H, *ddd*, $J_1$ = 13.5 Hz, $J_2$ = 8.5 Hz, $J_3$ = 1.5 Hz, H-3α), 1.73 (1H, *dddd*, $J_1$ = 13.5 Hz, $J_2$ = 6.5 Hz, $J_3$ = 3.5 Hz, $J_4$ = 0.7 Hz, H-6α), 1.89 (1H, *ddd*, $J_1$ = 13.5 Hz, $J_2$ = $J_3$ = 10 Hz, H-3β), 1.93 (1H, *dddd*, $J_1$ = $J_2$ = 13.5 Hz, $J_3$ = 6.5 Hz, $J_4$ = 3.5 Hz, H-6β), 2.04 (1H, *br dd*, $J_1$ = $J_2$ = 3.5 Hz, H-7α), 2.06 (3H, *dd*, $J_1$ = 1.5 Hz, $J_2$ = 1 Hz, Me-1), 2.16 (1H, *ddq*, $J_1$ = 12 Hz, $J_2$ = 6.5 Hz, $J_3$ = 6.5 Hz, H-4β), 2.44 (1H, *dddq*, $J_1$ = 18.5 Hz, $J_2$ = 10 Hz, $J_3$ = 1.5 Hz, $J_4$ = 1 Hz, H-2α), 2.78 (1H, *dddq*, $J_1$ = 18.5 Hz, $J_2$ = 10 Hz, $J_3$ = 8.5 Hz, $J_4$ = 1.5 Hz, H-2β). $^{13}$C NMR: δ15.2 (Me-1), 17.9 (Me-4), 18.9 (Me-9$^A$), 25.9 (C-6), 26.2 (C-3), 26.4 (Me-9$^B$), 28.0 (C-5), 34.6 (C-4), 41.4 (C-9), 43.4 (C-2), 63.0 (C-7), 63.7 (C-3a), 139.6 (C-8a), 148.5 (C-1), 207.4 (C-8). Isolated also from extract B.

*Spathulenol* (**4**). Oil (11 mg). TLC: $R_f$ 0.21 (S-5); anisaldehyde reagent: blue. $[\alpha]_D$ + 7° ($CHCl_3$; *c* 1.0) (ref. [12] $[\alpha]_D^{22}$ + 5.7°). IR, $^1$H, $^{13}$C NMR in agreement with published data [12]. Also isolated from extract E.

*Mixture of fatty acids*. Solid (*ca* 0.5 g). TLC: $R_f$ 0.25 (tailing) (S-4); anisaldehyde reagent: blue. Methylation in MeOH soln with $CH_2N_2$ in $Et_2O$ (room temp.; 15 min) yielded a mixt. of Me esters. Identification by GC (co-injection with authentic substances and/or by GC-MS; quantification by FID-integration). See Table 7, column a.

N,N′-*Dimethylurabaine* (**5**). Powder (11 mg). Mp 254° (ref. [13] mp 254°). TLC: $R_f$ 0.14 (S-7); $Ce^{IV}$ reagent [43]: pale yellow. UV, $^1$H NMR ($CDCl_3$), MS in agreement with published data [13]. $^1$H NMR ($C_6D_6$), $^{13}$C NMR ($C_6D_6$): see Tables 3 and 4.

*Heteropsine* (**6**). Powder (5 mg). Mp 262–264°. TLC: $R_f$ 0.21 (S-7); $Ce^{IV}$ reagent: orange. IR, UV, $^1$H NMR ($CDCl_3$), MS in agreement with published data [14]. $^1$H NMR ($C_6D_6$), $^{13}$C NMR ($C_6D_6$): see Tables 3 and 4.

N-*Methylheteropsine* (**7**). Powder (2.5 mg). Mp 267–269°. TLC: $R_f$ 0.25 (S-7); $Ce^{IV}$ reagent: pale orange. IR $\nu_{max}$ cm$^{-1}$: 3396 (NH). UV $\lambda_{max}$ nm (log ε): 201 (4.25), 213 (sh, 4.22), 255 (sh, 4.40), 260 (4.43), 332 (3.82), 399 (3.34). $^1$H NMR ($C_6D_6$), $^{13}$C NMR ($C_6D_6$): see Tables 3 and 4. MS *m/z* (rel. int.): 556 (8), 555 (34), 554.2205 (calcd for $C_{36}H_{30}N_2O_4$: 554.2205) $[M]^+$ (100), 293 (5), 292 (13), 280 (11), 277.1103 (calcd for $C_{36}H_{30}N_2O_4^{2+}$: 277.1103) (55), 276.1024 (calcd for $C_{18}H_{14}NO_2$: 276.1024) (84), 275 (6), 269 (42), 264 (23), 263 (24), 262 (40), 261 (25), 260 (13), 254 (10), 248 (14), 247 (16), 246 (13), 240 (15), 239 (11), 236 (7), 233 (13), 232 (19), 231 (7).

N-*Methylurabaine* (**8**). Powder (21 mg). Mp 262° (ref. [13] mp 262°). TLC: $R_f$ 0.18 (S-7); $Ce^{IV}$ reagent: deeply yellow. UV, $^1H$ NMR, MS in agreement with published data [13]. $^1H$ NMR ($C_6D_6$), $^{13}C$ NMR ($C_6D_6$): see Tables 3 and 4. Also isolated from extract B.

*Trivalvone* (**9**). Brown crystals (1.5 mg). Mp 258°. TLC: $R_f$ 0.09 (S-8). IR, UV/VIS, $^1H$, $^{13}C$ NMR ($CDCl_3$), MS in agreement with published data [15]. $^1H$ NMR ($C_6D_6$), $^{13}C$ NMR ($C_6D_6$): see Tables 3 and 4.

*Urabaine* (**10**). Powder (13 mg). Mp > 280° (ref. [13] mp > 280°). TLC: $R_f$ 0.12 (S-7); $Ce^{IV}$ reagent: pale yellow. UV, $^1H$ NMR, MS in agreement with published data [13]. $^1H$ NMR ($C_6D_6$), $^{13}C$ NMR ($C_6D_6$): see Tables 3 and 4.

*Extract B*

β-*Sitosterol*-3β-O-D-*glucoside*. Crystals (12 mg). Mp 288–290° (ref. [16] mp 292–293°). TLC: $R_f$ 0.27 (S-2); anisaldehyde reagent: violet. $[\alpha]_D$ −35° ($CHCl_3$; *c* 0.1). $^1H$ NMR, MS in agreement with published data [17]. Also isolated from extract C.

*Stigmasterol*-3β-O-D-*glucoside*. Crystals (16 mg). Mp 295–298° (ref. [16] mp 299°). TLC: $R_f$ 0.27 (S-2), anisaldehyde reagent: violet. $[\alpha]_D$ − 45° ($CHCl_3$; *c* 0.21). $^1H$ NMR, MS in agreement with published data [17]. Also isolated from extract C.

*Mixture of* 6′-O-*acyl*-β-*sitosterol*-3β-O-D-*glucosides*. Amorphous powder (10 mg). TLC: $R_f$ 0.56 (S-2); anisaldehyde reagent: violet. IR, $^1H$ NMR, MS in agreement with published data [18, 19]. Material (2 mg) was suspended in 2 ml NaOMe–MeOH (5%) and stirred at room temp. for 1 hr. After neutralization with 2 M HOAc, $H_2O$ was added, the mixt. of fatty acid Me esters extracted with $Et_2O$, concd and analysed by GC (co-injection with authentic substances or structure determination by GC-MS; quantification by FID-integration). See Table 7, column b.

*Mixture of* 6′-O-*acylstigmasterol*-3β-O-D-*glucosides*. Amorphous powder (5 mg). TLC: $R_f$ 0.56 (S-2); anisaldehyde reagent: violet. IR, $^1H$ NMR, MS in agreement with published data [18, 19]. The structures of the acyl groups were determined by GC and GC-MS after methanolysis as described above. See Table 7, column c.

*Extract C*

*Liriodenine* (**15**). Yellow crystals (2 mg). Mp 280° (dec.) (ref. [24] mp 280–282° (dec.)). TLC: $R_f$ 0.33 (S-1); $Ce^{IV}$ reagent: orange. IR, UV/VIS, $^1H$ NMR, MS in agreement with published data [24]. Also isolated from extract F.

*Lysicamine* (**16**). Yellow crystals (5 mg). Mp 210° (dec.) (ref. [24] mp 210–211° (dec.)). TLC: $R_f$ 0.25 (S-1); $Ce^{IV}$ reagent: orange. IR, UV/VIS, $^1H$ NMR, MS in agreement with published data [24]. Also isolated from extract F.

*Nornuciferine* (**18**). Solid (16 mg). Mp 129° (ref. [26] mp 128–129°). TLC: $R_f$ 0.19 (S-1); $Ce^{IV}$ reagent: orange. $[\alpha]_D$ − 140° (EtOH; *c* 0.8) (ref. [26] $[\alpha]_D$ − 140°). IR, UV, $^1H$, $^{13}C$ NMR, MS in agreement with published data [26]. Also isolated from extract F.

2,7-*Dihydroxyonychine* (**19**). Orange crystals (4 mg). Mp > 300°. TLC: $R_f$ 0.54 (S-2); Dragendorff's reagent: positive. IR $\nu_{max}$ $cm^{-1}$: 3403 (OH), 1709 (C = O). UV/VIS $\lambda_{max}^{EtOH}$ nm (log ε): 205 (4.28), 226 (sh, 3.95), 265 (4.56), 305 (sh, 3.84), 318 (3.95), 329 (3.85); + HCl: 207 (4.08), 227 (4.18), 234 (4.16), 261 (4.34), 282 (4.09), 358 (4.19); + NaOH: 210 (4.77), 2.83 (4.55), 354 (4.19). $^1H$ NMR: see Table 5. $^{13}C$ NMR: see Table 6. MS *m/z* (rel. int.): 228 (14), 227.0583 (calcd for $C_{13}H_9NO_3$: 227.0582) $[M]^+$ (100), 199 (33), 198.0555 (calcd for $C_{12}H_8NO_2$: 198.0555) (39), 170 (9), 115.0547 (calcd for $C_9H_7$: 115.0548) (14), 114 (6), 113 (6), 100 (5).

N-*Carbamoyl*-2-*methoxypyrrolidine*. solid (15 mg). Mp 92–95° (ref. [26] mp 96–98°). TLC: $R_f$ 0.33 (S-1); anisaldehyde reagent: deep yellow. $[\alpha]_D$ ± 0° ($CHCl_3$; *c* 0.9). IR, $^1H$, $^{13}C$ NMR, MS in agreement with published data [26]. Also isolated from extract F.

trans-*Feruloyltyramine*. Oil (7 mg). TLC: $R_f$ 0.25 (S-1). UV, $^1H$, $^{13}C$ NMR, MS in agreement with published data [28].

*Indole*-3-*carbaldehyde*. Needles (1 mg). Mp 196° (ref. [29] mp 196°). TLC: $R_f$ 0.29 (S-1). IR, $^1H$ NMR, MS in agreement with published data [29]. Also isolated from extract F.

*Extract D*

*Dipterine* ( = N-*methyltryptamine*). Crystals (45 mg). Mp 88° (ref. [27] mp 87–88°). TLC: $R_f$ 0.45 (S-3); anisaldehyde reagent: red-violet. IR, UV, $^1H$, $^{13}C$ NMR, MS in agreement with an authentic sample synthesized from tryptamine. Also isolated from extract G.

*Stepharanine* (**22**). Orange crystals (2 mg). Mp 270° (dec.) (ref. [30] mp 266° (dec.)). TLC: $R_f$ 0.56 (S-3). IR, UV/VIS, $^1H$ NMR in agreement with published data [30]. Also isolated from extract G.

*Extract E* contained β-sitosterol, stigmasterol and **4** as the major components; see extract A.

*Extract F*

5α-*Cycloart*-24-*ene*-3β,16β,21-*triol* (**11**). Needles (11 mg). Mp 171–173°. TLC: $R_f$ 0.19 (petrol–$Me_2CO$, 4:1); anisaldehyde reagent: violet. $[\alpha]_D$ + 53° ($CHCl_3$; *c* 0.35). IR $\nu_{max}$ $cm^{-1}$: 3400 (OH). $^1H$ NMR: δ0.34 (1H, *d*, *J* = 4.5 Hz, H-19$^A$), 0.60 (1H, *d*, *J* = 4.5 Hz, H-19$^B$), 0.81 (3H, *s*, Me-28), 0.89 (3H, *s*, Me-29), 0.97 (3H, *s*, Me-30), 1.17 (3H, *s*, Me-18), 1.38 (1H, *dd*, $J_1$ = 13.5 Hz, $J_2$ = 5 Hz, H-15α), 1.63 (3H, *s*, Me-26), 1.70 (3H, *s*, Me-27), 1.84 (1H, *m*, H-20β), 1.98 (1H, *dd*, $J_1$ = 11.5 Hz, $J_2$ = 7 Hz, H-17), 2.04 (1H, *dd*, $J_1$ = 13.5 Hz, $J_2$ = 8 Hz, H-15β), 3.29 (1H, *dd*, $J_1$ = 11 Hz, $J_2$ = 4.5 Hz, H-3α), 3.76 (1H, *dd*, $J_1$ = 11.5 Hz, $J_2$ = 4 Hz, H-21$^A$), 3.84 (1H, *dd*, $J_1$ = 11.5 Hz, $J_2$ = 3 Hz, H-21$^B$), 4.40 (1H, *ddd*, $J_1$ = 8 Hz, $J_2$ = 7 Hz, $J_3$ = 5 Hz, H-16α), 5.20 (1H, *br t*, *J* = 6.5 Hz, H-24). $^{13}C$ NMR: δ14.0 (C-30), 17.7 (C-26), 19.0 (C-28), 19.7 (C-18), 20.1 (C-9), 20.9 (C-6), 25.2 (C-23), 25.4 (C-27), 25.7 (C-29), 26.0 (C-7), 26.1 (C-10), 26.3 (C-11), 29.8 (C-19), 30.1 (C-22), 30.3 (C-2), 31.8 (C-1), 31.9 (C-12), 36.5 (C-20), 40.5 (C-4), 45.1 (C-13), 47.0 (C-14), 47.0 (C-5), 47.8 (C-15),

47.9 (C-8), 50.9 (C-17), 61.8 (C-21), 72.9 (C-16), 78.7 (C-3), 124.6 (C-24), 132.5 (C-25). MS *m/z* (rel. int.): 458.3760 (calcd for $C_{30}H_{50}O_3$: 458.3759) $[M]^+$ (3), 443 (22), 440 (8), 425 (10), 315 (16), 313 (10), 303 (11), 292 (22), 203 (16), 201 (17), 189 (15), 187 (33), 175 (32), 173 (25), 161 (28), 159 (28), 149 (20), 147 (32), 145 (28), 135 (29), 133 (38), 131 (20), 123 (26), 121 (42), 119 (39), 109 (95), 108 (68), 107 (58), 105 (45), 95 (71), 93 (51), 91 (36), 82 (39), 81 (50), 78 (37), 69 (100), 67 (45), 55 (73), 43 (78).

4-*Hydroxy*-4,7-*dimethyl*-1-*tetralone* (**12**). Oil (1.3 mg). TLC: $R_f$ 0.40 (S-4); anisaldehyde reagent: dark-grey, orange after 30 min. $[\alpha]_D$ ± 0° ($CHCl_3$; *c* 0.08). IR $\nu_{max}$ $cm^{-1}$: 3590 (OH), 1683 (C = O). UV $\lambda_{max}$ nm (log ε): 250 (3.52), 296 (2.83). $^1H$ NMR: δ 1.62 (3H, *s*, Me-4), 2.28 (2H, *m*, H-3$^A$, H-3$^B$), 2.38 (3H, *br s*, Me-7), 2.69 (1H, *ddd*, $J_1$ = 18 Hz, $J_2$ = 9 Hz, $J_3$ = 7 Hz, H-2ax), 2.88 (1H, *ddd*, $J_1$ = 18 Hz, $J_2$ = $J_3$ = 5.5 Hz, H-2eq), 7.43 (1H, *br dd*, $J_1$ = 8 Hz, $J_2$ = 2 Hz, H-6), 7.60 (1H, *d*, *J* = 8 Hz, H-5), 7.81 (1H, *br d*, *J* = 2 Hz, H-8). $^{13}C$ NMR: δ20.8 (Me-7), 28.9 (Me-4), 35.8 (C-2), 38.3 (C-3), 70.0 (C-4), 125.0 (C-8), 127.0 (C-5), 130.2 (C-8a), 135.1 (C-6), 137.6 (C-7), 146.6 (C-4a), 197.4 (C-1). MS *m/z* (rel. int.): 190.0995 (calcd for $C_{12}H_{14}O_2$: 190.0994) $[M]^+$ (6), 175.0760 (calcd for $C_{11}H_{11}O_2$: 175.0759) (100), 162.0680 (calcd for $C_{10}H_{10}O_2$: 162.0681) (28), 157 (5), 147 (6), 131 (7), 129 (14), 128 (10), 119.0497 (calcd for $C_8H_7O$: 119.0497) (47), 115 (12), 91 (28), 89 (8), 77 (8), 65 (12), 63 (8), 55 (6).

Synthetic **12** (0.4 mg) was subjected to HPLC on a Chiralcel® OD column (250 × 4.6 mm; flow rate 0.5 ml $min^{-1}$; 42 injs) with petrol–isoPrOH (9:1) to yield the enantiomers. (*R*)-**12**: $R_t$ = 17.3 min, *ca* 170 μg; assignment of absolute configuration by CD [$\lambda_{max}$ nm (Δε) = 285 (+ 2.93), 325 (− 3.78)] in combination with conformational considerations [47]; (*S*)-**12**: $R_t$ = 20.0 min, *ca* 150 μg.

*Vanillic acid* Me *ester*. Oil (1 mg). TLC: $R_f$ 0.51 ($CHCl_3$–MeOH, 19:1). IR, UV, $^1H$ NMR, MS identical with an authentic sample.

N-*Formylnornuciferine* (**14**) [22, 23]. Oil (1.1 mg). TLC: $R_f$ 0.60 (S-1); $Ce^{IV}$ reagent: orange. $[\alpha]_D$ − 281° ($CHCl_3$; *c* 0.36) [ref. [23] $[\alpha]_D$ − 413.9° ($CHCl_3$)]. IR, UV, $^1H$, $^{13}C$ NMR, MS identical with those of a sample obtained by formylation of **18** and in agreement with published data [23]. According to the NMR ($CDCl_3$): *S-cis* rotamer (~ 65%), *S-trans* rotamer (~ 35%); rotation barrier determined by line form analysis [48]: 82 kJ $mol^{-1}$.

O-*Methylmoschatoline* (**17**). Orange crystals (0.7 mg). Mp 186° (dec.) (ref. [24] mp 188° (dec.)). TLC: $R_f$ 0.39 (S-1); $Ce^{IV}$ reagent: red. IR, UV/VIS, $^1H$ NMR, MS in agreement with published data [24, 25].

7-*Hydroxy*-2-*methoxyonychine* (**20**). Yellow needles (1.5 mg). Mp > 300°. TLC: $R_f$ 0.75 (S-1), Dragendorff's reagent: positive. IR $\nu_{max}$ $cm^{-1}$: 3468 (OH), 1713 (C = O). UV/VIS $\lambda_{max}^{EtOH}$ nm (log ε): 227 (sh, 3.64), 265 (4.13), 280 (sh, 3.96), 305 (sh, 3.53), 318 (3.56), 330 (sh, 3.49); + HCl: 205 (3.90), 228 (3.78), 236 (sh, 3.76), 265 (4.05), 284 (sh, 3.95), 315 (sh, 3.57), 332 (3.52), 358 (3.47) + NaOH: 240 (sh, 3.89), 282 (4.16), 3.09 (sh, 3.92), 355 (sh, 3.99). $^1H$ NMR: see Table 5. Diff. NOE: irradiation on 2-MeO and H-3: NO-enhancement observed on H-3, 1-Me and 2-MeO. $^{13}C$ NMR: see Table 6. MS *m/z* (rel. int.): 242 (15), 241.0739 (calcd for $C_{14}H_{11}NO_3$: 241.0739) $[M]^+$ (100), 226.0503 (calcd for $C_{13}H_8NO_3$: 226.0504) (27), 199 (10), 198.0555 (calcd for $C_{12}H_8NO_2$: 198.0555) (68), 115 (13).

7-*Hydroxy*-2,8-*dimethoxyonychine* (**21**). Orange-red needles (0.9 mg). Mp 206°. TLC: $R_f$ 0.37 ($CHCl_3$–MeOH, 49:1); Dragendorff's reagent: positive. IR $\nu_{max}$ $cm^{-1}$: 3520 (OH), 1708 (C = O). UV/VIS $\lambda_{max}^{EtOH}$ nm (log ε): 237 (3.75), 270 (4.08), 318 (3.63), 450 (2.34); + HCl: 209 (3.84), 236 (3.75), 270 (4.04), 319 (3.61), 359 (3.01), 450 (2.47); + NaOH: 252 (4.01), 285 (4.14), 337 (3.85), 360 (sh, 3.73). $^1H$ NMR: see Table 5. Diff. NOE: irradiation on 2-MeO and H-3; NO-enhancement observed on H-3, 1-Me and 2-MeO. $^{13}C$ NMR: see Table 6. MS *m/z* (rel. int.): 272 (16), 271.0846 (calcd for $C_{15}H_{13}NO_4$: 271.0845) $[M]^+$ (100), 256 (11), 253.0740 (calcd for $C_{15}H_{11}NO_3$: 253.0739) (42), 228.0662 (calcd for $C_{13}H_{10}NO_3$: 228.0661) (34), 225 (13), 213 (9), 198 (6).

### *Extract G*

*Shikimic acid*. Crystals (20 mg). Mp 188° (ref. [20] mp 184.5°). TLC: $R_f$ 0.21 ($CHCl_3$–MeOH–$H_2O$, 6:4:1); anisaldehyde reagent: blue-green. $[\alpha]_D$ − 157° ($H_2O$; *c* 1.3) (ref. [20] $[\alpha]_D$ − 166.2°). IR, $^1H$, $^{13}C$ NMR, MS in agreement with published data [20].

3,4,5-*Trimethoxyphenyl* β-D-*apiofuranosyl*-(1 → 6)-β-D-*glucopyranoside* (**13**). Amorphous (5 mg). TLC: $R_f$ 0.39 (S-3); anisaldehyde reagent: brown. $[\alpha]_D$ − 29° (MeOH; *c* 0.3) (ref. [21] $[\alpha]_D^{26}$ − 26.2°). IR, UV, $^1H$, $^{13}C$ NMR, MS in agreement with published data [21].

### *Compounds prepared synthetically*

4-*Hydroxy*-4,7-*dimethyl*-1-*tetralone* (**12**). 6-Methyl-2,3-dihydro-1,4-naphthoquinone (0.5 g, 2.9 mmol) [34] were reacted with MeMgI (from 540 mg (3.8 mmol) MeI) in $Et_2O$ [49]. Work-up with $NH_4Cl$ soln and purification by CC on Fractogel PVA 500 (MeOH) yielded 350 mg (64%) of a mixt. of **12** (40%, according to $^1H$ NMR) and 4-hydroxy-4,6-dimethyl-1-tetralone (60%). Acetylation with $Ac_2O$–pyridine, evapn and subsequent separation by HPLC on Nucleosil 50, 10 μ, (hexane-tert. butylmethyl ether, 9:1) yielded 105 mg (25%) 4-acetoxy-4,7-dimethyl-1-tetralone, which was submitted to methanolysis in KOH–MeOH (2%). Purification by CC on Fractogel PVA 500 (MeOH) gave 58 mg (64%) **12** as a pale yellow oil, which was found identical in all physicochemical properties with the compound isolated from *P. fugax*.

2,7-*Dimethoxyonychine* (**23**). Compound **19** (2 mg) was stirred in $Me_2CO$ with MeI–$K_2CO_3$ (room temp., 15 hr) and purified by CC on silica gel to yield orange needles (2 mg), mp 204–206°. TLC: $R_f$ 0.12 ($CHCl_3$); Dragendorff's reagent: positive. IR $\nu_{max}$ $cm^{-1}$: 1713 (C=O). UV/VIS $\lambda_{max}^{EtOH}$ nm (log ε): 255 (sh, 4.32), 263 (4.39), 280 (sh, 4.18), 300 (3.79), 316 (3.78), 330 (3.71); + HCl: 204 (4.04), 256 (sh, 4.26), 263 (4.33), 280 (sh, 4.12), 299 (sh, 3.79), 317 (3.73), 331 (3.71), 356 (3.47). $^1H$ NMR: see Table 5. $^{13}C$ NMR: see Table 6. MS *m/z* (rel. int.): 256 (12),

255.0895 (calcd for $C_{15}H_{13}NO_3$: 255.0895) $[M]^+$ (70), 240.0662 (calcd for $C_{14}H_{10}NO_3$: 240.0661) (36), 213 (14), 212.0711 (calcd for $C_{13}H_{10}NO_2$: 212.0711) (100), 197 (26), 169 (27), 141 (12), 127 (15), 114 (17), 85 (10), 83 (17).

3,7-*Dimethoxy*-4-*methyl*-5H-*indeno*[1,2-b]*pyridin*-5-ol ( = 2,7-*dimethoxy*-1-*methyl*-9H-4-*azafluoren*-9-*ol*) (**24**). Compound **23** (2 mg) was stirred in dry MeOH with $NaBH_4$ (room temp., 5 min). Excess $NaBH_4$ was destroyed with $Me_2CO$. After addition of $H_2O$, the product was extracted with $Et_2O$. Purification by CC on silica gel gave needles (1.8 mg), mp 235–237°. TLC: $R_f$ 0.24 (S-2); Dragendorff's reagent: positive. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3450 (OH). UV $\lambda_{max}^{EtOH}$ (log $\varepsilon$): 269 (sh, 4.14), 280 (4.32), 295 (4.39), 323 (4.23), 334 (sh, 4.18); + HCl: 211 (4.49), 219 (4.51), 264 (4.06), 282 (3.98), 304 (4.11), 356 (4.56). $^1H$ NMR: see Table 5. $^{13}C$ NMR: see Table 6. MS *m/z* (rel. int.): 258 (17), 257 $[M^+]$ (100), 256 (17), 243 (8), 242 (53), 227 (9), 226 (32), 214 (30), 199 (16), 198 (5), 186 (5), 183 (6), 171 (10), 170 (6), 154 (7), 128 (14), 115 (10).

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