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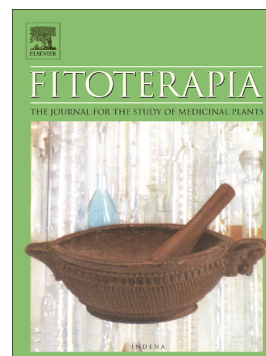
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New diterpenoids and phenolic amides from *Icacina mannii* Oliv.

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Abstract

Fourteen undescribed compounds including five *neo*-clerodanes (**1–5**), three labdanes (**12–14**), three pimarane (**15–17**) derivatives, one carbamate (**24**) and two clovamide-type amides (**25** and **26**), along with twenty-two known compounds (**6–11**, **18–23** and **27–36**) were isolated from the tuber and stem of *Icacina mannii*. Their structures were elucidated by 1D and 2D NMR and HR-ESI-MS data analysis, and by comparing their NMR data with those of the literature.

Keywords: *Icacina mannii*, Icacinaceae, diterpenoids, labdane, *neo*-clerodane, pimarane, clovamide.

1. Introduction

Icacinaceae is a pan-tropical family of trees, shrubs and lianas, with 23 genera including the genus *Icacina* with only six species (Burkill 1994). The *Icacina* species could be used as a food source because of the nutritional contents of their seeds. The roots are toxic and are used in traditional medicine after detoxifying according to local means by macerating them in water or ethanol for about three days (Fay, 1991). Previous chemical and pharmacological investigations on some *Icacina* species indicated the presence of diterpenes with pimarane skeleton (Monday Onakpa et al., 2014; On'Okoko et al., 1977; 1980; 1985b; Zhao et al.,

2015a, 2015b, 2015c), flavonoids and clovamide (Manga et al., 2013), exhibiting various pharmacological activities (Akuodor et al., 2014; 2017; Zhao et al., 2015c, 2017).

Icacina mannii Oliv. (Icacinaceae) is a scandent shrub up to 6 m high, growing from a large underground tuber and widely distributed in African tropical regions (Burkill, 1994). The different parts (stem bark, roots, and leaves) of this plant are widely used as a food source or medicinal plant to treat many diseases (Adjanohoun et al., 1979). Traditional healers in Ivory Coast used *Icacina mannii* against oedema, women sterility, sexual asthenia and haemorrhoids, as well as a laxative and a powerful diuretic (Bouquet A. et Debray, Malan et al., 2015). In Congo (RDC), the leaves are used as expectorant and emetic to relieve bronchial affections and coughs. The tubers are used to treat gastrointestinal disorders, dysentery, fibrous tumors and dysmenorrhea (On'Okoko et al., 1977; 1980, 1985a; 1985b). To the best of our knowledge, very few chemical studies have been carried out on *I. mannii* and only icacinone, a diterpene with pimarane skeleton (On'Okoko et al., 1985), was reported.

In the course of continuing efforts to discover novel natural products from medical plants, we report the isolation and structure elucidation of thirty-six compounds including fourteen undescribed compounds from the stems and the tuber rinds of *I. mannii*.

2. Results and discussion

2.1 Identification of compounds

Methanol/water (80/20, v/v) and ethyl acetate extracts of the stems and of the tuber rinds of *I. mannii* resulted after fractionation, to the isolation of thirty-six (**1–36**) compounds including fourteen undescribed structures (**1–5**, **12–17**, **24–26**) (Fig.1). Their structures were elucidated by 1D and 2D-NMR experiments in combination with HR-ESI-MS spectrometry data analysis and by comparison with literature values. The known compounds were identified as six neoclerodanes (**6–11**), six pimarane (**18–23**) derivatives, three clovamides (**27–29**), four labdanes (**30–33**) and three lignanes (**34–36**) (Table 1).

Insert figure 1 here

Compound **1** was isolated as an amorphous white powder. Its molecular formula was assigned as $C_{20}H_{30}O_4$, with 6 indices of hydrogen deficiency, on the basis of the high-resolution ESI-MS experiment (negative-ion mode) by observation of pseudo-molecular ion peak at m/z 333.2069 $[M-H]^-$ (calcd $C_{20}H_{29}O_4$, 333.2066). The 1H NMR (Table 2) spectrum of **1** showed signals of one oxygenated methylene at δ_H 4.81 (H-15), and an α,β -unsaturated γ -lactone with the diagnostic peak at δ_H 7.34 (H-14). The ^{13}C NMR spectrum (Table 3) displayed 20 carbon signals

assigned, with the aid of HSQC spectrum, to three methyl groups at δ_c 16.3 (C-17), 15.3 (C-19) and 18.5 (C-20), eight methylene groups (including one oxygenated at δ_c 72.1 (C-15), four methine groups (including one olefinic at δ_c 147.3 (C-14), three quaternary (including one olefinic at δ_c 134.9 (C-13) and two carbonyls at δ_c 178.3 (C-18) and 176.9 (C-16). The lactone ring was confirmed by the HMBC correlations between H-14 and C-13, C-15 and C-16. Of the required six double bond equivalents, three accounted for the α,β -unsaturated carbonyl group and a carboxylic acid function while the remaining three were satisfied by the bicyclic and lactone rings. The characteristic features of ^1H and ^{13}C NMR together with the molecular formula suggesting that **1** was a *neo*-clerodane type diterpenoid (Li et al., 2016, Merritt et al., 1992) The ^1H - ^1H COSY spectrum of **1** included three fragments consisting of H-1 to H-4/H-10 to H-12, H-6 to H-8/H-17, and H-14/H-15 (Fig. 2). The presence of a carbonyl at C-18 was confirmed by HMBC correlations from H-3 and H-4 to C-18. In the NOESY experiment, the cross-peak between H-10 and H-6 β , and between H-8 and H-11, indicated that H-8, H-10, and C-11 were β -oriented. The absolute structure of compound **1** was determined as 4*S*, 5*R*, 8*R*, 9*S*, 10*R*, 15*R*. Therefore, **1** was identified as (4*S*, 5*R*, 8*R*, 9*S*, 10*R*)-*neo*-clerod-13-en-15,16-olide-18-oic acid and named icacimannitin A.

The molecular formula of compound **2** was established as $\text{C}_{21}\text{H}_{32}\text{O}_5$ based on the pseudo-molecular ion peak at m/z 363.2173 [$\text{M}-\text{H}]^-$ (calcd $\text{C}_{21}\text{H}_{31}\text{O}_5$, 363.2710) observed in the HR-ESI-MS spectrum, indicating a gain of 30 *uma* compared to **1**. The ^1H and ^{13}C NMR spectra (Tables 2 and 3) of **2** were very similar to those of **1**, differing in the presence of a methoxy group at δ_H 3.55 (s) in **2** linked to C-15 (δ_c 104.5) in the HMBC spectrum. The final structure was confirmed by analysis of correlations observed in COSY, HSQC and HMBC spectra. The relative configuration of **2** was determined by ROESY NMR correlations, except for the hemiacetal proton (H-15) which did not result in any informative cross-peaks. Accordingly, the structure of **2** was assigned as (4*S*, 5*R*, 8*R*, 9*S*, 10*R*)-methoxy-*neo*-clerod-13-en-15,16-olide-18-oic acid and named icacimannitin B.

Compound **3** had the same chemical formula as compound **1**, assigned by the negative HR-ESI-MS (m/z 333.2068 [$\text{M}-\text{H}]^-$; calcd $\text{C}_{20}\text{H}_{29}\text{O}_4$, 333.2066). Their main difference was the position of the lactone function. According to ^1H and ^{13}C NMR data (Tables 2 and 3) and HMBC correlations, the lactone function in **3** was located on C-15 (Table 3), in agreement with *neo*-clerodane diterpenoids bearing an 3-ethyl-2-butenolide-based side chain at C-9 (Li et al., 2016). Thus, **3** was unambiguously identified as (4*S*, 5*R*, 8*R*, 9*S*, 10*R*)-*neo*-clerod-13-en-16,15-olide-18-oic acid and named icacimannitin C.

The molecular formula of compound **4** was established as $\text{C}_{20}\text{H}_{32}\text{O}_2$ based on ESI-MS at m/z 304.3 [$\text{M}-\text{H}]^-$. Compound **4** differs from the known compound **6** (Tables 2 and 3) by the

replacement of the acid function in **6** with an alcohol function in **4**. The presence of a β -monosubstituted furan ring was clearly indicated by the ^1H and ^{13}C signals at δ_{H} 6.28 (H-14), 7.38 (H-15) and 7.26 (H-16) and δ_{C} 125.6 (C-13), 110.5 (C-14), 142.5 (C-15) and 138.2 (C-16), which were in agreement with those of crolechnic acid (**6**) (Cai et al., 1993). In addition, a hydroxy group was involved in the molecule as shown by a ^{13}C signal at δ_{C} 62.1 (C-18) compared to the carboxylic acid group at δ_{C} 180.4 in **6**. Furthermore, all analyses confirmed the structure of compound **4** as (4*S*, 5*R*, 8*R*, 9*S*, 10*R*)-*neo*-15,16-epoxy-clerod-13(16),14-dien-18-ol or 3,4-dihydro-bacchalineol and named icacimannitol A.

Compound **5**, named 18-hydroxy-kolavenol, had the molecular formula $\text{C}_{20}\text{H}_{34}\text{O}_2$ exhibiting two rings and two C=C bonds, as evidenced by analysis of ESI-MS (m/z 306.25 [M-H] $^-$) and NMR data (Tables 2 and 3). The ^1H NMR spectrum of **5** containing four methyl signals at δ_{H} 1.69 (s, H₃-16), 0.86 (d, $J = 6.4$ Hz, H₃-17), 1.12 (s, H₃-19) and 0.80 (s, H₃-20), attributed to a vinyl methyl and three methyl groups linked to sp^3 C-atoms respectively, suggested a bicyclic diterpenoid carbon framework. The presence of an allylic hydroxy methylene (HO-C-15) located on the lateral alkyl chain was indicated by the signal at δ_{H} 4.08 (d, $J = 6.7$, H₂-15), which was coupled in the COSY spectrum to a vicinal olefinic proton (H-14, δ_{H} 5.38, m). A signal at δ_{H} 5.57 (m) was assigned to an another olefinic proton (H-3) coupled with two methylenes (H-2) resonating at δ_{H} 2.17–2.11 (m), in turn linked to the methylene (H-1) at δ_{H} 1.67–1.50 (m). A methyl (H-19) had direct correlation with the signals at δ_{C} 148.6 (C-4), δ_{C} 38.8 (C-5) and δ_{C} 47.6 (C-10), and whose carbon in turn showed significant long-range cross-peaks with H-2, in the HMBC spectrum, supporting the location of the second double bond in the ring A of a rearranged *neo*-clerodane diterpenoid. Particularly diagnostic were the long-range HMBC correlations of the quaternary carbon C-9 (δ_{C} 39.7) with H-8, H-11a, H-17, and H-20 as well as C-10 (δ_{C} 47.6) with H-6a. The geometry of the double bond in the lateral chain was determined to be (*E*) as in kolavenol (**7**) by the chemical shift of the vinyl proton H-16 (δ_{C} 16.4) (Lopes et al., 1987; Salah et al., 2003; Tschritzis and Jakupovic, 1991). Compound **5** was identified as 18-hydroxy-kolavenol or (5*R*, 8*R*, 9*S*, 10*R*)-*neo*-13-methyl-clerod-3,13*E*-dien-15,18-diol and named icacimannitol B.

Compounds 12 to 14 have the similar basic skeleton as compounds **5** and **7**, according to their NMR spectra (Fig 1).

Compound **12** had the same molecular formula (ESI-MS m/z 290.3 [M] $^+$) as **7**. The ^1H NMR spectrum of **12** (Table 4) was similar to that of **7**. The two compounds differed by the position of the methyl groups C-18 and C-19 positioned at C-4 in compound **12**, thus suggesting it to have a labdane-type diterpenoid skeleton (Freiburghaus et al., 1998). Of the required four

double bond equivalents, two double bonds were attributable to (C-1=C-10) and (C-13=C-14), while the remaining two were satisfied by the bicyclic rings. The methyls H₃-18 at δ_{H} 0.91 and H₃-19 at δ_{H} 0.85 had direct correlation with the signals at δ_{C} 32.4 (C-4), δ_{C} 44.8 (C-5), and δ_{C} 34.2 (C-3) in the HMBC spectrum (Figure 2). Total NMR assignment of **12** (Table 4), suggested its bicyclic halimene backbone (Hara et al., 1995). Thus, **12** was identified as *neo*-halima-1(10),13*E*-dien-15-ol.

Compound **13** had the same molecular formula (ESI-MS m/z 290.3 [M]⁺) as **12**. The NMR spectra of **13** (Table 4) were similar to those of **12**. However, **13** differed from **12** by the position of the double bond at C-5-C-10 in **13** instead of C-1-C-10 in **12**. Total assignment of NMR data (Table 4) identified **13** as *neo*-halima-5(10),13*E*-dien-15-ol.

Compound **14** had the same molecular formula (ESI-MS m/z 306.35 [M]⁺) as **5**. The ¹H NMR spectrum of **14** (Table 4) was similar to that of **13** described above, except the presence of hydroxyl group at C-19 characterized by oxygenated methylene protons at δ_{H} 3.26 and 3.49 in **14**. Total assignment of NMR data (Table 4) attributed **14** to *neo*-19-hydroxy-halima-5(10),13*E*-dien-15-ol.

Compound **15** was obtained as colourless amorphous solid. A molecular formula of C₁₉H₂₆O₇ with 7 indices of hydrogen deficiency, was suggested by the positive HR-ESI-MS (m/z 389.1579 [M+Na]⁺; calcd C₁₉H₂₆O₇Na, 389.1576). The ¹H NMR and HSQC spectra of **15** revealed the presence of two methyl groups as singlets at δ_{H} 0.99 and 1.22 corresponding to the methyl carbons at δ_{C} 16.4 (C-15) and 19.2 (C-16), respectively (Table 5). Four methylene group signals were observed in the ¹H NMR spectrum at $\delta_{\text{H-1}}$ 1.54 and 1.42, $\delta_{\text{H-2}}$ 1.92 and 1.64, $\delta_{\text{H-11}}$ 1.62 and 1.16, and $\delta_{\text{H-12}}$ 1.72 and 1.48. Signals at δ_{H} 5.06 (dd, $J = 7.5, 4.5$ Hz), 3.55 (d, $J = 4.5$ Hz) and δ_{H} 3.66 (d, $J = 4.6$ Hz) corresponded to the oxygenated methine carbons C-6, C-7 and C-14, respectively. Signals at δ_{H} 2.21 (d, $J = 7.5$ Hz) and 1.55 (dd, $J = 12.8, 4.4$ Hz) were assigned to the methine carbons C-5, and C-9, respectively (Fig. 2). The ¹³C NMR spectrum also exhibited a singlet of a methoxy group at δ_{H} 3.20 linked to C-19, and two protons at δ_{H} 4.51 (dd, $J = 9.1, 3.4$ Hz) and δ_{H} 3.34 (dt, $J = 9.1, 1.5$ Hz), corresponding to an oxygenated methylene group (C-18). The ¹³C NMR spectrum of compound **15** showed the presence of 19 carbons. One lactone resonance at δ_{C} 178.3 was attributed to C-17. The carbon resonances at δ_{C} 96.9, 65.2 and 77.7 were attributed to oxygenated quaternary carbons C-3, C-8, and C-13, respectively after analysis of HMBC spectrum (Fig. 2). In the NOESY experiment, the cross-peak between H-18 β and H-11 and H-9, indicated that H-9 was in β -orientation. The COSY and HMBC correlations were in agreement with the seven degrees of unsaturation, including the carboxylic acid function of the lactone, the tricyclic rings, while the remaining two were identified as a tetrahydropyran and an epoxide (Fig 2). These

assignments were consistent with the structure of reported (9 β -H)-pimarane derivative (Zhang et al., 2022). Accordingly, compound **15** was identified as 16-*nor*-(9 β -H)-pimarane and named Icacinlactone O.

Compound **16** was isolated as a colourless amorphous solid. The HR-ESI-MS indicated a molecular formula of C₁₈H₂₄O₁₀ (m/z 399.1288 [M-H]⁻; calcd C₁₈H₂₃O₁₀, 399.1291). Its ¹H NMR spectrum was similar to that of **15** (Table 5), differing in the resonances at δ_C 65.9 (C-1), 78.8 (C-5), 68.4 (C-11) and 71.3 (C-13), suggesting their oxygenated substitution. The final structure was confirmed using correlations observed in COSY, HSQC and HMBC spectra. Therefore, the structure of **16** has been established as icacinlactone P.

Compound **17** was obtained as a white amorphous powder and had a molecular formula of C₂₅H₃₀O₁₂, established by its negative ion HR-ESI-MS at m/z 521.1655 [M-H]⁻ (calcd for C₂₅H₂₉O₁₂, 521.1659), with 11 indices of hydrogen deficiency. The ¹H and ¹³C NMR spectra displayed resonances due to the icacinone aglycone as in **19** (Table 5) with two olefinic protons (δ_H 6.67 (H-15) and 7.72 (H-16)) of the tetrahydropyran, one oxygenated methine proton (δ_H 3.90, H-2), two methylene protons bearing an oxygen (δ_H 4.21, H-19b and 3.50, H-19a), and one methyl group (δ_H 1.24, H₃-17), showing correlations in the HSQC spectrum with their corresponding carbon at δ_C 106.9, 144.5, 76.7, 72.1 and 16.8, respectively. Furthermore, other characteristic signals were observed such as two oxygen-bearing carbons at δ_C 193.1 (C-12) and δ_C 177.1 (C-18), confirming the existence of two carbonyl groups, and one carbon at δ_C 96.6 (C-3) suggesting the presence of a hemiacetalic function. Extensive 2D NMR analysis confirmed the structure of the aglycone to be icacinone (On'Okoko et al., 1985). The presence of one sugar moiety in compound **17** was evidenced by the presence of one anomeric proton at δ_H 4.32 (α , $J = 7.8$ Hz, H-1') (Table 5). Full sugar assignment was achieved by extensive 1D and 2D NMR spectra analyses (¹H-¹H-COSY, HSQC and HMBC) and by optical rotation measurement, allowing characterization of a β -D-glucopyranosyl. The large coupling constant (>7 Hz) for glucose indicated their β -configuration (Agrawal, 1992; Bock and Pedersen, 1983). The HMBC correlation between Glc-H-1 (δ_H 4.32) and C-2 (δ_C 76.7) of icacinone indicated the glycosidic linkage at the C-2 position of icacinone (Fig. 1). Therefore, the structure of **17** was established as 2-*O*- β -D-glucopyranosyl-icacinone.

The molecular formula of compound **24** was established as C₁₄H₂₀N₂O₅, based on the negative ion HR-ESI-MS at m/z 295.1295 [M-H]⁻ (calcd for C₁₄H₁₉N₂O₅, 295.1294). The ¹H-NMR spectrum (Table 6) showed a 1,3,4-trisubstituted benzene ring due to the presence of three aromatic signals from an ABX spin system, consisting of a broad singlet at δ_H 6.81 (brs, H-3), and two doublets at δ_H 6.72 ($J = 7.2$ Hz, H-5), δ_H 6.65 ($J = 7.2$ Hz, H-6). The ¹H-NMR spectrum displayed two singlets at δ_H 3.86 and 3.65 ascribed to two methoxyl groups. The ¹H-NMR

spectrum also exhibited a triplet at δ_{H} 2.42 (2H, H-1') and a multiplet at δ_{H} 2.10 (2H, H-2'), each corresponding to nitrogen-bearing protons, and two methylene protons at δ_{H} 2.72 (2H, t, $J = 6.4$ Hz, H-7) and 3.39 (2H, t, $J = 6.4$ Hz, H-8) correlated each other in COSY spectrum (Fig. 2). The ^{13}C NMR spectrum of **24** (Table 6) showed 14 signals including: six aromatic carbons, two methoxyl carbons, four carbons assigned to methylenes, and two carboxylic amides. The presence of oxygen on the aromatic carbons C-3 and C-4 was reflected by their deshielding at δ_{C} 147.5 and 144.6, respectively. The HMBC experiment showed the linkages of the methoxyl group at δ_{H} 3.86 (OCH₃) with the carbon at δ_{C} 147.5 (C-3) of the benzene ring, and HMBC correlations between H-7 at δ_{H} 2.72 and the carbons at δ_{C} 130.5 (C-1), 111.9 (C-2), and 120.8 (C-6) (Fig. 2). Other correlations were observed from H-7 and H-1' to C-9 (δ_{C} 173.4) and from H-2' and the methoxyl group (δ_{H} 3.65) to C-3' (δ_{C} 172.1). The above data led to identified the compound **24** as methyl *N*-[2-[3-(4-hydroxy-3-methoxyphenyl)propyl amido]ethyl]carbamate and named Icaninamate.

Compound **25** had a molecular formula of C₁₈H₁₇NO₇ assigned by observation of the pseudo-molecular ion peak in the HR-ESI-MS at m/z 358.0927 [M-H]⁻ (calcd for 358.0927). The ^1H and ^{13}C NMR spectra displayed resonances due to the clovamide (El-Sharawy et al., 2017, Manga et al., 2013, Sanbongi et al., 1998) with six aromatic protons at δ_{H} 6.70 (d, $J = 2.1$ Hz), 6.69 (d, $J = 8.3$ Hz), 6.84 (dd, $J = 8.3, 2.1$ Hz), 6.70 (d, $J = 2.1$ Hz), 6.70 (d, $J = 8.3$ Hz), and 6.84 (dd, $J = 8.3, 2.1$ Hz) showing correlations in the HSQC spectrum with their corresponding carbon at δ_{C} 117.2 (C-2), 116.0 (C-5), 121.7 (C-6), 115.1 (C-2'), 116.3 (C-5'), and 123.5 (C-6') (Table 6). Furthermore, other characteristic signals were observed such as two olefinic protons at δ_{H} 6.44 (H-7', d, $J = 12.7$ Hz), δ_{H} 5.81 (H-8', d, $J = 12.7$ Hz), one methylene proton at δ_{H} 3.10 (H-7b, dd, $J = 14.0, 5.3$ Hz) and 2.90 (H-7a, dd, $J = 14.0, 8.5$ Hz) and one nitrogen-bearing methine proton at δ_{H} 4.71 (H-8, dd, $J = 8.6, 5.3$ Hz) showing HSQC correlation with carbons at δ_{C} 139.5 (C-7'), 120.8 (C-8'), 37.8 (C-7) and 55.4 (C-8), respectively. The coupling constant ($J = 12.7$ Hz) between the ethylenic doublets at δ_{H} 5.81 and 6.44, suggested that the double bond was of *Z* configuration. Extensive 2D NMR analysis confirmed the structure of **25** to be clovamide (Fig. 2). According to the above-described results, the structure of compound **25** was elucidated as (+)-*N*-(*Z*)-caffeoyl-L-dopamine. It was isolated in mixture with (-)-*N*-(*E*)-caffeoyl-L-dopamine (**28**).

Compound **26** exhibited, in the negative ion-mode HR-ESI-MS, a pseudo-molecular ion peak at m/z 372.1082 [M-H]⁻ (calcd C₁₉H₁₈NO₇, 372.1083) compatible with the molecular formula C₁₉H₁₉NO₇. The ^1H NMR spectrum of **26** (Table 6) was similar to that of **25**, except for the presence of the signal of methyl ester group at δ_{H} 3.70. Based on the above spectral data, the

structure of **26** was identified as (-)-(Z)-caffeoyl-L-dopamine methyl ester. It was isolated in mixture with its isomer *E* (**29**).

2.3 Chemotaxonomic significance

Icacine (**19**) have been previously identified in the tubers of *I. mannii* (On'Okoko et al., 1985a). Compounds **18**, **19**, **20**, **22** and **23**, were previously isolated in the genus *Icacina* (On'Okoko et al., 1985; Sun, 2019; Zhao et al., 2015). Deoxyclovamid (**27**) [*N*-(*E*)-caffeoyl-L-dopamine] was previously identified in the leaves of *I. senegalensis* (Manga et al., 2013), but this is the first report of annonalide (**21**), phenolic amides compounds (**24–29**) from *I. mannii*. In addition, this study is the first structural elucidation of *neo*-clerodanes (**6–11**), labdanes (**30–33**), and lignans (**34–36**) from the genus *Icacina*.

3. Conclusion

In conclusion, we have isolated eleven new diterpenoids (**1-5**, **12-17**) and three new clovamide-type amides, (**24-26**) from peeling of tubers and stems of *I. mannii*. Many of the isolated compounds were *neo*-clerodane type diterpenoids. Indeed, this finding showed that the diterpene and amide derivatives could play a key role in chemotaxonomic classification of *Icacina* genus. The presence of these molecules can explain the different medicinal properties of *I. mannii*. Further chemical and biological studies are necessary for promoting these molecules.

4. Experimental

4.1. General experimental procedures

Optical rotations were measured on a Perkin-Elmer 341 polarimeter. 1D and 2D-NMR spectra were recorded in MeOH-*d*₄ or DMSO-*d*₆ on Bruker Avance DRX III 500 or 600 instrument using standard Bruker microprograms (Karlsruhe, Germany). (–) and (+)-HR-ESI-MS were obtained from Micromass Q-TOF micro-instrument (Manchester, UK). Flash chromatography was performed on a Grace Reveleris system equipped with dual UV and ELSD detection using Grace cartridges (silica gel or RP-C₁₈), and the monitored wavelengths were at 205 and 254 nm. The medium-pressure liquid chromatography (MPLC) was employed using a Buchi pump system AP250/500 (Buchi, France), with a RP-C₁₈ silica gel Merck column (15 × 230 and 26 × 460 mm). Semi-preparative HPLC was performed on an apparatus equipped with an ASI-100 Dionex autosampler, an Ultimate 3000 pump ThermoFisher Scientific, a diode array detector

UVD 340S and a Chromeleon software (Dionex, ThermoFisher Scientific, France). RP-C₁₈ column (Phenomenex 250 ×15 mm, Luna 5 μ, Interchim, France) was used for the semi-preparative HPLC with a binary gradient eluent (H₂O pH 2.4 with TFA; CH₃CN) and a flow rate of 5 mL/min; the chromatogram was monitored at 205, 254, 300, and 360 nm. Analytical TLC was performed using silica gel plates (Merck Kieselgel 60 F254) and RP-C₁₈ plates (Kieselgel 60 F₂₅₄) and visualized at 254 and 366 nm and by spraying the dried plates with vanillin and 50% of H₂SO₄, followed by heating.

4.2. Plant material

Peeling of tubers and stems of *I. mannii* Oliv. (Icacinaceae) were collected in December 2018 from Abidjan (South Ivory Coast) during the wet season, and identified at the National Floristic Center of the University Félix Houphouët Boigny of Cocody Abidjan (Ivory Coast), where a voucher specimen (UCJ008642) has been deposited.

4.3. Extraction and isolation

4.3.1. Fractionation of the tuber rinds of *I. mannii*

The tuber rinds of *I. mannii* (295.5 g) were milled and extracted with 80% aqueous methanol (4L) by maceration (72 h) followed by leaching. After evaporation of the MeOH, the aqueous phase was successively partitioned with CH₂Cl₂ and *n*-BuOH. The CH₂Cl₂ extract (19.7 g) was subjected to vacuum liquid chromatography (VLC) over silica gel (318 g, 9 cm) and eluted with petroleum ether-CH₂Cl₂-MeOH (from 1:0:0 to 0:0:1, v/v/v) to give six fractions (F1-F6). The combined fractions (F2+ F3) (1.2 g), eluted with petroleum ether-CH₂Cl₂ (9:1 and 8:2), was separated over a silica gel column using a gradient of petroleum ether-CH₂Cl₂ (from 1:0 to 0:1, v/v; 25 mL each) to give 19 subfractions (Fa-Fs). The subfraction Fi gave **6** (508 mg). Compounds **7** (26 mg), **12** (10 mg) and **30** (70 mg) were obtained from Fj (2.4 g) by preparative HPLC (CH₃CN-H₂O, 8:2 to 10:0, v/v; 10 mL/min). The subfraction Fn (761 mg) was purified by preparative HPLC eluted with CH₃CN-H₂O (7:3 to 10:0, v/v; 10 mL/min) to afford compounds **4** (12 mg) and **9** (70 mg). Fraction F5, eluting with petroleum ether-CH₂Cl₂-MeOH (0:1:0) was fractionated into 24 subfractions (E₁-E₂₄) by RP₁₈ flash chromatography (40 g) using a gradient of CH₃CN-H₂O (2:8 to 8:2, v/v; 25 mL each). Compound **15** (*t*_r=12.9 min, 3 mg) was purified by semi-preparative HPLC from subfraction E₂, eluted with CH₃CN-H₂O (2:8 to 4:6 v/v, during 35 min). The subfraction E₄ was purified by semi-preparative HPLC eluted with CH₃CN-H₂O (25:75 to 50:50, v/v, during 35 min) to afford **20** (*t*_r=11.4 min, 11 mg), **18** (*t*_r=13.3 min, 5 mg), and **21** (*t*_r=13.6 min, 5 mg). Compounds **22** (*t*_r=15.1 min, 6 mg), and **2** (*t*_r=20.1 min, 1 mg) were obtained from subfraction E₁₀ by semi-preparative HPLC (CH₃CN-H₂O, 5:5 to 7:3, v/v, during 35 min). The combined subfractions (E₁₂ and E₁₃) was further purified by semi-preparative HPLC (CH₃CN-H₂O, 65:35 to 75:25, v/v, during 35 min) to

give compounds **3** ($t_r=11.3$ min, 6 mg) and **1** ($t_r=12.6$ min, 6 mg). The combined subfractions ($E_{14} - E_{16}$) was purified by preparative HPLC eluted with $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ (6:4 to 10:0, v/v; 10 mL/min) to yield compounds **8** (4 mg), **5** (13 mg) and **11** (13 mg). Compounds **31** ($t_r=13.2$ min, 2 mg) and **14** ($t_r=14$ min, 2 mg) were purified from subfraction E_{17} by semi-preparative HPLC ($\text{CH}_3\text{CN}-\text{H}_2\text{O}$, 8:2 to 10:0, v/v, during 35 min).

A part of the *n*-BuOH extract (18.5 g) was passed through a macroporous resin Diaion HP-20 column (5×45.5 cm) eluted with EtOAc-MeOH- H_2O (from 0:2:8 to 1:0:0, v/v/v, 1.5 L each) to give six fractions (B1-B6). The fraction B1 (15.7 g) was separated into 29 subfractions named M_1-M_{29} using RP_{18} flash chromatography eluted with $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ (from 5/95 to 40/60, v/v). The combined subfractions $M_{11}-M_{14}$ was chromatographed by PLC eluted with $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ (5:95 to 40:60, v/v; 10 mL/min) to afford compounds **16** (6 mg) and **21** (2 mg). Compounds **17** (147 mg), **19** (27 mg), **34** (4 mg), **35** (2 mg), **36** (6 mg), and **26** (5 mg) were purified from combined subfractions $M_{16}-M_{18}$ by PLC ($\text{CH}_3\text{CN}-\text{H}_2\text{O}$, 10:90 to 50:50, v/v; 10 mL/min). Compound **23** (57 mg) was precipitated from the subfraction M_{24} . Fraction B2, eluting with EtOAc-MeOH- H_2O (0:40:60), was further purified by semi-preparative HPLC ($\text{CH}_3\text{CN}-\text{H}_2\text{O}$, 2:8 to 4:6 v/v, during 30 min) to yield compounds **25** ($t_r=5.6$ min, 8 mg), **28** ($t_r=13.3$ min, 12 mg), **27** ($t_r=17$ min, 2 mg) and **29** ($t_r=20.5$ min, 9 mg).

4.3.2. Fractionation of the stems of *I. mannii*

Powdered air-dried stems (2 kg) were extracted by maceration with EtOAc (20L) at room temperature for 72h. The extract (100 g) was fractionated by VLC on silica gel with a gradient of petroleum ether- CH_2Cl_2 -MeOH (from 1:0:0 to 0:0:1, v/v/v) to give eight fractions (S1-S8). Fraction S4 (120 g), obtained with the mixture petroleum ether- CH_2Cl_2 -MeOH (7:3:0), was separated into 16 subfractions (Sa-Sp) by RP_{18} flash chromatography eluted with a gradient $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ (8:2 to 10:0, v/v). The subfraction Sc (3.075 g) contain the pure compound **6**. Compounds **10** ($t_r=17$ min, 5 mg), **33** ($t_r=17.7$ min, 3.2 mg), and **32** ($t_r=19.3$ min, 4.2 mg), were purified by semi-preparative HPLC of subfraction Sf, eluted with $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ (95:5 to 100:0, v/v, during 30 min). The subfraction Sg was chromatographed by PLC eluted with $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ (8:2 to 10:0, v/v; 10 mL/min) to afford compounds **7** (13 mg) and **12** (1.2 mg). The subfraction Sh was purified by semi-preparative HPLC eluted with $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ (98:2 to 100:0, v/v, during 35 min) to yield compounds **30** ($t_r=19.4$ min, 4 mg) and **13** ($t_r=20.5$ min, 2 mg).

4.3.3. icacimannitin A (**1**)

$[\alpha]_{\text{D}}^{20}$ - 41 (c 0.3, MeOH); ^1H NMR (500 MHz, MeOH- d_4) and ^{13}C NMR (125 MHz, MeOH- d_4), see (Table 2 and Table 3); HR-ESI-MS m/z 333.2069 $[\text{M}-\text{H}]^-$ (calcd $\text{C}_{20}\text{H}_{29}\text{O}_4$, 333.2066).

4.3.4. icacimannitin B (2)

$[\alpha]_{\text{D}}^{20}$ -142 (c 0.05, MeOH); ^1H NMR (600 MHz, MeOH- d_4) and ^{13}C NMR (150 MHz, MeOH- d_4), see (Table 2 and Table 3); HR-ESI-MS m/z 363.2173 $[\text{M}-\text{H}]^-$ (calcd $\text{C}_{21}\text{H}_{31}\text{O}_5$, 363.271).

4.3.5 icacimannitin C (3)

$[\alpha]_{\text{D}}^{20}$ -41.6 (c 0.3, MeOH); ^1H NMR (500 MHz, MeOH- d_4) and ^{13}C NMR (125 MHz, MeOH- d_4), see (Table 2 and Table 3); HR-ESI-MS m/z 333.2068 $[\text{M}-\text{H}]^-$ (calcd $\text{C}_{20}\text{H}_{29}\text{O}_4$, 333.2066).

4.3.6. 3,4-dihydro-bacchalineol (4)

$[\alpha]_{\text{D}}^{20}$ -32.8 (c 0.6, MeOH); ^1H NMR (500 MHz, MeOH- d_4) and ^{13}C NMR (125 MHz, MeOH- d_4), see (Table 2 and Table 3); EI-MS m/z 304.3 $[\text{M}]^+$; (calcd $\text{C}_{20}\text{H}_{32}\text{O}_2$, 304.3).

4.3.7. 18-hydroxy-kolavenol (5)

$[\alpha]_{\text{D}}^{20}$ -24.4 (c 0.65, MeOH); ^1H NMR (500 MHz, MeOH- d_4) and ^{13}C NMR (125 MHz, MeOH- d_4), see (Table 2 and Table 3); ESI-MS 306.25 $[\text{M}]^+$; (calcd $\text{C}_{20}\text{H}_{34}\text{O}_2$).

4.3.8. (13E)-halima-1(10),13-dien-15-ol (12)

$[\alpha]_{\text{D}}^{20}$ +18.6 (c 0.5, MeOH); ^1H NMR (500 MHz, MeOH- d_4) and ^{13}C NMR (125 MHz, MeOH- d_4), see Table 4.

4.3.9. (13E)-halima-5(10),13-dien-15-ol (13)

$[\alpha]_{\text{D}}^{20}$ +22 (c 0.05, MeOH); ^1H NMR (600 MHz, MeOH- d_4) and ^{13}C NMR (150 MHz, MeOH- d_4), see Table 4; EI-MS m/z 290.3 $[\text{M}]^+$; (calcd $\text{C}_{20}\text{H}_{34}\text{O}$).

4.3.10. (13E)-19-hydroxy-halima-5(10),13-dien-15-ol (14)

$[\alpha]_{\text{D}}^{20}$ +11 (c 0.1, MeOH); ^1H NMR (600 MHz, MeOH- d_4) and ^{13}C NMR (150 MHz, MeOH- d_4), see Table 4; ESI-MS m/z 306.35 $[\text{M}]^+$; (calcd $\text{C}_{20}\text{H}_{34}\text{O}_2$).

4.3.11. icacinlactone O (15)

$[\alpha]_{\text{D}}^{20}$ -6 (c 0.15, DMSO); ^1H NMR (600 MHz, DMSO- d_6) and ^{13}C NMR (150 MHz, DMSO- d_6), see Table 5; HR-ESI-MS m/z 389.1579 $[\text{M}+\text{Na}]^+$ (calcd $\text{C}_{19}\text{H}_{26}\text{O}_7\text{Na}$, 389.1576).

4.3.12. icacinlactone P (16)

$[\alpha]_D^{20}$ -27.3 (c 0.3, MeOH); ^1H NMR (500 MHz, DMSO- d_6) and ^{13}C NMR (125 MHz, DMSO- d_6), see Table 5; HR-ESI-MS m/z 399.1288 $[\text{M}-\text{H}]^-$ (calcd $\text{C}_{18}\text{H}_{23}\text{O}_{10}$, 399.1291).

4.3.13. 2-O- β -D-glucopyranosyl-icacinone (17)

$[\alpha]_D^{20}$ +6.9 (c 7.1, DMSO); ^1H NMR (500 MHz, DMSO- d_6) and ^{13}C NMR (125 MHz, DMSO- d_6), see Table 5; HR-ESI-MS m/z 521.1655 $[\text{M}-\text{H}]^-$ (calcd $\text{C}_{25}\text{H}_{29}\text{O}_{12}$, 521.1659).

4.3.14. Icaninamate (24)

^1H NMR (600 MHz, MeOH- d_4) and ^{13}C NMR (150 MHz, MeOH- d_4), see Table 6; HR-ESI-MS m/z 295.1295 $[\text{M}-\text{H}]^-$ (calcd $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_5$, 295.1294).

4.3.15. (+)-N-(Z)-caffeoyl-L-dopamine (25)

$[\alpha]_D^{20}$ +5.5 (c 0.4, MeOH); ^1H NMR (500 MHz, MeOH- d_4) and ^{13}C NMR (125 MHz, MeOH- d_4), see Table 6; HR-ESI-MS m/z 358.0926 $[\text{M}-\text{H}]^-$ (calcd $\text{C}_{22}\text{H}_{16}\text{NO}_7$, 358.0927).

4.3.16. (-)-(Z)-caffeoyl-L-dopamine methyl ester (26)

$[\alpha]_D^{20}$ -9.6 (c 0.25, MeOH); ^1H NMR (600 MHz, MeOH- d_4) and ^{13}C NMR (150 MHz, MeOH- d_4), see Table 6; HR-ESI-MS m/z 372.1082 $[\text{M}-\text{H}]^-$ (calcd $\text{C}_{19}\text{H}_{18}\text{NO}_7$, 372.1083).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online

References

Adou, E., Williams, R.B., Schilling, J.K., Malone, S., Meyer, J., Wisse, J.H., Frederik, D., Koese, D., Werkhoven, M.C.M., Snipes, C.E., Werk, T.L., Kingston, D.G.I., 2005. Cytotoxic

diterpenoids from two lianas from the Suriname rainforest. *Bioorg. Med. Chem.* 13, 6009–6014. <https://doi.org/10.1016/j.bmc.2005.07.026>

Adjanooun E, Aké Assi L. Contribution au recensement des plantes médicinales de Côte d'Ivoire. Abidjan: CNF; 1979.

Agrawal, P.K., 1992. NMR Spectroscopy in the structural elucidation of oligosaccharides and glycosides. *Phytochemistry*, 31, 3307–3330. [https://doi.org/10.1016/0031-9422\(92\)83678-R](https://doi.org/10.1016/0031-9422(92)83678-R)

Akuodor, G.C., Essien, D.-O., Nkorroh, J.A., Essien, A.D., Nkanor, E.E., Ezeunala, M.N., Chilaka, K.C., 2017. Antiplasmodial activity of the ethanolic root bark extract of *Icacina senegalensis* in mice infected by *Plasmodium berghei*. *J. Basic Clin. Physiol. Pharmacol.* 28, 181–184. DOI: 10.1515/jbcpp-2016-0109

Akuodor, G.C., Nwobodo, N.N., Megwas, A.U., Akpan, J.L., Chwchukwu, D.C., Asika, E.C., Chilaka, K.C., 2018. Antidiarrheal and antimicrobial activities of the ethanol extract from the *Icacina senegalensis* root bark. *J. basic clin. physiol. pharmacol.* 29, 211–216. DOI: 10.1515/jbcpp-2016-0174

Akuodor, G.C., Udia, P.M., Bassey, A., Chilaka, K.C., Okezie, O.A., 2014. Antihyperglycemic and antihyperlipidemic properties of aqueous root extract of *Icacina senegalensis* in alloxan induced diabetic rats. *J. Acute Dis.* 3, 99–103. [https://doi.org/10.1016/S2221-6189\(14\)60025-1](https://doi.org/10.1016/S2221-6189(14)60025-1)

Alemanno, L., Ramos, T., Gargadeneç, A., Andary, C., Ferriere, N., 2003. Localization and identification of phenolic compounds in *Theobroma cacao* L. somatic embryogenesis. *Ann. Bot.* 92, 613–623. <https://doi.org/10.1093/aob/mcg177>

Bock, K., Pedersen, C., 1983. Carbon-13 nuclear magnetic resonance spectroscopy of monosaccharides, in: Tipson, R.S., Horton, D. (Eds.), *Advances in Carbohydrate Chemistry and Biochemistry*. Academic Press, pp. 27–66. [https://doi.org/10.1016/S0065-2318\(08\)60055-4](https://doi.org/10.1016/S0065-2318(08)60055-4)

Bohlmann, F., Zdero, C., Gupta, R.K., King, R.M., Robinson, H., 1980. Diterpenes and tetranorditerpenes from *Acritopappus* species. *Phytochemistry* 19, 2695–2705. [https://doi.org/10.1016/S0031-9422\(00\)83946-1](https://doi.org/10.1016/S0031-9422(00)83946-1)

Bouquet A. et Debray M, 1974. Plantes médicinales de la Côte d'Ivoire, Travaux et documents de l'O.R.S.T.O.M., O.R.S.T.O.M. PARIS 32 :96 pp.

Burkill, H.M., 1994. *The useful plants of West Tropical Africa*. 2nd Edition. Volume 2, Families E–I. Royal Botanic Gardens, Kew, Richmond, United Kingdom. 636 pp.

Cai, Y., Chen, Z. P., Phillipson, J. D. (1993). *Diterpenes from Croton lechleri*. *Phytochemistry*, 32(3), 755–760. [https://doi.org/10.1016/S0031-9422\(00\)95166-5](https://doi.org/10.1016/S0031-9422(00)95166-5)

- Cao, S., Hou, Y., Brodie, P., Miller, J.S., Randrianaivo, R., Rakotobe, E., Rasamison, V.E., Kingston, D.G.I., 2011. Antiproliferative compounds of *Cyphostemma greveana* from a Madagascar dry forest. *Chem. Biodivers.* 8, 643–650. <https://doi.org/10.1002/cbdv.201000061>
- Chen-Loung, C., Hou-Min, C., 1978. Lignans and aporphine alkaloids in bark of *Liriodendron tulipifera*. *Phytochemistry* 17, 779–782. [https://doi.org/10.1016/S0031-9422\(00\)94226-2](https://doi.org/10.1016/S0031-9422(00)94226-2)
- David, J.P., David, J.M., Yang, S.-W., Cordell, G.A., 1999. A bis-labdenic diterpene from *Moldenhawera nutans*. *Phytochemistry* 50, 443–447. [https://doi.org/10.1016/S0031-9422\(98\)00590-1](https://doi.org/10.1016/S0031-9422(98)00590-1)
- Du, K., De Mieri, M., Neuburger, M., Zietsman, P.C., Marston, A., van Vuuren, S.F., Ferreira, D., Hamburger, M., van der Westhuizen, J.H., 2015. Labdane and clerodane diterpenoids from *Colophospermum mopane*. *J. Nat. Prod.* 78, 2494–2504. <https://doi.org/10.1021/acs.jnatprod.5b00729>
- El-Sharawy, R.T., Elkhateeb, A., Marzouk, M. M., El-Latif, R. R. A., Abdelrazig, S. E., El-Ansari, M.A. (2017). Antiviral and antiparasitic activities of clovamide: the major constituent of *Dichrostachys cinerea* (L.) Wight et Arn. *J. App. Pharm. Sci.* 7, 219-223.
- Fay, J.M. 1991. *Icacina oliviformis* (Icacinaceae): A close look at an under exploited food plant II. Analysis of food products. *Econ. Bot.* 43, 15-26
- Freiburghaus, F., Steck, A., Pfander, H., Brun, R., 1998a. Bioassay-guided isolation of a diastereoisomer of kolavenol from *Etida abyssinica* active on *Trypanosoma brucei rhodesiense*. *J. Ethnopharmacol.* 61, 179–183. [https://doi.org/10.1016/S0378-8741\(98\)00035-X](https://doi.org/10.1016/S0378-8741(98)00035-X)
- Graebner, I.B., Mostardeiro, M.A., Ethur, E.M., Burrow, R.A., Dessoy, E.C.S., Morel, A.F., 2000. Diterpenoids from *Humirianthera ampla*. *Phytochemistry* 53, 955–959. [https://doi.org/10.1016/S0031-9422\(99\)00585-3](https://doi.org/10.1016/S0031-9422(99)00585-3)
- Hara, N., Asaki, H., Fujimoto, Y., Gupta, Y.K., Singh, A.K., Sahai, M., 1995. Clerodane and ent-halimane diterpenes from *Polyalthia longifolia*. *Phytochemistry* 38, 189–194. [https://doi.org/10.1016/0031-9422\(94\)00583-F](https://doi.org/10.1016/0031-9422(94)00583-F)
- Inui, T., Wang, Y., Nikolic, D., Smith, D.C., Franzblau, S.G., Pauli, G.F., 2010. Sesquiterpenes from *Oplopanax horridus*. *J. Nat. Prod.* 73, 563–567. <https://doi.org/10.1021/np900674d>
- Li, R., Morris-Natschke S. L., Lee K-H. (2016). Clerodane diterpenes: sources, structures, and biological activities. *Nat. Prod. Rep.*, 28, 33(10), 1166–1226. doi:10.1039/c5np00137d

- Lopes, L.M.X., Bolzani, V. da S., Trevisan, L.M.V., 1987. Clerodane diterpenes from *Aristolochia* species. *Phytochemistry* 26, 2781–2784. [https://doi.org/10.1016/S0031-9422\(00\)83590-6](https://doi.org/10.1016/S0031-9422(00)83590-6)
- Manga, A., Gassama, A., Yoro SY, G., Bassene, E., Lavaud, C., 2013. Détermination structurale de nouvelles flavones C-glycosides et le *trans* -(S, E)-clovamide isolés de la feuille de *Icacina senegalensis* Juss. (Icacinaceae). *J. Soc. Ouest-Afr. Chim.* 35, 15-27.
- Malan, D.F., Neuba, D.F., Kouakou, K.L., 2015. Medicinal plants and traditional healing practices in ehotile people, around the aby lagoon (eastern littoral of Côte d'Ivoire). *J. Ethnobiol. Ethnomed.* 11, 21.
- Merritt, A. T., Ley, S. V. (1992). *Clerodane diterpenoids*. *Nat. Prod. Rep.* 9, 243. doi:10.1039/np9920900243
- Monday Onakpa, M., Zhao, M., Gödecke, T., Chen, W.-L., Che, C.-T., Santarsiero, B.D., Swanson, S.M., Uzoma Asuzu, I., 2014. Cytotoxic (9 β H)-pimarane and (9 β H)-17-norpimarane diterpenes from the tuber of *Icacina trichantha*. *Cnem. Biodivers.* 11, 1914–1922. <https://doi.org/10.1002/cbdv.201400151>
- Mussini, P., Orsini, F., Pelizzoni, F., Buckwalter, B.L., Wenkert, E., 1973. The C-13 configuration of annonalide. *Tetrahedron Lett.* 14, 4849–4851. [https://doi.org/10.1016/S0040-4039\(01\)87353-6](https://doi.org/10.1016/S0040-4039(01)87353-6)
- On'Okoko, P., Hans, M., Colau, B., Houllé, C., Declercq, J.-P., Germain, G., Meerssche, M. van, 1977. icacine, nouvel alcaloïde diterpenique de *Icacina gussfeldtii*. *Bull. Soc. Chim. Belges*, 86, 655-661. <https://doi.org/10.1002/bscb.19770860902>.
- On'Okoko, P., Vanhaelen, M., 1980. Two new diterpene-based alkaloids from *Icacina gussfeldtii*. *Phytochemistry* 19, 303–305. [https://doi.org/10.1016/S0031-9422\(00\)81979-2](https://doi.org/10.1016/S0031-9422(00)81979-2)
- On'Okoko, P., Vanhaelen M., Vanhaelen-Fastré, R., Declercq, J.-P., Van Meerssche, M., 1985a. Icacenone, a furanoditerpene with a pimarane skeleton from *Icacina mannii*. *Phytochemistry* 24, 2452–2453. [https://doi.org/10.1016/S0031-9422\(00\)83067-8](https://doi.org/10.1016/S0031-9422(00)83067-8)
- On'okoko, P., Vanhaelen, M., Vanhaelen-Fastre, R., Declercq, J.-P., Van Meerssche, M., 1985b. The constitution of icacinol, a new diterpene with a pimarane skeleton from *Icacina claessensis*. *Tetrahedron* 41, 745–748. [https://doi.org/10.1016/S0040-4020\(01\)96452-X](https://doi.org/10.1016/S0040-4020(01)96452-X)
- Park, S.-H., Oh, H.-S., Kang, M.-A., Cho, H., Prasad, J.B., Won, J., Lee, K.-H., 2007. The structure–activity relationship of the series of non-peptide small antagonists for p56lck SH2 domain. *Bioorg. Med. Chem.* 15, 3938–3950. <https://doi.org/10.1016/j.bmc.2006.06.059>

- Salah, M.A., Bedir, E., Toyang, N.J., Khan, I.A., Harries, M.D., Wedge, D.E., 2003. Antifungal clerodane diterpenes from *Macaranga monandra* (L) Muell. et Arg. (Euphorbiaceae). *J. Agric. Food Chem.* 51, 7607–7610. <https://doi.org/10.1021/jf034682w>
- Sanbongi, C., Osakabe, N., Natsume, M., Takizawa, T., Gomi, S., Osawa, T. Antioxidative polyphenols isolated from *Theobroma cacao* *J. Agric. Food Chem.* 1998, 46, 454–457.
- San-Martín, A., Givovich, A., Castillo, M., 1985. Neo-clerodane diterpenoids from *Baccharis incarum*. *Phytochemistry* 25, 264–266. [https://doi.org/10.1016/S0031-9422\(00\)94546-1](https://doi.org/10.1016/S0031-9422(00)94546-1)
- Stark, T., Hofmann, T., 2005. Isolation, structure determination, synthesis, and sensory activity of N-phenylpropenoyl-l-amino acids from cocoa (*Theobroma cacao*). *J. Agric. Food Chem.* 53, 5419–5428. <https://doi.org/10.1021/jf050458q>
- Sun, M., 2019. Identification of diterpenoids from *lCACINA OLIVIFORMIS*, Thesis B.S., China Pharmaceutical University.
- Tong, W., Liang, H., Wu, G., Wang, B., Zhao, Y., 2015. RP-HPLC determination of (-)-syringaresinol-4-O- β -D-glucopyranoside in the stem bark of *Albizia julibrissin* Durazz. *Chinese Journal of Pharmaceutical Analysis* 25, 1061–1063
- Toshima, H., Oikawa, H., Toyomasu, T., Sassa, T., 2000. Total synthesis of both enantiomers of copalol via optical resolution of a general synthetic intermediate for drimane sesquiterpenes and labdane diterpenes. *Tetrahedron* 56, 8443–8450. [https://doi.org/10.1016/S0040-4020\(00\)00791-2](https://doi.org/10.1016/S0040-4020(00)00791-2)
- Tsichritzis, F., Jakupovic, J., 1995. Diterpenes from *Leyssera gnaphaloides*. *Phytochemistry* 30, 211–213. [https://doi.org/10.1016/0031-9422\(91\)84127-E](https://doi.org/10.1016/0031-9422(91)84127-E)
- Xin, Z., Lu, Y., Xing, X., Long, J., Li, J., Xue, X., 2016. Synthesis of (-)-agathic acid and (-)-copalic acid from andrographolide via a regioselective Barton-McCombie reaction. *Tetrahedron* 72, 555–562. <https://doi.org/10.1016/j.tet.2015.12.022>
- Xiong, L., Zhu, C., Li, Y., Tian, Y., Lin, S., Yuan, S., Hu, J., Hou, Q., Chen, N., Yang, Y., Shi, J., 2011. Lignans and neolignans from *Sinocalamus affinis* and their absolute configurations. *J. Nat. Prod.* 74, 1188–1200. <https://doi.org/10.1021/np200117y>
- Zhang, Y., Li, M., Liu, Q., Huang, J., Chen, Y. (2022) A Synthetic view on momilactones and related 9 β -H pimarane skeleton diterpenoids. *Front. Chem.*,10, 882404. doi: 10.3389/fchem.2022.882404
- Zhao, M., Onakpa, M.M., Chen, W.-L., Santarsiero, B.D., Swanson, S.M., Burdette, J.E., Asuzu, I.U., Che, C.-T., 2015a. 17-Norpimaranes and (9 β H)-17-norpimaranes from the tuber of *lCACINA trichantha*. *J. Nat. Prod.* 78, 789–796. <https://doi.org/10.1021/np5010328>

Zhao, M., Onakpa, M.M., Santarsiero, B.D., Chen, W.-L., Szymulanska-Ramamurthy, K.M., Swanson, S.M., Burdette, J.E., Che, C.-T., 2015b. (9 β H)-Pimaranes and derivatives from the tuber of *Icacina trichantha*. J. Nat. Prod. 78, 2731–2737. <https://doi.org/10.1021/acs.jnatprod.5b00688>

Zhao, M., Onakpa, M.M., Santarsiero, B.D., Huang, X.-J., Zhang, X.-Q., Chen, J., Cheng, J.-J., Longnecker, R., Che, C.-T., 2015c. Icacinlactone H and icacintrichantholide from the tuber of *Icacina trichantha*. Org. Lett. 17, 3834–3837. <https://doi.org/10.1021/acs.orglett.5b01806>

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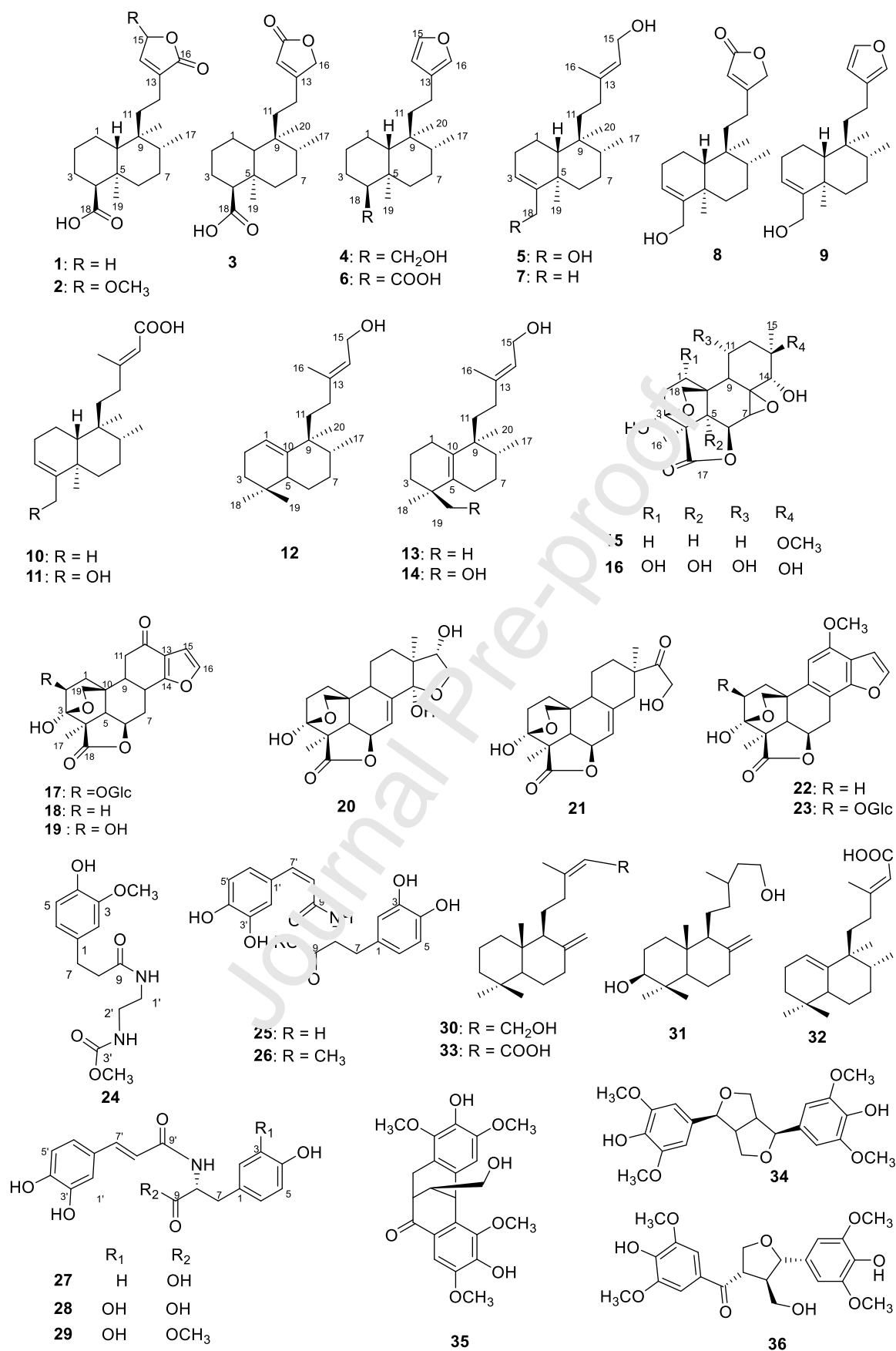


Fig. 1: Compounds 1–36 isolated from *Icacina mannii*

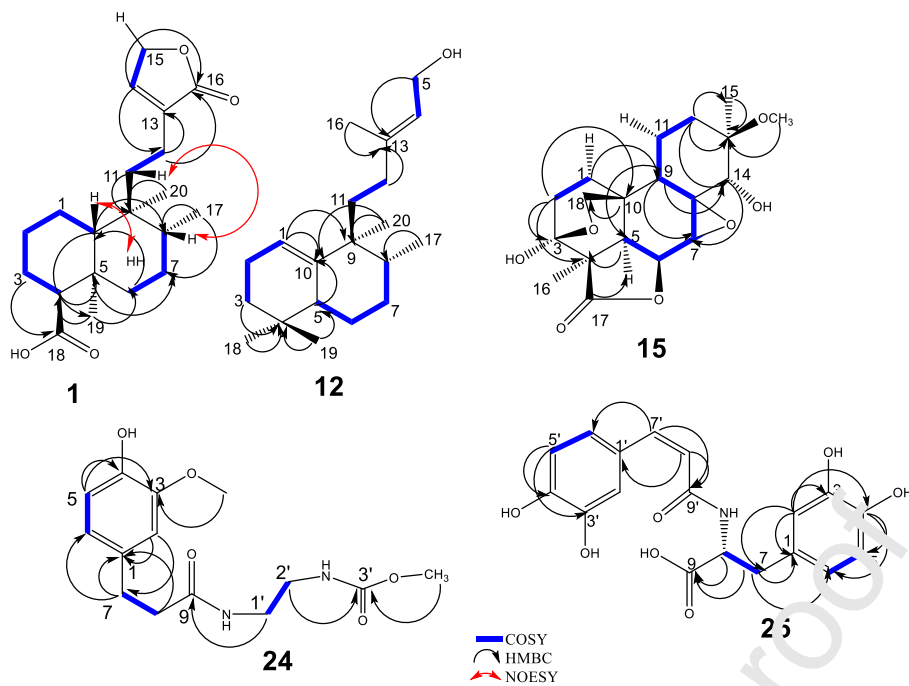


Fig 2: Selected key HMBC, COSY and NOESY interactions for compound 1, 12, 15, 24 and 25.

Table 1Known compounds from *I. mannii*.

| Compounds | Name | References |
|-----------|--|---|
| 6 | Crolechinic acid | Cai et al., 1993 |
| 7 | (+)-Kolavenol | Freiburghaus et al., 1998 |
| 8 | 18-Hydroxykolavenoic acid lactone | Cao et al., 2011; Bohlmann et al., 1980 |
| 9 | Bacchalineol | San-Martin et al., 1985 |
| 10 | (<i>E</i>)-(+)-Kovalenic acid | Salah et al., 2003; Lopes et al., 1987 |
| 11 | (-)-18-Hydroxycleroda-3,13 <i>E</i> -dien-15-oic acid | Du et al., 2015 |
| 18 | Icacinlactone E | Zhao et al., 2015 |
| 19 | Icacinone | On'Okoko et al., 1985 |
| 20 | Icacinol | On'Okoko et al., 1985 |
| 21 | Annonalide | Mussini et al., 1973; Adou et al., 2005 |
| 22 | Icacinlactone B | Zhao et al., 2015 |
| 23 | 2- <i>O</i> - β -D-glucopyranosyl-Icacinlactone H | Meng S., 2019 |
| 27 | <i>N</i> -(<i>E</i>)-caffeoyl-L-dopamine | Alemanno et al., 2003 |
| 28 | (-)- <i>N</i> -(<i>E</i>)-caffeoyl-L-dopamine | Stark and Hofmann, 2005 |
| 29 | (-)-(<i>E</i>)-caffeoyl-L-dopamine methyl ester | Park et al., 2007 |
| 30 | (-)-Copalol | Toshima et al., 2000 |
| 31 | 3 β ,15-dihydroxy-labda-8(17)-ene | David et al., 1999 |
| 32 | (+)- <i>ent</i> -halima-1(10), 13 <i>E</i> -dien-15-oic acid | Hara et al., 1995 |
| 33 | (<i>E</i>)-(-)-copalic acid | Xin et al., 2016 |
| 34 | Syringaresinol | Tong et al., 2005 ; Inui et al., 2010 |
| 35 | Lirionol | Chen-Loung and Hou-Min, 1978 |
| 36 | (7' <i>S</i> , 8 <i>S</i> , 8' <i>R</i>)-4,4'-dihydroxy-3,3',5,5'-tetrahydroxy-7',9-epoxylignan-9'-ol-7-one | Xiong et al., 2011 |

Table 2¹H (500 MHz, MeOH-*d*₄) NMR spectroscopic data for compounds 1-5.

| | 1 | 2 | 3 | 4 | 5 |
|-------------------|---------------------------------|---------------------------------|--|--|---------------------------------|
| | δ_{H} m (J in Hz) | δ_{H} m (J in Hz) | δ_{H} m (J in Hz) | δ_{H} m (J in Hz) | δ_{H} m (J in Hz) |
| 1 | 1.59 m 1.36 m | 1.60 m 1.39 m | 1.52 m 1.37 m | 1.59 m 1.35 m | 1.67 m 1.50 m |
| 2 | 1.86 m 1.35 m | 1.88 dm (9.3) 1.40 m | 1.86 m 1.35 tt (12.6, 3.4) | 1.89 m 1.33 m | 2.17 m 2.10 m |
| 3 | 1.74 m 1.56 m | 1.75 tm (13.2) 1.59 m | 1.73 td (13.2, 4.2) 1.55 m | 1.85 m 1.22 m | 5.57 m |
| 4 | 2.11 dd (12.8, 3.1) | 2.12 dm (12.8) | 2.11 dd (12.9, 3.2) | 1.20 m | - |
| 5 | - | - | - | - | - |
| 6 | 1.61 m 1.37 m | 1.62 m 1.39 m | 1.62 dt (13.3, 3.1) 1.38 m | 1.82 tt (13.0, 3.2) 1.20 m | 1.78 m 1.35 m |
| 7 | 1.46 m 1.40 m | 1.50 m 1.40 m | 1.49 m 1.41 m | 1.47 td (12.1, 3.3) 1.40 m | 1.53 m 1.47 m |
| 8 | 1.57 m | 1.58 m | 1.57 m | 1.60 m | 1.53 m |
| 9 | - | - | - | - | - |
| 10 | 1.17 dd (11.7, 2.2) | 1.17 dd (11.7, 2.2) | 1.15 dq (12.0, 2.5) | 1.19 dd (12.1, 2.3) | 1.42 m |
| 11 | 1.58 m 1.47 m | 1.59 m 1.48 m | 1.66 m 1.55 m | 1.62 d, d (14.8, 12.7, 4.5) 1.50 m | 1.59 m 1.45 m |
| 12 | 2.20 tm (13.7) 2.10 m | 2.22 tm (13.3) 2.12 m | 2.41 ddd (16.8, 12.4, 3.4) 2.27 ddd (16.8, 13.0, 4.7) | 2.35 dd (13.0, 4.4) 2.23 td (13.0, 5.1) | 1.92 m 1.84 m |
| 13 | - | - | - | - | - |
| 14 | 7.34 q (1.5) | 6.98 brs | 5.88 q (1.5) | 6.28 m | 5.38 m |
| 15 | 4.81 q (1.7) | 5.85 brs | - | 7.28 s (1.5) | 4.08 d (6.7) |
| 16 | - | - | 4.87 d (1.6) | 7.26 s | 1.69 s |
| 17 | 0.84 d (6.7) | 0.84 d (6.7) | 0.84 d (6.4) | 0.35 d (6.8) | 0.86 d (6.4) |
| 18 | - | - | - | 3.79 dd (10.6, 2.7) 3.17 dd (10.6, 8.5) | 4.06 d (13.6) 4.01 d (13.6) |
| 19 | 1.05 s | 1.07 s | 1.06 s | 0.87 s | 1.12 s |
| 20 | 0.75 s | 0.77 s | 0.79 s | 0.75 s | 0.80 s |
| O-CH ₃ | | 3.55 s | | | |

Table 3¹³C (125 MHz, MeOH-*d*₄) NMR spectroscopic data for compounds 1-5.

| | 1 | 2 | 3 | 4 | 5 |
|-------------------|---------------------|---------------------|---------------------|---------------------|---------------------|
| | δ_{C} | δ_{C} | δ_{C} | δ_{C} | δ_{C} |
| 1 | 22.1 | 22.1 | 22.2 | 21.3 | 19.3 |
| 2 | 27.2 | 27.2 | 27.2 | 25.3 | 27.5 |
| 3 | 26.3 | 26.2 | 26.2 | 26.7 | 22.2 |
| 4 | 58.9 | 58.9 | 58.8 | 54.1 | 48.6 |
| 5 | 38.1 | 38.1 | 38.1 | 36.6 | 38.8 |
| 6 | 41.1 | 41.1 | 41.0 | 39.1 | 31.4 |
| 7 | 28.3 | 28.3 | 28.2 | 27.5 | 28.4 |
| 8 | 37.9 | 37.9 | 37.8 | 36.3 | 37.5 |
| 9 | 40.0 | 40.0 | 40.0 | 38.6 | 39.7 |
| 10 | 50.6 | 50.6 | 50.5 | 41.7 | 47.6 |
| 11 | 37.1 | 36.9 | 36.3 | 38.6 | 38.4 |
| 12 | 19.8 | 19.8 | 23.0 | 17.6 | 34.1 |
| 13 | 134.9 | 139.7 | 175.1 | 125.6 | 140.6 |
| 14 | 147.3 | 144.2 | 115.0 | 110.5 | 124.4 |
| 15 | 72.1 | 104.5 | 176.9 | 142.5 | 59.4 |
| 16 | 176.9 | 173.5 | 75.0 | 138.2 | 16.4 |
| 17 | 16.3 | 16.3 | 16.3 | 15.1 | 16.3 |
| 18 | 178.3 | 178.5 | 178.2 | 62.1 | 62.7 |
| 19 | 15.3 | 15.3 | 15.3 | 14.1 | 21.7 |
| 20 | 18.5 | 18.5 | 18.4 | 17.3 | 18.9 |
| O-CH ₃ | | 57.1 | | | |

Table 4¹H (500 MHz) and ¹³C (125 MHz), spectroscopic data for compounds **12-14** (in MeOH-*d*₄).

| | 12 | | 13 | | 14 | |
|----|--|---------------------|---------------------------------|---------------------|---------------------------------|---------------------|
| | δ_{H} m (J in Hz) | δ_{C} | δ_{H} m (J in Hz) | δ_{C} | δ_{H} m (J in Hz) | δ_{C} |
| 1 | 5.36 t (3.6) | 121.0 | 2.10 m 1.88 m | 25.6 | 2.07 m 1.85 m | 25.6 |
| 2 | 2.05 m | 24.1 | 1.65 m | 19.6 | 1.69 m 1.55 m | 19.2 |
| 3 | 1.39 m 1.15 m | 34.2 | 1.59 m 1.40 m | 39.8 | 1.71 m 1.35 m | 33.4 |
| 4 | - | 32.4 | - | 34.1 | - | 39.7 |
| 5 | 1.74 dd (13.3, 4.0) | 44.8 | - | 137.0 | - | 134.0 |
| 6 | 1.60 m 1.29 dd (12.8, 4.5) | 24.9 | 2.11 m | 25.1 | 2.04 m 1.97 m | 25.0 |
| 7 | 2.04 m 1.37 m | 30.2 | 1.58 m 1.38 m | 27.0 | 1.49 m 1.38 m | 27.0 |
| 8 | 1.55 m | 40.6 | 1.69 m | 33.5 | 1.71 m | 33.3 |
| 9 | - | 44.1 | - | 40.3 | - | 40.6 |
| 10 | - | 142.9 | - | 132.5 | - | 135.7 |
| 11 | 2.06 m 1.24 td (12.8, 4.8) | 39.0 | 1.60 m | 34.3 | 1.50 m | 34.2 |
| 12 | 1.87 td (13.4, 4.8) 1.73 dt (13.4, 4.8) | 35.5 | 1.98 m 1.70 m | 34.0 | 1.96 m 1.75 m | 34.0 |
| 13 | - | 140.8 | - | 139.4 | - | 139.6 |
| 14 | 5.32 tq (6.9, 1.2) | 124.2 | 5.35 t (6.9) | 122.8 | 5.35 t (6.8) | 122 |
| 15 | 4.06 d (6.9) | 59.4 | 4.08 d (6.9) | 58.0 | 4.08 d (6.8) | 58.0 |
| 16 | 1.65 s | 16.5 | 1.68 s | 15.0 | 1.67 s | 15.1 |
| 17 | 0.84 d (7.0) | 16.0 | 0.88 d (6.9) | 15.1 | 0.87 d (6.4) | 15.1 |
| 18 | 0.91 s | 28.7 | 1.00 s | 28.3 | 0.96 s | 21.7 |
| 19 | 0.85 s | 26.6 | 1.01 s | 26.6 | 3.49 d (10.4) 3.26 d (10.4) | 28.5 |
| 20 | 0.93 s | 22.8 | 0.85 s | 20.1 | 0.86 s | 20.0 |

Table 5
¹H (500 MHz) and ¹³C (125 MHz) NMR spectroscopic data for compounds **15-17** (in DMSO-*d*₆).

| | 15 | | 16 | | 17 | |
|-----|--|---------------------|---------------------------------|---------------------|--|---------------------|
| | δ_{H} m (J in Hz) | δ_{C} | δ_{H} m (J in Hz) | δ_{C} | δ_{H} m (J in Hz) | δ_{C} |
| 1 | 1.54 m 1.42 td (12.2, 4.0) | 31.0 | 4.75 m | 65.9 | 2.25 m 1.58 m | 40.1 |
| 2 | 1.92 ddd (13.3, 12.2, 8.6) 1.64 m | 29.0 | 2.40 dd (13.3, 10.3) 1.64 m | 37.9 | 3.90 m | 76.7 |
| 3 | - | 96.9 | - | 97.0 | - | 96.6 |
| 4 | - | 49.4 | - | 54.7 | - | 50.4 |
| 5 | 2.21 d (7.5) | 43.8 | - | 78.8 | 2.20 m | 43.1 |
| 6 | 5.06 dd (7.5, 4.5) | 73.1 | 4.69 m | 80.7 | 4.68 m | 73.4 |
| 7 | 3.55 d (4.5) | 49.9 | 3.85 m | 50.5 | 2.35 dd (16.1, 4.8) 1.95 m | 27.0 |
| 8 | - | 65.2 | - | 64.2 | 3.20 m | 27.0 |
| 9 | 1.55 dd (12.8, 4.4) | 37.6 | 1.81 d (9.7) | 44.3 | 2.14 d (11.6) | 37.5 |
| 10 | - | 32.1 | - | 42.5 | - | 32.6 |
| 11 | 1.62 m 1.16 qd (13.2, 3.6) | 21.8 | 4.60 m | 68.4 | 2.59 t (15.5) 2.22 m | 34.4 |
| 12 | 1.72 dt (12.8, 3.2) 1.48 td (13.2, 4.0) | 33.3 | 2.14 dd (12.7, 5.2) 1.66 m | 49.0 | - | 193.1 |
| 13 | - | 77.7 | - | 71.3 | - | 120.3 |
| 14 | 3.66 d (4.6) | 72.0 | 3.70 m | 76.3 | - | 170.8 |
| 15 | 0.99 s | 16.4 | 1.15 s | 19.7 | 6.67 m | 106.9 |
| 16 | 1.22 s | 19.2 | 1.24 s | 14.1 | 7.72 m | 144.9 |
| 17 | - | 178.3 | - | 179.2 | 1.24 s | 16.8 |
| 18 | 4.51 dd (9.1, 3.4) 3.34 dt (9.1, 1.5) | 72.6 | 4.39 d (9.7) 3.96 d (9.7) | 66.2 | - | 177.1 |
| 19 | 3.20 s | 49.2 | - | - | 4.21 t (8.7) 3.50 t (8.7) | 72.1 |
| Glc | | | | | | |
| 1' | - | - | - | - | 4.32 a (7.8) | 105.7 |
| 2' | - | - | - | - | 3.15 m | 74.2 |
| 3' | - | - | - | - | 3.23 t (8.8) | 76.7 |
| 4' | - | - | - | - | 3.13 t (9.2) | 70.4 |
| 5' | - | - | - | - | 3.20 m | 77.3 |
| 6' | - | - | - | - | 3.74 dd (11.7, 2.1) 3.53 dd (11.3, 5.8) | 61.5 |

Table 6
¹H (500 MHz) and ¹³C (125 MHz) NMR spectroscopic data for compounds **24-26** (in MeOH-*d*₄).

| | 24 | | 25 | | 26 | |
|----------------------|---------------------------------|---------------------|--|---------------------|--|---------------------|
| | δ_{H} m (J in Hz) | δ_{C} | δ_{H} m (J in Hz) | δ_{C} | δ_{H} m (J in Hz) | δ_{C} |
| 1 | - | 130.5 | - | 129.7 | - | 129.3 |
| 2 | 6.81 brs | 111.9 | 6.70 d (2.1) | 117.2 | 6.63 d (2.1) | 117.1 |
| 3 | - | 147.5 | - | 146.2 | - | 145.3 |
| 4 | - | 144.6 | - | 145.1 | - | 143.3 |
| 5 | 6.72 d (7.2) | 114.7 | 6.65 d (8.3) | 116.0 | 6.67 d (8.0) | 116.3 |
| 6 | 6.65 d (7.2) | 120.8 | 6.54 dd (8.3, 2.1) | 121.7 | 6.52 dd (8.0, 2.1) | 121.6 |
| 7 | 2.72 d (6.4) | 31.7 | 3.11 dd (14.0, 5.3) 2.90 dd (14.0, 8.5) | 37.8 | 3.02 dd (13.9, 5.9) 2.89 dd (13.9, 8.0) | 37.9 |
| 8 | 3.39 d (6.4) | 40.9 | 4.71 dd (8.6, 5.3) | 55.4 | 4.69 dd (8.0, 5.9) | 55.5 |
| 9 | - | 173.1 | - | 175.2 | - | 173.6 |
| 1' | 2.42 t (6.4) | 31.6 | - | 128.2 | - | 128.3 |
| 2' | 2.10 m | 26.5 | 7.08 d (2.1) | 115.1 | 7.08 d (2.1) | 117.8 |
| 3' | - | 172.1 | - | 146.7 | - | 146.3 |
| 4' | - | - | - | 147.5 | - | 147.5 |
| 5' | - | - | 6.70 d (8.3) | 116.3 | 6.70 d (8.3) | 115.9 |
| 6' | - | - | 6.84 dd (8.3, 2.1) | 123.5 | 6.85 dd (8.3, 2.1) | 123.5 |
| 7' | - | - | 6.44 d (12.7) | 139.5 | 6.60 d (12.7) | 139.5 |
| 8' | - | - | 5.81 d (12.7) | 120.8 | 6.41 d (12.7) | 120.5 |
| 9' | - | - | - | 169.8 | - | 169.9 |
| 9-O-CH ₃ | - | - | - | - | 3.70 s | 52.6 |
| 3-O-CH ₃ | 3.86 s | 54.9 | - | - | - | - |
| 3'-O-CH ₃ | 3.65 s | 53.9 | - | - | - | - |

Credit Author Statement

| Author name | Credit 1 | Credit 2 | Credit 3 | Credit 4 | Credit 5 |
|---------------------------------|---------------|-------------|------------------------|--------------------------|------------------------|
| Zachée Louis Evariste Akissi | Investigation | Methodology | Writing-Original Draft | Writing-Review & Editing | Project administration |
| Abdulmagid Alabdul Magid | Validation | Resources | Writing-Original Draft | Writing-Review & Editing | Supervision |
| Akoua Philomène Kouassi-Yao | Validation | Supervision | Writing-Original Draft | Writing-Review & Editing | Funding acquisition |
| Nangouban Ouattara | Investigation | | | | |
| Jean-Michel Kouamé Koffi | Investigation | | | | |
| Laurence Voutquenne-Nazabadioko | Validation | Resources | Writing-Original Draft | Writing-Review & Editing | Supervision |

Zachée Louis Evariste Akissi: Investigation, Methodology, Writing- Original draft, Writing- Review and Editing. **Abdulmagid Alabdul Magid:** Validation, Resources, Writing- Original draft, Writing- Reviewing and Editing, Supervision. **Akoua Philomène Kouassi-Yao:** Validation, Supervision, Writing- Original draft, Writing- Reviewing and Editing, Funding acquisition. **Nangouban Ouattara:** Investigation. **Jean-Michel Kouamé Koffi:** Investigation. **Laurence Voutquenne-Nazabadioko:** Validation, Resources, Writing-Original Draft, Writing- Reviewing and Editing, Supervision.

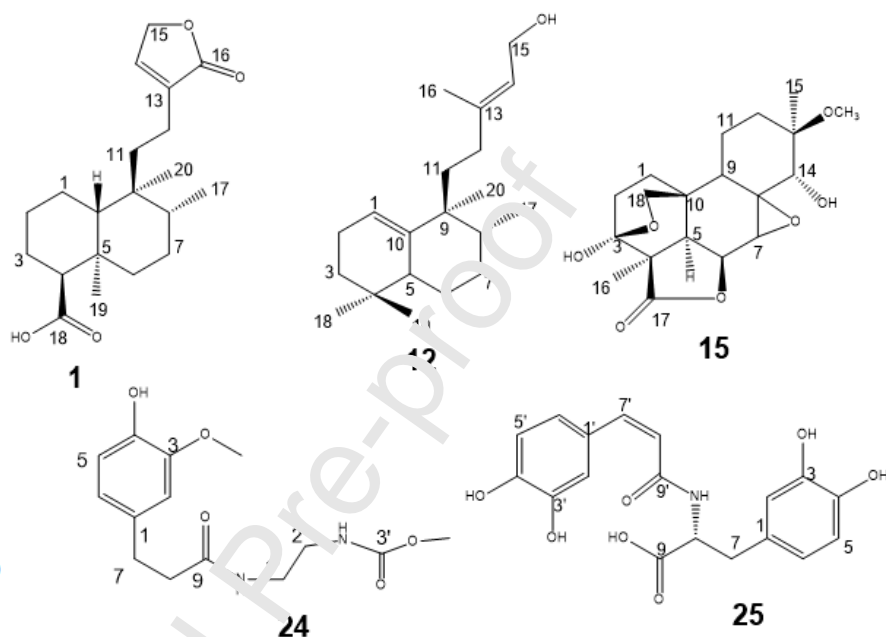
Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Graphical abstract



Icacina Oliv. (Icacinaceae)



Highlights

- Thirty-six compounds were isolated from *Icacina mannii* Oliv.
- Eleven diterpenoids including five *neo-clerodanes*, three *labdanes*, three *pimarane* are newly described
- Two phenolic amides and a rare carbamate are newly described
- This is the first report of *labdane* and *neo-clerodane* diterpenes and *lignans* in the genus *Icacina*