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## Antiplasmodial Oleanane Triterpenoids from *Terminalia albida* Root Bark

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**ABSTRACT:** Phytochemical investigation of the *n*-BuOH extract of the roots of *Terminalia albida* Sc. Elliot (Combretaceae) led to the isolation and identification of 10 oleanane triterpenoids (**1-10**), among which six new compounds, i.e. albidanoside A (**2**), albidic acid A (**4**), albidinolic acid (**5**), albidienic acid (**8**), albidolic acid (**9**), albidiolic acid (**10**); two triterpenoid aglycones, i.e. albidic acid B (**6**) and albidic acid C (**7**) isolated here for the first time from a natural source; and two known compounds. The structures of these constituents were established by means of 1D and 2D NMR spectroscopy and ESI - mass spectrometry. The isolated compounds were evaluated for their antiplasmodial and antimicrobial activity against the chloroquine-resistant strain *Plasmodium falciparum* K1, *Candida albicans*, and *Staphylococcus aureus*. Compounds **1 - 4, 6, 7,** and **8** showed moderate antiplasmodial activity with IC<sub>50</sub> values between 5 and 15 μM. None of the tested compounds was active against *C. albicans* or *S. aureus*. These findings emphasize the potential of *T. albida* as a source for discovery of new antiplasmodial compounds.

The genus *Terminalia* comprises about 250 species, mostly medium-sized or large trees. It is the second largest genus in the Combretaceae family.<sup>1</sup> The name “Terminalia” is derived from the Latin word “terminus”, since the leaves are located at the tip of the branch.<sup>2</sup> Species of this genus are widely distributed throughout the tropical and subtropical regions of Asia, Australia, and Africa, and are frequently used in traditional medicine in many countries for the treatment of both communicable and non-communicable diseases.<sup>3</sup> Several *Terminalia* species have been investigated for their phytochemical constituents, which resulted in the identification of around 368 compounds, including terpenoids, tannins, flavonoids, lignans, and simple phenols, amongst others. Some of the isolated compounds have demonstrated various bioactivities, in vitro or in vivo, such as antimalarial, antifungal, antibacterial, antitumor, anti-HIV-1, antioxidant, antidiarrheal, and analgesic.<sup>1</sup> In the Guinean flora, around 11 *Terminalia* species have been inventoried and most of them are widely used for their medicinal properties. Among these, *Terminalia albida* Sc. Elliot, a savannah shrub up to 12 m high, is distributed in all Guinean regions, where it is widely used in traditional medicine for the management of several diseases.<sup>4,5,6,7</sup> Previous pharmacological studies suggested that *T. albida* extracts were active against *Plasmodium falciparum*, *Candida albicans*, and *Staphylococcus aureus* and considerably increased the survival rate of mice infected with *Plasmodium berghei*.<sup>8,9</sup> Among the current research strategies for new biologically active natural products, dereplication is vital to effectively distinguish known from new compounds. The rapid development of modern hyphenated techniques and various novel bioinformatics approaches such as molecular networking (MN) and *in silico* tools to predict fragmentation during mass spectrometric analysis have emerged recently and provide new perspectives for early metabolite identification in natural products (NPs) research.<sup>10,11</sup>

During our continuing research towards the discovery of novel antiplasmodial and antimicrobial agents, we have previously reported on the bioassay-guided isolation of antiplasmodial constituents from the roots of *Terminalia albida*, resulting in the isolation of the triterpenoids arjunolic acid, arjungenin, arjunic acid, and arjunglucoside II, showing IC<sub>50</sub> values in the range of 5 – 15  $\mu$ M against *P. falciparum* strain K1, among other active constituents. These compounds were isolated from the CH<sub>2</sub>Cl<sub>2</sub> and EtOAc fractions of the total 80% MeOH extract.<sup>12</sup> Although the *n*-BuOH fraction was not active, the possibility cannot be excluded that this polar fraction contains inactive glycosides, which may release active aglycones after removal of the glycosidic moieties in the gastrointestinal tract, more in particular in the colon.<sup>13</sup> Therefore, in the present study the *n*-BuOH fraction of the total root extract of *T. albida* has

been subjected to extensive dereplication studies. Liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) combined with molecular networking and *in silico* MS/MS analysis was performed prior to subsequent isolation of the target compounds. Several molecular masses and their respective fragmentations patterns did not correlate with known compounds, thus revealing potentially new natural products which could be studied in more detail. Reported herein are the targeted isolation guided by mass spectrometry and the structure elucidation of oleanane-type triterpenoids, as well as their antiplasmodial and antimicrobial properties.

## RESULTS AND DISCUSSION

In order to obtain a complete overview of the phytochemical composition of the *n*-BuOH extract of the root of *T. albida*, its fractions were subjected to extensive dereplicative studies by LC-MS/MS combined with *in silico* MS/MS analysis using MS-FINDER and molecular networking. The potential candidates obtained for each constituent by consulting the natural product databases integrated in MS-FINDER were ranked according to their similarity score, which was based on comparison between experimental MS/MS fragments and *in silico* spectra of candidates. Next, the molecular structures of compounds which could not be identified by using MS-FINDER were manually searched in different databases such as the Dictionary of Natural Products, ChemSpider, and SciFinder. The dereplicative analysis led to the characterization of 45 constituents (Table S1, Supporting Information). Compounds which did not have a match in the databases during the dereplication process were considered to be unknown. The establishment of the molecular network (MN) of MS/MS data revealed correlations of these compounds with known compounds indicating their possible similarity to oleanane triterpenoids. Detailed analysis of the MN allowed to highlight a cluster consisting essentially of oleanane triterpenoids (Figure S1, Supporting Information). They were tentatively identified by comparison with *in silico* fragmentation data using MS-FINDER. Although these compounds showed correlations with known compounds within the network, it is important to stress that in this way it is not possible to fully identify them. Nowadays, it is well known that MN can provide more structural information by assigning similar chemical scaffolds to their related neighbours and eventually give potential chemical scaffolds for unknown nodes, but MN cannot provide insights into the annotation of similar structures.<sup>14</sup> Therefore, a complementary identification strategy using preparative LC-MS and 1D (<sup>1</sup>H and <sup>13</sup>C NMR, DEPT-135, DEPT-90) and 2D (COSY, HSQC, HMBC) NMR data analysis has

been applied, resulting in the isolation and complete identification of 10 target compounds.  $^1\text{H}$  and  $^{13}\text{C}$  NMR assignments are listed in Tables 1 and 2, respectively.

Compound **1** was obtained as a white powder and the molecular formula ( $\text{C}_{36}\text{H}_{56}\text{O}_{12}$ ) was determined by HR-ESIMS, yielding deprotonated ion at  $m/z$  679.3710  $[\text{M}-\text{H}]^-$ . The  $^1\text{H}$  NMR spectrum recorded in pyridine- $d_5$  showed six methyl singlets at  $\delta_{\text{H}}$  1.67, 1.46, 1.37, 1.06, 1.06, and 0.85, which were attributed to methyl groups C-27, C-25, C-26, C-24, C-29 and C-30, respectively (Table 1). Additional proton resonances observed included those attributed to an olefinic proton at  $\delta_{\text{H}}$  6.11 (1H, br s), three oxymethine protons at  $\delta_{\text{H}}$  4.38 (1H, m), 4.23 (1H, m), and 3.59 (1H, d,  $J = 5.2$  Hz), two oxymethylene protons at  $\delta_{\text{H}}$  4.22 (1H, m) and 3.69 (1H, d  $J = 10.9$  Hz) (H-23a and H-23b, respectively), which showed HMBC correlations with C-3 ( $\delta_{\text{C}}$  77.5) and C-24 ( $\delta_{\text{C}}$  14.6). In addition, two oxymethylene protons at  $\delta_{\text{H}}$  4.40 (1H, m) and 4.44 (1H, m) were attributed to C-6' of the sugar moiety. An anomeric proton signal at  $\delta_{\text{H}}$  6.35 (1H, d,  $J = 8.0$  Hz) correlated in the HSQC spectrum with an anomeric carbon at  $\delta_{\text{C}}$  95.8. The  $^{13}\text{C}$  NMR spectrum displayed 36 carbon signals, among which six were attributed to a glucopyranosyl moiety and the remaining 30 to the triterpenoid skeleton. The structure of compound **1** was established as  $2\alpha,3\beta,19\alpha,23$ -tetrahydroxy-11-oxo-olean-12-en-28-oic acid 28- $O$ - $\beta$ -D-glucopyranosyl ester, previously isolated from *Pteleopsis suberosa*.<sup>16</sup>

The HR-ESIMS spectrum of compound **2** (molecular formula  $\text{C}_{36}\text{H}_{56}\text{O}_{12}$ ) showed a formic acid adduct at  $m/z$  725.3723 corresponding to the formic acid adduct  $[\text{M}-\text{H}+\text{HCOOH}]^-$  and a fragment at  $m/z$  517.3159 resulting from the loss of a hexosyl unit  $[\text{M}-\text{H}-\text{HCOOH}-162]^-$ , suggesting that compound **2** was an isomer of **1**. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra (Table 1 and 2) in pyridine- $d_5$  were similar to those of compound **1**. The  $^1\text{H}$  NMR spectrum of **2** showed six methyl singlets at  $\delta_{\text{H}}$  1.00, 1.04, 1.17, 1.37, 1.39, and 1.45. An olefinic proton at  $\delta_{\text{H}}$  6.36 (1H, br s), three oxymethine protons at  $\delta_{\text{H}}$  4.34 (1H, m), 4.18 (1H, m), and 3.76 (1H, m), two oxymethylene protons at  $\delta_{\text{H}}$  3.69 (1H, m) and 4.25 (1H, m) linked to C-23, which showed HMBC correlations with C-3 ( $\delta_{\text{C}}$  77.8) and C-24 ( $\delta_{\text{C}}$  14.5). In addition, two oxymethylene protons at  $\delta_{\text{H}}$  4.42 (1H, m) and  $\delta_{\text{H}}$  4.46 (1H, m) were attributed to C-6' of the glucosyl moiety. An anomeric proton signal at  $\delta_{\text{H}}$  6.32 (1H d,  $J = 8.3$  Hz), indicating a  $\beta$ -configuration, correlated in the HSQC spectrum with an anomeric carbon at  $\delta_{\text{C}}$  96.1. The  $^{13}\text{C}$  NMR spectrum displayed 36 carbon signals, among which six were attributed to a glucopyranosyl moiety and the remaining 30 to the triterpenoid skeleton. Signals observed at  $\delta_{\text{C}}$  199.8 (C-11), 131.8 (C-12), and 162.3 (C-13) were indicative of the presence of an  $\alpha,\beta$ -unsaturated carbonyl functionality in the C-ring, which was supported by the HMBC correlations observed between H-12 and C-

9, C-13, C-14 and C-18, and also between H-9 and C-11.<sup>15,16</sup> The C-19 assignment was also confirmed by its HMBC correlations with H-29, H-30 and its COSY correlation with H-18 (Figure 1). The linkage of the sugar moiety to C-28 was confirmed by the HMBC correlation between the anomeric proton H-1' ( $\delta_{\text{H}}$  6.32,  $J = 8.3$  Hz), indicating a  $\beta$ -configuration, and the signal at  $\delta_{\text{C}}$  175.6 (C-28). Comparison of the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of this compound with those of **1** revealed some differences in the C- and E-rings of their aglycone moieties. Indeed, the doublet at  $\delta_{\text{H}}$  3.23 (H-18,  $J = 10.8$  Hz) in **2** was shifted compared to  $\delta_{\text{H}}$  3.57 ( $J = 5.2$  Hz) in **1**, while the resonance of H-19 was observed at  $\delta$  3.76, compared to  $\delta_{\text{H}}$  3.59 ( $J = 5.2$  Hz) for **1**. Furthermore, the difference between compounds **2** and **1** could be explained in terms of configurational dissimilarity at C-19. Indeed, the chemical shift of C-19 ( $\delta$  74.7) in compound **2** displayed a difference of -5.3 ppm to that of compound **1** ( $\delta_{\text{C}}$  80.0). Moreover, the chemical shift values of C-12, C-13, and the methyl groups C-29 and C-30 were different both in the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound **2** in comparison with those of **1**. The coupling constant of H-18 (d,  $J = 10.8$  Hz) and H-19 confirmed the  $\beta$ -orientation of the hydroxyl group at C-19 of compound **2**. Therefore, **2** (albidanoside A) could be identified as a new epimer of **1**, i.e.  $2\alpha,3\beta,19\beta,23$ -tetrahydroxy-11-oxo-olean-12-en-28-oic acid 28-*O*- $\beta$ -D-glucopyranosyl ester.

The molecular formula of compound **3** was deduced as  $\text{C}_{36}\text{H}_{56}\text{O}_{12}$  based on the HR-ESIMS ion ( $m/z$  679.3724  $[\text{M}-\text{H}]^-$ ). The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **3** were highly similar to those of **2**, except for the assignments of the methyl- and hydroxymethyl substituents at C-4. Indeed, the chemical shift of the methyl group ( $\delta_{\text{C}}$  14.5 for C-24 in compound **2**,  $\beta$ -orientation) was shifted to  $\delta_{\text{C}}$  23.8, assigned to the C-23 methyl in compound **3** ( $\alpha$ -orientation). Moreover, the chemical shift values of carbons C-3 ( $\delta_{\text{C}}$  85.1) and C-5 ( $\delta_{\text{C}}$  55.9) of the A-ring in compound **3** were deshielded compared to  $\delta$  77.8 and 47.6, respectively, in compound **2**. The structure of **3** was established as  $2\alpha,3\beta,19\beta, 24$ -tetrahydroxy-11-oxo-olean-12-en-28-oic acid 28-*O*- $\beta$ -D-glucopyranosyl ester (ivorenoside C), previously isolated from *Terminalia ivorensis*.<sup>16</sup>

Compound **4** displayed a molecular ion at  $m/z$  517.3154  $[\text{M}-\text{H}]^-$  in its HR-ESIMS data, revealing a difference of 162 mass units in comparison with the above mentioned compounds, which displayed a deprotonated ion at  $m/z$  679.3724  $[\text{M}-\text{H}]^-$  indicating that compound **4** is an aglycone. The  $^1\text{H}$  NMR data (Table 1) showed six methyl singlets ( $\delta_{\text{H}}$  1.04, 1.12, 1.21, 1.24, and 1.43 x 2), one olefinic proton at  $\delta_{\text{H}}$  6.39 (1H, br s), three hydroxymethine protons at  $\delta_{\text{H}}$  4.35 (1H, m), 4.18 (1H, m), and 3.81 (1H, d,  $J = 10.6$  Hz) and two oxymethylene protons at  $\delta_{\text{H}}$  3.68 (1H, d,  $J = 10.6$  Hz) and 4.21 (1H, d,  $J = 10.6$  Hz) linked to C-23, which showed HMBC

correlations with C-3 ( $\delta$  77.8) and C-24 ( $\delta$  14.5). The  $^{13}\text{C}$  NMR data (Table 2) displayed 30 carbon signals which were assigned to a triterpenoid moiety. Signals observed at  $\delta_{\text{C}}$  199.9 (C-11),  $\delta_{\text{C}}$  131.5 (C-12), and  $\delta_{\text{C}}$  163.0 (C-13) were indicative of the presence of an  $\alpha,\beta$ -unsaturated carbonyl functionality in the C-ring, which was supported by HMBC correlations observed between H-12 and C-14/C-18, between H-27 and C-14, and also between H-9 and C-11. The C-19 assignment has been confirmed by its HMBC correlations with H-29 and H-30 and its COSY correlation with H-18. Comparison of the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound **4** with those of the above mentioned compounds indicated that albidic acid A (**4**) is the aglycone of compound **2** and identified as *2\alpha,3\beta,19\beta,23*-tetrahydroxy-11-oxo-olean-12-en-28-oic acid.

Compound **5** displayed a deprotonated ion at  $m/z$  519.3328  $[\text{M-H}]^-$  in HR-ESIMS. The  $^1\text{H}$  NMR data (Table 1) showed six methyl singlets ( $\delta_{\text{H}}$  0.69, 0.79, 0.97, 1.02, 1.12 and 1.27), one olefinic proton at  $\delta_{\text{H}}$  5.33 (1H, br s), four hydroxymethine protons at  $\delta_{\text{H}}$  3.68 (1H, m), 3.55 (1H, m), 3.41 (1H, m) and 3.34 (1H, m), two oxymethylene protons at  $\delta_{\text{H}}$  3.49 (1H, d,  $J = 10.8$  Hz) and 3.26 (1H, m) linked to C-23. These oxymethylene protons showed HMBC correlations with C-3 ( $\delta_{\text{C}}$  77.5), C-24 ( $\delta_{\text{C}}$  14.6), C4 ( $\delta_{\text{C}}$  44.0), C5 ( $\delta_{\text{C}}$  48.2) (Figure 2). The  $^{13}\text{C}$  NMR spectrum of compound **5** displayed 30 carbon resonances, which were assigned to a triterpenoid skeleton (Table 2). Examination of the spectrum revealed that compound **5** lacks the  $\alpha,\beta$ -unsaturated carbonyl functionality in the C-ring present in compounds **1** - **4**. The presence of hydroxyl groups at C-19 and C-21 of the E-ring was supported by HMBC correlations of H-19 and H-21 with C-20 ( $\delta_{\text{C}}$  39.2), C-29 ( $\delta_{\text{C}}$  19.5), and C-30 ( $\delta_{\text{C}}$  28.4). This was also supported by the COSY correlation observed between H-18 ( $\delta_{\text{H}}$  1.99) and H-19 ( $\delta_{\text{H}}$  3.55). Therefore the structure of albidinolic acid (**5**) was defined as *2\alpha,3\beta,19\alpha,21\beta,23*-pentahydroxyolean-12-en-28-oic acid.

Compound **6** revealed the same monoisotopic mass as compound **4** and the same fragmentation pattern in the HRESI-MS spectrum:  $m/z$  517.3163  $[\text{M-H}]^-$  consistent with a molecular formula of  $\text{C}_{30}\text{H}_{46}\text{O}_7$ , suggesting that compound **6** was an isomer of compound **4**. However, the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra showed some differences in the A-ring, especially due to the orientation of the C-23 methyl group. Indeed, the chemical shift of C-23 ( $\delta_{\text{C}}$  24.1) ( $\alpha$ -orientation) in compound **6** is 9.6 ppm different from the methyl group at  $\delta$  14.5 ( $\beta$ -orientation), assigned to C-24 in compound **4**. Moreover, the chemical shifts of C-3 ( $\delta$  85.4) and C-5 ( $\delta$  56.1) were deshielded compared to compound **4** ( $\delta$  77.8 and  $\delta$  47.7, respectively). The aforementioned spectroscopic analysis suggested that the structure of compound **6** was identical to the aglycone of compound **3**. Therefore, albidic acid (**6**) was identified as

*2α,3β,19β,23* tetrahydroxy-11-oxo-olean-12-en-28-oic acid, isolated for the first time as an aglycone.

The HR-ESIMS spectrum of compound **7** showed a deprotonated ion at  $m/z$  517.3154 [M-H]<sup>-</sup> (molecular formula C<sub>30</sub>H<sub>46</sub>O<sub>7</sub>) suggesting that compound **7** was an isomer of compounds **4** and **6**. Furthermore, its <sup>1</sup>H and <sup>13</sup>C NMR data (Table 1, and 2) were similar to those of compound **6** except for the configuration of C-19. Indeed, the chemical shift of C-19 ( $\delta_C$  80.5) in compound **7** shows a difference of 5.5 ppm to that of compound **6** ( $\delta_C$  75.0). Furthermore, the chemical shifts of C-12 and C-13 and the methyl groups C-29 and C-30 attached to the E-ring were shifted both in the <sup>1</sup>H and <sup>13</sup>C NMR spectra in comparison with compound **7**. Comparison of the coupling constants of H-19 of compounds **7** ( $\delta$  3.66 d,  $J$  = 5.1 Hz) and **6** ( $\delta$  3.83 d,  $J$  = 10.2 Hz) confirmed the  $\alpha$ -orientation of the hydroxy group linked to C-19 in compound **7**. The identity of albidic acid C (**7**) was confirmed as *2α,3β,19α,24*-tetrahydroxy-11-oxo-olean-12-en-28-oic acid, isolated for the first time as an aglycone.

The HR-ESIMS spectrum of compound **8** exhibited a deprotonated ion at  $m/z$  499.3065 [M-H]<sup>-</sup> (molecular formula C<sub>30</sub>H<sub>46</sub>O<sub>6</sub>) and a fragment at  $m/z$  455.3160 due to the loss of a hydroxycarboxyl moiety. Compared to the other aglycones, compound **8** bears an additional olefinic proton but lacks one hydroxyl group. The <sup>1</sup>H NMR data (Table 1) in pyridine-*d*<sub>5</sub> displayed six methyl groups ( $\delta_H$  0.96, 1.01, 1.21, 1.24, 1.46, and 1.60), two olefinic protons ( $\delta_H$  5.74 and 6.21), two hydroxymethine protons at  $\delta_H$  3.62 (1H, m), 4.46 (1H, m) and two oxymethylene protons at  $\delta_H$  3.77 (1H, m) and 4.49 (1H, m). The <sup>13</sup>C NMR data (Table 2) showed 30 carbon signals, including six methyl signals, and two olefinic carbons at  $\delta_C$  123.0 (C-12) and  $\delta_C$  138.9 (C-19). Signals observed at  $\delta$  199.7 (C-11), 123.0 (C-12) and 163.8 (C-13) revealed the presence of an  $\alpha,\beta$ -unsaturated carbonyl functionality. The presence of an olefinic proton at C-19 was supported by the HMBC correlations observed between H-19 ( $\delta_H$  5.74), C-29 ( $\delta$  27.9) and C-30 ( $\delta$  30.0) (Figure 1). Accordingly, albidienic acid (**8**) was identified as *2α,3β,23*-trihydroxyolean-12-19-dien-28-oic acid.

Compound **9** displayed a deprotonated ion at  $m/z$  503.3373 [M-H]<sup>-</sup>, corresponding to a molecular formula of C<sub>30</sub>H<sub>47</sub>O<sub>6</sub> in HR-ESIMS. The molecular ion of compound **9** revealed a difference of 16 mass units in comparison with compound **5** ( $m/z$  519.3330 [M-H]<sup>-</sup>). The <sup>1</sup>H NMR data (Table 1) showed six methyl singlets ( $\delta_H$  0.68, 0.82, 0.92, 0.92, 1.02, 1.18 and 1.43), one olefinic proton at  $\delta_H$  5.25 (1H, br s), three hydroxymethine protons at  $\delta_H$  3.68 (1H, m), 3.34



(1H, m) and 3.18 (1H, s), and two oxymethylene protons at  $\delta_{\text{H}}$  3.48 (1H, d,  $J = 11.0$  Hz) and 3.25 (1H, d,  $J = 11.0$  Hz) linked to C-23. The  $^{13}\text{C}$  NMR data (Table 2) displayed 30 carbon signals which were assigned to a triterpenoid skeleton. Comparison of the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of this compound with previously reported data suggested that compound **9** is a new oleanane triterpenoid. The presence of a hydroxyl group at C-21 was supported by the HMBC correlations of H-21 with C-29 ( $\delta_{\text{C}}$  28.4) and C-30 ( $\delta_{\text{C}}$  19.5). This was also supported by the COSY correlation observed between the protons linked to carbons C-18 ( $\delta$  42.09) and C-19 ( $\delta$  41.5). Therefore, the new albidolic acid (**9**) was identified as  $2\alpha,3\beta, 21\alpha,23$ -tetrahydroxyolean-12-en-28-oic acid.

The HR-ESIMS spectrum of compound **10** exhibited a deprotonated ion at  $m/z$  503.3370  $[\text{M}-\text{H}]^-$  (molecular formula  $\text{C}_{30}\text{H}_{47}\text{O}_6$ ). Compared to compound **9**, compound **10** has two additional oxymethylene protons at  $\delta_{\text{H}}$  3.56 (2H, s) but lacks one hydroxyl group. The  $^{13}\text{C}$  NMR data (Table 2) of compound **10** displayed 30 carbons. The presence of an oxymethylene group at C-30 was supported by HMBC correlations of H-30 with C-20 ( $\delta_{\text{C}}$  36.6) and C-29 ( $\delta_{\text{C}}$  19.8). This was also supported by the COSY correlation between H-18 and H-19 (Figure 2). The position of the hydroxymethylene groups was confirmed by HMBC correlations observed between H-3 ( $\delta_{\text{H}}$  4.19, m) and C-2 ( $\delta_{\text{C}}$  68.9), H-23 ( $\delta_{\text{H}}$  3.70, 4.18) and C-3 ( $\delta_{\text{C}}$  78.2) and C-24 ( $\delta_{\text{C}}$  14.4), and H-29 ( $\delta_{\text{H}}$  1.19) and C-30 ( $\delta_{\text{C}}$  73.9). Comparison of the  $^1\text{H}$  and  $^{13}\text{C}$  NMR reported data suggested that albidolic acid (**10**) was a new triterpenoid, and was identified as  $2\alpha,3\beta,23,30$ -tetrahydroxy-11-oxo-olean-12-en-28-oic acid. Two isomers  $2\alpha, 3\alpha, 23, 30$ -tetrahydroxy-11-oxo-olean-12-en-28-oic acid and  $2\beta, 3\beta, 23, 30$ -tetrahydroxy-11-oxo-olean-12-en-28-oic acid of this compound were previously identified in other plant species.<sup>17,18</sup>

The compounds isolated in this study have been tested against *P. falciparum*, *C. albicans*, and *S. aureus*, and their cytotoxicity was determined against MRC-5 cells (human foetal lung fibroblast cells) (Table 3). It emerges from these results that compounds **1 - 4**, **6,7**, and **8** possess moderate antiplasmodial activity with  $\text{IC}_{50}$  values between 5 and 15  $\mu\text{M}$ , while compound **10** was weakly active ( $\text{IC}_{50}$  48.9  $\mu\text{M}$ ). Notably, albidanoside B (**2**) is the C-28 glucosyl ester of albidic acid A (**4**), and ivorenoside C (**3**) is the C-28 glucosyl ester of albidic acid B (**6**). None of the active compounds were cytotoxic. Furthermore, all the tested compounds were inactive against *S. aureus* and *C. albicans*.

In conclusion, molecular networking and *in silico* MS/MS dereplication aided in the targeted semipreparative HPLC-MS-DAD purification of oleanane triterpenoids from the *n*-BuOH fraction of *T. albida*. This resulted in the isolation of six new oleanane triterpenoids named albidanoside A, albidic acid A, albidinol acid, albidienic acid, albidol acid, and albidiolic acid, together with two triterpenoid aglycones (albidic acid B, albidic acid C) reported here for the first time as aglycones, and two known compounds. The isolated compounds were evaluated for their activity against *P. falciparum*, *C. albicans*, and *S. aureus*. Compounds **1-4**, **6,7**, and **8** demonstrated moderate antiplasmodial activity with IC<sub>50</sub> values between 5 and 15 μM. None of the tested compounds was active against *C. albicans* or *S. aureus*. These findings emphasize the potential of *T. albida* as a source for discovery of new antiplasmodial compounds.

## EXPERIMENTAL SECTION

**General Experimental Procedures.** Purification of extracts and fractions was carried out using an MCI column and a Grace Reveleris X2 flash chromatographic system (Lokeren, Belgium) equipped with an evaporative light scattering detector (ELSD), a diode array detector (DAD), and a fraction collector. The ELSD carrier solvent was isopropyl alcohol and the column used was a pre-packed Flash Pure BUCHI C<sub>18</sub> with a particle size of 40 μm. A semi-preparative HPLC system equipped with DAD and ESI-MS detectors was used for the isolation of compounds. The system was composed of a sample manager, injector, and collector (2767), a quaternary gradient module (2545), a System Fluidics Organizer, a HPLC pump (515), a diode array detector (2998), and a Micromass Quattro TQD mass spectrometer, all supplied by Waters (Milford, MA, USA). For data processing MassLynx version 4.1 was used. Optical rotations were measured on a JASCO P-2000 spectropolarimeter (Easton, MD, USA). 1D and 2D NMR spectra were recorded on a Bruker DRX-400 NMR spectrometer (Rheinstetten, Germany) equipped with either a 3 mm inverse broadband (BBI) probe or a 5 mm dual <sup>1</sup>H/<sup>13</sup>C probe using standard Bruker pulse sequences and operating at 400 MHz for <sup>1</sup>H and at 100 MHz for <sup>13</sup>C NMR spectra. The spectra were processed with Topspin version 4.0.6). Chemical shifts are expressed in δ (ppm) and referenced to the residual solvent signals.

MeCN and MeOH (all HPLC grade) were purchased from Fisher Scientific (Leicestershire, UK). All reagents, such as TFA and formic acid (eluent additive for HPLC) were purchased from Acros Organics (Geel, Belgium) or Sigma-Aldrich (St. Louis, MO, USA). MeCN and formic acid (both for UPLC-MS) were obtained from Biosolve Chimie (Dieuze, France).

Ultrapure water was obtained using a Milli-Q system from Millipore (Bedford, MA, USA). NMR solvents (methanol-*d*<sub>4</sub>, pyridine-*d*<sub>5</sub>) were obtained from Sigma-Aldrich.

**Plant Material.** Roots of *T. albida* were harvested in Dubréka, Republic of Guinea in June 2016. The plant was identified by the botanists from the Research and Valorization Center on Medicinal Plants, Dubréka, where a voucher specimen (D36HK13) is kept. The collected root samples were dried at room temperature and milled. A “Material Transfer Agreement” has been established between the University of Antwerp and the Department of Pharmacy, University Gamal Abdel Nasser of Conakry / Research and Valorization Center on Medicinal Plants.

**LC-ESI-MS Analysis.** Fractions were dissolved in UPLC/MS grade MeOH at a concentration of 1 mg/mL, which was diluted with water in order to obtain a final concentration of 0.1 mg/mL. Analyses were performed on a Xevo-G2-XS-QToF mass spectrometer (Waters) coupled to an Acquity LC system equipped with MassLynx version 4.1 software. A Waters Acquity UHPLC BEH Shield RP18 column (3.0 mm x 150 mm, 1.7 μm) was used with a mobile phase consisting of water + 0.1% formic acid (A) and MeCN + 0.1% formic acid (B), which were pumped at a rate of 0.4 mL/min. The gradient system was set as follows: 2% B (0-1 min), 2-100% B (1-5 min), 100% B (5-7 min), 100-2% B (7-8 min), 2% B (8-10 min). For all analyses, full scan data were recorded in ESI (–) and ESI (+) mode from *m/z* 50 to 1500 in sensitivity mode (approximate resolution: 22000 FWHM) using a spray voltage at either –1.0 kV and +1.5 kV, respectively. Cone gas flow and desolvation gas flow were set at 50.0 L/h and 1000.0 L/h, respectively; and source temperature and desolvation temperature at 120 °C and 550 °C, respectively. Leucine enkephalin was used as lock mass during the analysis.

### **Molecular Networking and In-silico MS/MS Dereplication of the *n*-BuOH Fraction.**

***In-Silico Ms/Ms Dereplication.*** The UHPLC–HR-MS raw data were firstly converted to Abf files (Reifycs Abf Converter) and processed with MS-DIAL version 4.16<sup>19</sup> for mass signal extraction between 50 and 1500 Da from 0 to 25 min. Respective MS1 and MS2 tolerance were set to 0.01 and 0.05 Da in centroid mode. The optimised detection threshold was set to  $3 \times 10^4$  for MS1. The peaks were finally aligned on a quality control (QC) reference file with a retention time tolerance of 0.1 min and a mass tolerance of 0.025 Da. MS-FINDER software ([http://prime.psc.riken.jp/Metabolomics\\_Software/](http://prime.psc.riken.jp/Metabolomics_Software/))<sup>20</sup> was used for *in silico* fragmentation predictions. Compounds were tentatively identified according to their similarity score, which was based on comparison between experimental MS/MS fragments and *in silico* spectra. To

find the potential candidates, only compounds consisting essentially of C, H, and O have been considered. The MS1 and MS2 tolerances were set at 0.01 and 0.25 Da, respectively. An isotopic ratio tolerance of 20% has been considered. The natural product databases integrated in MSFINDER ( PlantCyc, UNPD, KNApSAcK and NANPDB) have been used for compound identification. The molecular formulas determined by using MS-FINDER software have been queried in different natural product databases such as Dictionary of Natural Products, ChemSpider and SciFinder in order to obtain the molecular structures of the compounds.

**GNPS Molecular Networking.** After MS-DIAL processing, two files (the feature quantification table “TXT file” and the MS/MS spectral summary “MGF file” have been exported and uploaded to the GNPS website (<http://gnps.ucsd.edu>). The molecular network was created using the GNPS web platform.<sup>21</sup> All MS/MS signals within 17 Da of the precursor *m/z* were removed, and only the top six fragment peaks were compared for analysis. The data were clustered with MS-Cluster with a precursor ion mass tolerance of 0.05 Da and an MS/MS fragment ion tolerance of 0.5 Da. Next, consensus spectra that contained less than 2 spectra were discarded. A network was then created where edges were filtered to have a cosine score above 0.65 and more than one matched peak. Edges between two nodes were kept in the network if, and only if, each of the nodes appeared in each other’s respective top 10 most similar nodes. The spectra in the network were then searched against the spectral libraries of GNPS. The library spectra were filtered in the same manner as the input data. The data were imported into Cytoscape v3.7.2 (The Cytoscape Consortium, New York, NY, USA) for visualisation. All matches kept between network spectra and library spectra were required to have a score above 0.6 and at least 1 matched peak. Analogue search was enabled against the library with a maximum mass shift of 100.0 Da.

**Extraction and Isolation.** The dried and milled root bark of *T. albida* (470.9 g) defatted with *n*-hexane (4 x 2.5 L) was extracted 4 times with 80% MeOH (4 x 2L; each for 24 h). The filtrate was concentrated under reduced pressure and freeze-dried to obtain a crude 80% MeOH extract (110 g), which was redissolved in water (1 L) and successively partitioned with EtOAc (2 x 8 L) and *n*-BuOH (2 x 8 L) to give an EtOAc soluble fraction (15.1 g), an *n*-BuOH soluble fraction (24.2 g), and a residual H<sub>2</sub>O phase. The *n*-BuOH fraction (15 g) (Figure 3) was subjected to MCI column chromatography and eluted with 5, 10, 20, 30, 40, 50, 60, 70, 80, and 100% MeOH-H<sub>2</sub>O to give 10 pooled fractions, A to J.

The LC-MS profile of all the fractions was recorded and the fractions F and H containing the products of interest were selected and further purified. Indeed, the purification of fraction F (0.3 g) by semi-preparative HPLC-MS operated with a C<sub>18</sub> Kinetex column and eluted with H<sub>2</sub>O + 0.1% formic acid (A) and MeCN (B) resulted in the isolation of compounds **1** (9.4 mg), **2** (4.2 mg), and **3** (3.5 mg). Mass-based fraction collection was used to enable highly specific peak triggering with the fragment masses of *m/z* 499 (compounds **1**, **2**, and **3**) set as the target masses with a threshold of 6.58e5. The flow rate was set at 3 mL/min and the gradient was programmed as follows: (0-5 min) 30% B, (5-35min) 50% B, (35-40 min) 50% B, (40-50 min) 95% B. The sample concentration was 25 mg/mL and the injection volume was 400  $\mu$ L. The DAD spectrum was recorded from 200 to 450 nm, and mass spectra in the ESI modes, MS scan range: *m/z* 100 to 1000; capillary voltage 3.00 kV, cone voltage 50 V, extractor voltage 3 V, source temperature 135 °C, desolvation temperature 400 °C, desolvation gas flow 750 L/h, and cone gas flow 50 L/h. The fraction H (1.9 g) was subjected to a reverse phase flash chromatography using a C-18 pre-packed column (Flash Pure BUCHI-40  $\mu$ m) eluted with a gradient of H<sub>2</sub>O + 0.1% formic acid (A) and MeCN (B) at the flow rate of 40mL/min. This separation yielded five sub-fractions H<sub>1</sub> (0.28 g), H<sub>2</sub> (0.34 g), H<sub>3</sub> (0.37 g), H<sub>4</sub> (0.25 g), and H<sub>5</sub> (0.19 g). The gradient was set as follow (0-5 min) 5%B, (6-46 min) 50%B, (46-59 min) 50%B, (59-80 min) 100%B, (80-90 min) 100%B. Subfractions selected for further purification based on their LC-MS profile were subjected to a semi-preparative HPLC-MS system operated with a C<sub>18</sub> Kinetex column and eluted with a gradient of H<sub>2</sub>O + 0.1% formic acid (A) and MeCN (B). The purification of H<sub>1</sub> was performed with the following gradient (0-5 min) 30% B, (5-35min) 50% B, (35-40 min) 50% B, and (40-50 min) 95% B and resulted in the isolation of compounds **4** (3.5mg) and **5** (3.3 mg).

The purification of fraction H<sub>2</sub> by using the following gradient: (0-5 min) 30% B, (5-35 min) 35% B, (35-40 min) 35% B, and (40-50 min) 95% B afforded compounds **6** (4.6 mg), **7** (5.2 mg), and **8** (2.7mg). Fraction H<sub>3</sub> fractionated by using the following gradient (0-5 min) 20% B, (5-35min) 30% B, and (35-45 min) 95 % B, resulted in the isolation of compounds **9** (2.3 mg) and **10** (4.5 mg). The flow rate was set at 3.0 mL/min and samples were dissolved at the concentration of 20 mg/mL. For all fractions, 400  $\mu$ L was injected. The automatic collection was triggered by *m/z* 455 (compound **4**, **6**, and **7**); *m/z* 519 (compound **5**); *m/z* 499 (compound **8**), and *m/z* 503 (compound **9** and **10**) reaching a threshold of 4.94e5. The MS method described above was used during the whole purification process.

*2 $\alpha$ ,3 $\beta$ ,19 $\alpha$ ,23-tetrahydroxy-11-oxo-olean-12-en-28-oic acid 28-O- $\beta$ -D-glucopyranosyl ester (1)*: amorphous white solid;  $[\alpha]_D^{20} = + 4.2$  (c 0.01, MeOH);  $^1\text{H}$  NMR (pyridine-*d*<sub>5</sub>, 400 MHz) and  $^{13}\text{C}$  NMR (pyridine-*d*<sub>5</sub>, 100MHz), see Tables 1 and 2; HR-ESIMS  $m/z$  679.3710  $[\text{M-H}]^-$  (calculated for C<sub>36</sub>H<sub>55</sub>O<sub>12</sub>, 679.3694), major peak formic acid adduct ion at  $m/z$  725.3723  $[\text{M-H+HCOOH}]^-$  (calculated for C<sub>37</sub>H<sub>57</sub>O<sub>14</sub>, 725.3748).

*Albidanoside A (2)*: Amorphous white solid;  $[\alpha]_D^{20} = + 9.1$  (c 0.3, MeOH);  $^1\text{H}$  NMR (pyridine-*d*<sub>5</sub>, 400 MHz) and  $^{13}\text{C}$  NMR (pyridine-*d*<sub>5</sub>, 100MHz), see Tables 1 and 2, respectively; HR-ESIMS  $m/z$  679.3690  $[\text{M-H}]^-$  (calculated for C<sub>36</sub>H<sub>55</sub>O<sub>12</sub>, 679.3694), major peak formic acid adduct ion at  $m/z$  725.3739  $[\text{M-H+HCOOH}]^-$  (calculated for C<sub>37</sub>H<sub>57</sub>O<sub>14</sub>, 725.3748).

*Ivorenoside C (3)*: amorphous white powder;  $[\alpha]_D^{20} = + 23$  (c 0.2, MeOH);  $^1\text{H}$  NMR (pyridine-*d*<sub>5</sub>, 400 MHz) and  $^{13}\text{C}$  NMR (pyridine-*d*<sub>5</sub>, 100MHz), see Tables 1 and 2; HR-ESIMS  $m/z$  679.3690  $[\text{M-H}]^-$  (calculated for C<sub>36</sub>H<sub>55</sub>O<sub>12</sub>, 679.3694), major peak formic acid adduct ion at  $m/z$  725.3741  $[\text{M-H+HCOOH}]^-$  (calculated for C<sub>37</sub>H<sub>57</sub>O<sub>14</sub>, 725.3748).

*Albidic acid A (4)*: amorphous white powder;  $[\alpha]_D^{20} = + 39.5$  (c 0.3, MeOH);  $^1\text{H}$  NMR (pyridine-*d*<sub>5</sub>, 400 MHz) and  $^{13}\text{C}$  NMR (pyridine-*d*<sub>5</sub>, 100MHz), see Tables 1 and 2, respectively; HR-ESI-MS:  $m/z$  517.3156  $[\text{M-H}]^-$  (calculated for C<sub>30</sub>H<sub>45</sub>O<sub>7</sub>, 517.3165), fragments at  $m/z$  499.3062  $[\text{M-H-18}]^-$ , 455.3158  $[\text{M-H-18-44}]^-$ .

*Albidinolic acid (5)*: colourless powder;  $[\alpha]_D^{20} = + 6.9$  (c 0.2, MeOH);  $^1\text{H}$  NMR (methanol-*d*<sub>4</sub>, 400 MHz) and  $^{13}\text{C}$  NMR (methanol-*d*<sub>4</sub>, 100 MHz), see Tables 1 and 2; HR-ESIMS  $m/z$  519.3328  $[\text{M-H}]^-$  (calculated for C<sub>30</sub>H<sub>47</sub>O<sub>7</sub>, 519.3322), formic acid adduct ion at  $m/z$  565.3376  $[\text{M-H+HCOOH}]^-$  calculated for C<sub>31</sub>H<sub>49</sub>O<sub>9</sub>, 565.3377).

*Albidic acid B (6)*: amorphous white powder;  $[\alpha]_D^{20} = + 14.7$  (c 0.4, MeOH);  $^1\text{H}$  NMR (pyridine-*d*<sub>5</sub>, 400 MHz) and  $^{13}\text{C}$  NMR (pyridine-*d*<sub>5</sub>, 100MHz), see Tables 1 and 2; HR-ESIMS  $m/z$  517.3170  $[\text{M-H}]^-$  (calculated for C<sub>30</sub>H<sub>45</sub>O<sub>7</sub>, 517.3165), fragments at  $m/z$  499.3062  $[\text{M-H-18}]^-$ ,  $m/z$  455.3162  $[\text{M-H-18-44}]^-$ .

*Albidic acid C (7)*: amorphous white powder; ;  $[\alpha]_D^{20} = + 6.8$  (c 0.4, MeOH);  $^1\text{H}$  NMR (pyridine-*d*<sub>5</sub>, 400 MHz) and  $^{13}\text{C}$  NMR (pyridine-*d*<sub>5</sub>, 100MHz), see Tables 1 and 2; HR-ESIMS  $m/z$  517.3187  $[\text{M-H}]^-$  (calculated for C<sub>30</sub>H<sub>45</sub>O<sub>7</sub>, 517.3165), fragments at  $m/z$  499.3072  $[\text{M-H-18}]^-$ ,  $m/z$  455.3169  $[\text{M-H-18-44}]^-$ .

*Albidienic acid (8)*: amorphous white solid;  $[\alpha]_D^{20} = +109.7$  (c 0.2, MeOH);  $^1\text{H}$  NMR (pyridine-*d*<sub>5</sub>, 400 MHz) and  $^{13}\text{C}$  NMR (pyridine-*d*<sub>5</sub>, 100MHz), see Tables 1 and 2; HR-ESIMS  $m/z$  499.3067  $[\text{M-H}]^-$  (calculated for C<sub>30</sub>H<sub>43</sub>O<sub>6</sub>, 499.3060), fragments at  $m/z$  455.3162  $[\text{M-H-44}]^-$ .

*Albidolic acid (9)*: amorphous white powder;  $[\alpha]_D^{20} = +17.1$  (c 0.3, MeOH);  $^1\text{H}$  NMR (methanol- $d_4$ , 400 MHz) and  $^{13}\text{C}$  NMR (methanol- $d_4$ , 100 MHz), see Tables 1 and 2; HR-ESIMS  $m/z$  503.3373  $[\text{M}-\text{H}]^-$  (calculated for  $\text{C}_{30}\text{H}_{47}\text{O}_6$ , 503.3373), formic acid adduct ion at  $m/z$  549.3420  $[\text{M}-\text{H}+\text{HCOOH}]^-$  calculated for  $\text{C}_{31}\text{H}_{49}\text{O}_8$ , 549.3427).

*Albidiolic acid (10)*: colourless solid powder;  $[\alpha]_D^{20} = +23.5$  (c 0.2, MeOH);  $^1\text{H}$  NMR (pyridine- $d_5$ , 400 MHz) and  $^{13}\text{C}$  NMR (pyridine- $d_5$ , 100MHz), see Tables 1 and 2; HR-ESIMS  $m/z$  503.3370  $[\text{M}-\text{H}]^-$  (calculated for  $\text{C}_{30}\text{H}_{47}\text{O}_6$ , 503.3373), fragments at  $m/z$  549.3429  $[\text{M}-\text{H}+\text{HCOOH}]^-$  calculated for  $\text{C}_{31}\text{H}_{49}\text{O}_8$ , 549.3427).

### Biological Evaluation

**Antibacterial and antifungal activity.** The antimicrobial activity of all fractions and pure compounds was evaluated according to Cos et al. (2006) and Baldé et al. (2010).<sup>20,21</sup> Fractions and pure compounds were tested against the following microorganisms: *E. coli* ATCC8739 (Gram-negative), *S. aureus* ATCC 6538 (Gram-positive), and *C. albicans* ATCC59630 (yeast). The following positive controls were used: flucytosine for *C. albicans* ( $\text{IC}_{50}$   $0.7 \pm 0.01$   $\mu\text{M}$ ) and doxycycline for *S. aureus* ( $\text{IC}_{50}$   $0.28 \pm 0.2$   $\mu\text{M}$ ).

**Antiplasmodial and Cytotoxicity Assays.** Antiplasmodial activity and cytotoxicity were assessed as previously described<sup>22,24</sup>. Fractions and pure compounds were tested *in vitro* against the chloroquine-resistant strain *Plasmodium falciparum* K1 using the lactate dehydrogenase assay. Tamoxifen was used as the positive control for cytotoxicity on MRC-5 cells ( $\text{IC}_{50}$   $10.0 \pm 1.5$   $\mu\text{M}$ ), and chloroquine ( $\text{IC}_{50}$   $0.15 \pm 0.10$   $\mu\text{M}$ ) for *P. falciparum*. These reference compounds are routinely used in the screening platform and their activities were in the range that is usually observed.

**Table 1. <sup>1</sup>H NMR Assignments ( $\delta_{\text{H}}$  in ppm) for Compounds 2, 4-10 (400 MHz, Pyridine-*d*<sub>5</sub> and Methanol-*d*<sub>4</sub>)**

	<b>2<sup>b</sup></b>	<b>4<sup>b</sup></b>	<b>5<sup>b</sup></b>	<b>6<sup>b</sup></b>	<b>7<sup>b</sup></b>	<b>8<sup>b</sup></b>	<b>9<sup>b</sup></b>	<b>10<sup>c</sup></b>
Position	$\delta_{\text{H}}$ ( <i>J</i> in Hz)	$\delta_{\text{H}}$ ( <i>J</i> in Hz)	$\delta_{\text{H}}$ ( <i>J</i> in Hz)	$\delta_{\text{H}}$ ( <i>J</i> in Hz)	$\delta_{\text{H}}$ ( <i>J</i> in Hz)	$\delta_{\text{H}}$ ( <i>J</i> in Hz)	$\delta_{\text{H}}$ ( <i>J</i> in Hz)	$\delta_{\text{H}}$ ( <i>J</i> in Hz)
1a	1.38 <sup>a</sup>	1.38, m	0.89, m	1.29 <sup>a</sup>	1.46, m	1.52, d (12.9)	0.89, m	1.37, m
1b	3.76, m	3.78, m	1.91, m	3.72, m	3.90, m	3.81, m	1.92, m	2.27, m
2	4.34, m	4.35, m	3.68, m	4.39, m	4.41, m	4.46, m	3.68, m	4.22, m
3	4.18, m	4.18, m	3.35, m	3.54, d (8.7)	3.6, m	3.62, d (9.5)	3.34, m	4.19, m
4								
5	1.79, d (11.9)	1.79, m	1.29 <sup>a</sup>	1.08 <sup>a</sup>	1.17 <sup>a</sup>	1.18 <sup>a</sup>	1.27, br s	2.43, m
6a	1.17 <sup>a</sup>	1.44 <sup>a</sup>	1.45, m	0.91 <sup>a</sup>	0.91, m	1.55, m		1.43, s
6b	1.73, m	1.76, m	1.60, m	1.68, m	1.68, m	1.70, m		
7a	1.40, m	1.84, m	1.28, m	1.34, m	1.34, m	1.43, m	1.28, br s	1.28, m
7b	1.79, m	2.09, m	1.61, m	1.58, m	1.58, m	1.54, m		1.61, m
8								
9	2.67, s	2.68, s	1.99 <sup>a</sup>	2.6, s	2.83, s	2.65, s	1.68, m	1.78, m
10								
11			1.28 <sup>a</sup> , 1.77 br s					2.0, m
12	6.36, s	6.39, s	5.33, s	6.4, s	6.16, s	6.21, s	5.25, s	5.48, s
13								
14								
15a	1.30, m	1.24, m	1.0, m	1.32, m	1.32, m	1.29, m	1.06 <sup>a</sup>	1.12, m
15b	2.43, m	2.17, m	1.62, m	2.09, m	2.09, m	2.11, t (13.2)	1.80, m	
16a	1.52, m	2.09, m	0.92, m	1.34, m	1.34, m		0.90, m	1.98, m
16b	0.86, d (11.1)	2.17, m	1.7, m	1.58, m	1.58, m		1.27, m	2.16, m
17								
18	3.23, d (10.8)	3.37, d (10.6)	1.99 <sup>a</sup>	3.34, br d (10.2)	3.22, m		2.88, d (14.4)	3.38, dd (11.4, 11.4)



19	3.76, m	3.81, d (10.6)	3.55, m	3.83, br d (10.2)	3.66, (d, J = 5.1)	5.74, s	1.07, m 1.61, m	1.49, m 2.07, m
20								
21a	1.27 <sup>a</sup>	1.36, m	3.41, m	1.38 m	n.o	1.41, m	3.18, brs	1.39, m
21b	1.63 <sup>a</sup>	1.72, m		1.71 m	n.o	1.64, m		1.78, m
22a	1.75, m	1.84, m	n.o	1.71 m	1.5, m	1.67, m	1.14 m	1.91, m
22b	1.88, m	2.09, m	n.o	1.67 m	1.71, m	2.49, m	1.46 m	2.13, m
23a	3.69, m	3.68, d (10.6)	3.26, d (10.6)	1.55 s	1.60, s	1.60 s	3.25 d (11.02)	3.70, m
23b	4.25, m	4.21, d (10.6)	3.49, d (10.6)	n.o	n.o	n.o	3.48 d (11.02)	4.18, m
24a	1.04, s	1.04, s	0.69, s	3.71 m	3.74, m	3.77, d (10.6)	0.68, s	1.04, s
24b				4.44 m	4.45, m	4.49, d (10.6)		
25	1.45, s	1.43, s	1.02, s	1.34 s	1.38, s	1.46, s	1.02, s	1.35, s
26	1.37, s	1.24, s	0.79, s	1.19 s	1.20, s	1.21, s	0.82, s	1.03, s
27	1.39, s	1.43, s	1.27, s	1.50 s	1.78, s	1.24, s	1.18, s	1.20, s
28								
29	1.17, s	1.21, s	1.12, s	1.24, s	0.99, s	0.96, s	0.92, s	1.19, s
30	1.0, s	1.12, s	0.97, s	1.13, s	1.12, s	1.01, s	0.92, s	3.56, s
1'	6.32, d (8.3)							
2'	4.19 <sup>a</sup>							
3'	2.28, m							
4'	4.36 <sup>a</sup>							
5'	4.04, m							
6'	4.42 m, 4.46, m							

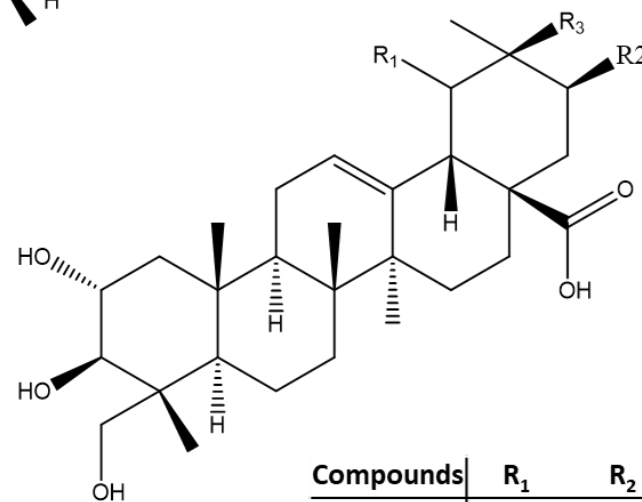
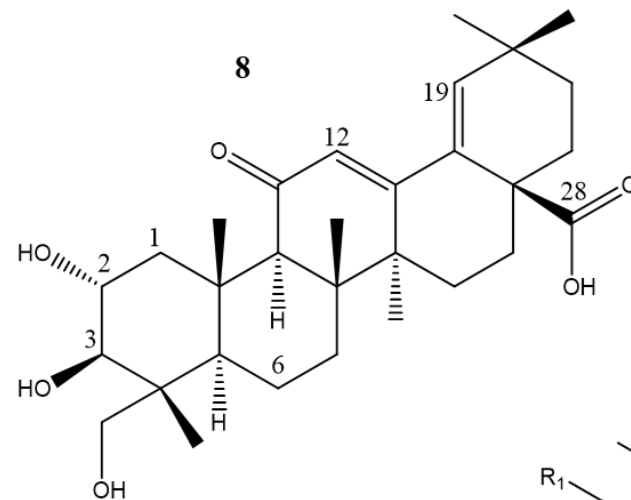
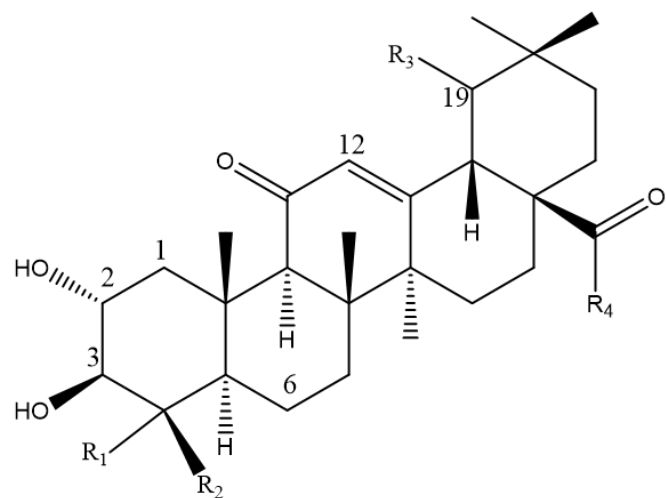
<sup>a</sup> Overlapping signals, <sup>b</sup>Pyridine-*d*<sub>5</sub>, <sup>c</sup>Methanol-*d*<sub>4</sub> n.o: not observed.

**Table 1.  $^{13}\text{C}$  NMR Assignments ( $\delta_c$  in ppm) for Compounds 2, 4-10 (100 MHz, Pyridine- $d_5$  and Methanol- $d_4$ )**

	<b>2<sup>b</sup></b>	<b>4<sup>b</sup></b>	<b>5<sup>c</sup></b>	<b>6<sup>b</sup></b>	<b>7<sup>b</sup></b>	<b>8<sup>b</sup></b>	<b>9<sup>c</sup></b>	<b>10<sup>b</sup></b>
Position	$\delta_c$ , Type	$\delta_c$ , Type	$\delta_c$ , Type	$\delta_c$ , Type	$\delta_c$ , Type	$\delta_c$ , Type	$\delta_c$ , Type	$\delta_c$ , Type
1	48.7, CH <sub>2</sub>	48.7, CH <sub>2</sub>	47.5, CH <sub>2</sub>	48.6, CH <sub>2</sub>	48.5, CH <sub>2</sub>	48.3, CH <sub>2</sub>	47.9, CH <sub>2</sub>	47.7, CH <sub>2</sub>
2	68.6, CH	68.7, CH	69.4, CH	68.4, CH	68.5, CH	68.1, CH	69.4, CH	68.9, CH
3	77.8, CH	77.8, CH	78.0, CH	85.4, CH	85.4, CH	85.2, CH	77.9, CH	78.2, CH
4	43.8, C	43.7, C	44.0, C	44.1, C	44.2, C	43.9, C	44.2, C	43.7, C
5	47.6, CH	47.7, CH	48.2, CH	56.1, CH	56.4, CH	56.1, CH	48.0, CH	48.2, CH
6	18.0, CH <sub>2</sub>	17.6, CH <sub>2</sub>	18.9, CH <sub>2</sub>	18.5, CH <sub>2</sub>	18.5, CH	18.4, CH <sub>2</sub>	18.3, CH <sub>2</sub>	18.5, CH <sub>2</sub>
7	33.0, CH <sub>2</sub>	33.2, CH <sub>2</sub>	33.2, CH <sub>2</sub>	33.8, CH <sub>2</sub>	33.8, CH	34.6, CH <sub>2</sub>	30.4, CH <sub>2</sub>	32.9, CH <sub>2</sub>
8	45.5, C	45.3, C	40.4, C	45.3, C	44.6, C	43.8, C	43.1, C	39.8, C
9	62.7, CH	62.2, CH	48.8, CH	62.1, CH	62.6, CH	61.1, CH	48.6, CH	48.0, CH
10	38.6, C	38.6, C	38.8, C	38.5, C	38.8, C	38.2, C	39.0, C	38.6, C
11	199.8, C	199.9, C	24.6, CH <sub>2</sub>	199.6, C	200.3, C	199.7, C	24.0, CH <sub>2</sub>	24.0, CH <sub>2</sub>
12	131.8, CH	131.5, CH	124.5, CH	131, CH	129.3, CH	123.0, CH	123.3, CH	122.5, CH
13	162.3, C	163.0, C	144.0, C	163.4, C	171.8, C	163.8, C	145.2, C	145.1, C
14	44.2, C	44.3, C	42.5, C	44.3, C	44.5, C	45.1, C	40.5, C	42.2, C
15	28.4, CH <sub>2</sub>	28.6, CH <sub>2</sub>	29.2, CH <sub>2</sub>	28.5, CH <sub>2</sub>	28.3, CH <sub>2</sub>	27.6, CH <sub>2</sub>	28.8, CH <sub>2</sub>	28.4, CH <sub>2</sub>
16	24.2, CH <sub>2</sub>	25.3, CH <sub>2</sub>	28.3, CH <sub>2</sub>	33.8, CH <sub>2</sub>	33.6, CH <sub>2</sub>	33.1, CH <sub>2</sub>	33.2, CH <sub>2</sub>	23.8, CH <sub>2</sub>
17	46.7, C	45.3, C	n.o	45.2, C	46.1, C	49.0, C	n.o	47.2, C
18	49.7, CH	50.2, CH	40.6, CH	50.1, CH	49.3, CH	136.9, C	41.5, CH	41.4, CH
19	74.7, CH	75.1, CH	76.4, CH	75.0, CH	80.5, CH	138.9, CH	42.1, CH <sub>2</sub>	41.2, CH
20	36.3, C	36.5, C	39.2, C	36.5, C	35.8, CH	n.o	36.5, C	36.6, C
21	34.5, CH <sub>2</sub>	34.9, CH <sub>2</sub>	85.4, CH	34.8, CH <sub>2</sub>	29.0, CH <sub>2</sub>	34.1, CH <sub>2</sub>	74.4, CH	29.2, CH <sub>2</sub>
22	31.4, CH <sub>2</sub>	32.2, CH <sub>2</sub>	25.9, CH <sub>2</sub>	31.2, CH <sub>2</sub>	31.4, CH <sub>2</sub>	33.1, CH <sub>2</sub>	29.4, CH <sub>2</sub>	32.7, CH <sub>2</sub>
23	66.0, CH <sub>2</sub>	66.0, CH <sub>2</sub>	66.0, CH <sub>2</sub>	24.1, CH <sub>3</sub>	24.2, CH <sub>3</sub>	23.9, CH <sub>3</sub>	66.2, CH <sub>2</sub>	66.5, CH <sub>2</sub>

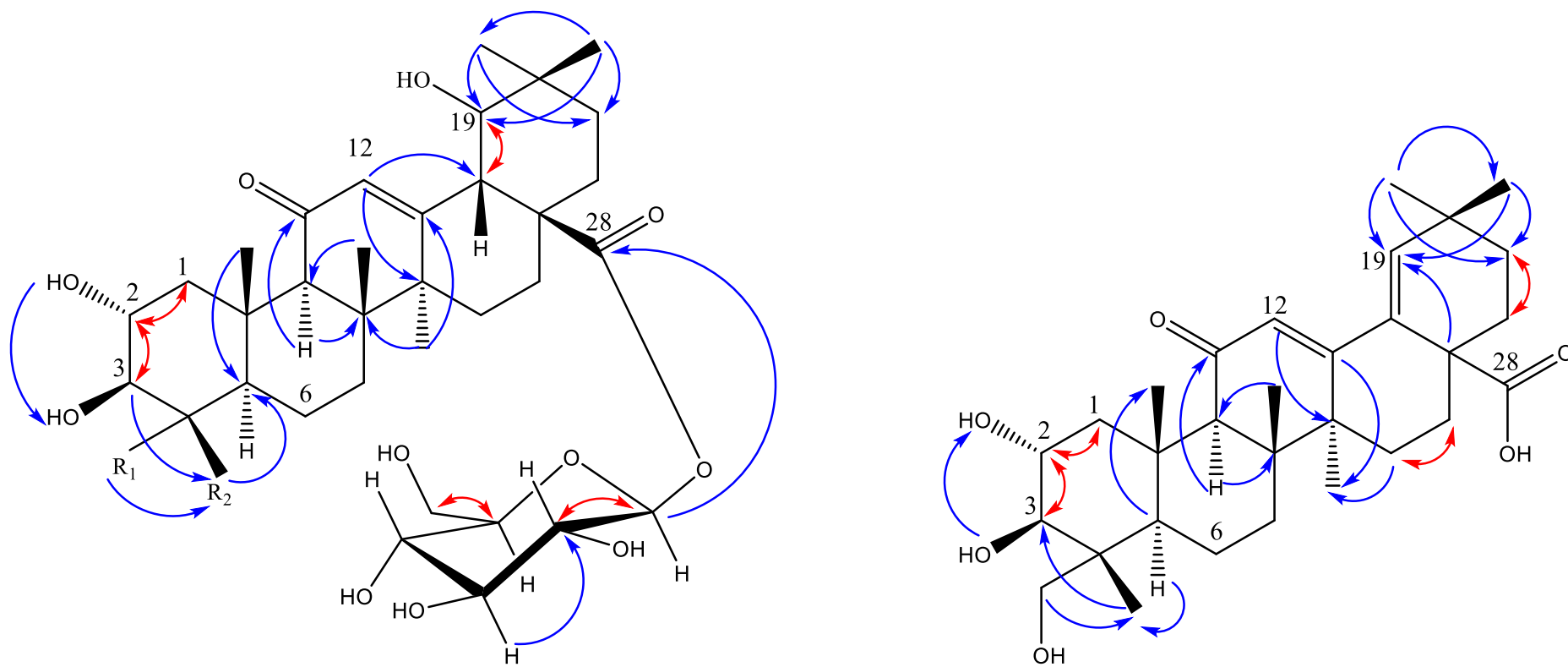
24	14.5, CH <sub>3</sub>	14.5, CH <sub>3</sub>	13.5, CH <sub>3</sub>	65.5, CH <sub>2</sub>	65.6, CH <sub>2</sub>	65.4, CH <sub>2</sub>	13.8, CH <sub>3</sub>	14.4, CH <sub>3</sub>
25	18.5, CH <sub>3</sub>	18.4, CH <sub>3</sub>	17.2, CH <sub>3</sub>	18.3, CH <sub>3</sub>	18.4, CH <sub>3</sub>	18.6, CH <sub>3</sub>	17.5, CH <sub>3</sub>	17.6, CH <sub>3</sub>
26	19.6, CH <sub>3</sub>	19.7, CH <sub>3</sub>	17.6, CH <sub>3</sub>	19.4, CH <sub>3</sub>	19.4, CH <sub>3</sub>	18.6, CH <sub>3</sub>	17.9, CH <sub>3</sub>	17.4, CH <sub>3</sub>
27	21.7, CH <sub>3</sub>	66.0 CH <sub>2</sub>	24.1, CH <sub>3</sub>	21.8, CH <sub>3</sub>	22.8, CH <sub>3</sub>	19.9, CH <sub>3</sub>	26.5, CH <sub>3</sub>	26.2, CH <sub>3</sub>
28	175.6, C	175.3, C	n.o	179.2, C	179.1, C	n.o	n.o	180.0, C
29	30.3, CH <sub>3</sub>	30.5, CH <sub>3</sub>	23.4, CH <sub>3</sub>	30.5, CH <sub>3</sub>	28.5, CH <sub>3</sub>	30.0, CH <sub>3</sub>	28.4, CH <sub>3</sub>	19.8, CH <sub>3</sub>
30	17.8, CH <sub>3</sub>	17.9, CH <sub>3</sub>	18.3, CH <sub>3</sub>	17.9, CH <sub>3</sub>	24.5, CH <sub>3</sub>	27.9, CH <sub>3</sub>	19.5, CH <sub>3</sub>	73.9, CH <sub>2</sub>
1'	96.1, CH							
2'	74.2, CH							
3'	78.8, CH							
4'	71.1, CH							
5'	79.5, CH							
6'	62.2 CH <sub>2</sub>							

<sup>a</sup> Overlapping signals, <sup>b</sup> Pyridine-*d*<sub>5</sub>, <sup>c</sup> Methanol-*d*<sub>4</sub>, n.o: not observed.

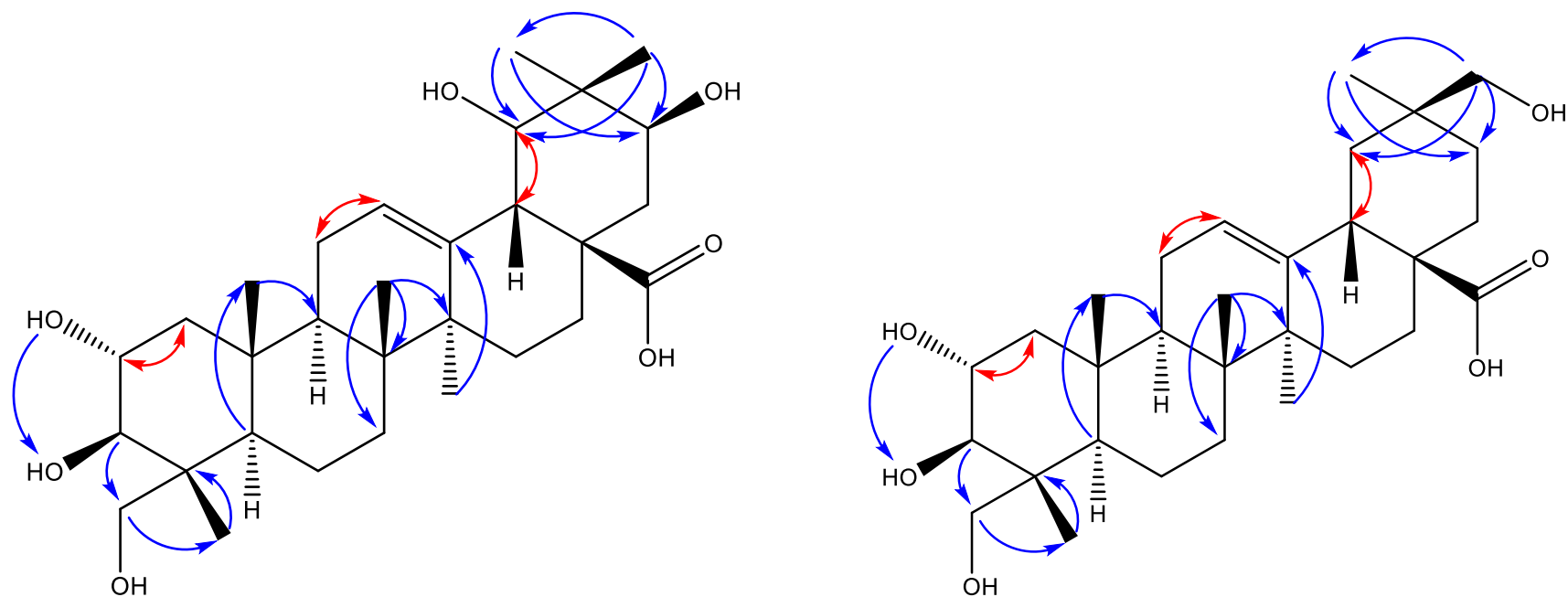


Compounds	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>
<b>1</b>	CH <sub>2</sub> OH	CH <sub>3</sub>	α-OH	β-D-glucopyranoside
<b>2</b>	CH <sub>2</sub> OH	CH <sub>3</sub>	β-OH	β-D-glucopyranoside
<b>3</b>	CH <sub>3</sub>	CH <sub>2</sub> OH	β-OH	β-D-glucopyranoside
<b>4</b>	CH <sub>2</sub> OH	CH <sub>3</sub>	β-OH	OH
<b>6</b>	CH <sub>3</sub>	CH <sub>2</sub> OH	β-OH	OH
<b>7</b>	CH <sub>3</sub>	CH <sub>2</sub> OH	α-OH	OH

Compounds	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>
<b>5</b>	α-OH	β-OH	CH <sub>3</sub>
<b>9</b>	H	α-OH	CH <sub>3</sub>
<b>10</b>	H	H	CH <sub>2</sub> OH



**Figure 1.**  $^1\text{H}$  -  $^1\text{H}$  COSY (red arrows), key HMBC (blue arrows) correlation of compound 2 and 8



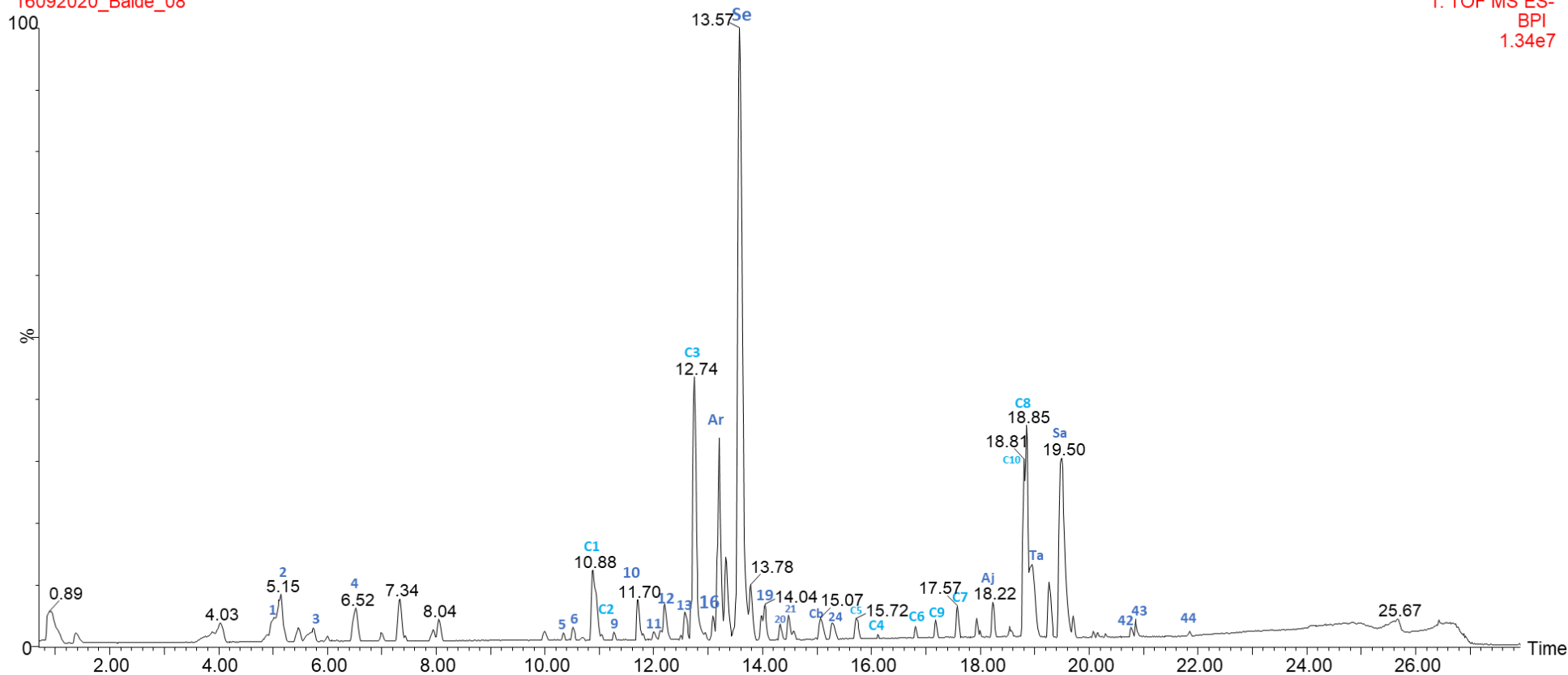
**Figure 2.**  $^1\text{H}$  -  $^1\text{H}$  COSY (red arrows), key HMBC (blue arrows) correlation of compound **5** and **10**

**Table 3.** *In vitro* Antimicrobial, Antiplasmodial and Cytotoxic activity of the *n*-BuOH Fraction and Isolated Compounds from *T. albida* Roots

Fraction and compound names	Antibacterial and antifungal activity (IC <sub>50</sub> μM)		Antiplasmodial activity (IC <sub>50</sub> μM)	Cytotoxicity (CC <sub>50</sub> μM)	Selectivity index
	<i>S. aureus</i>	<i>C. albicans</i>	<i>Pf-K1</i>	<i>MRC-5</i>	<i>MRC-5/ PfK1</i>
<i>n</i> -BuOH fraction	>64.0	>64.0	>64.0	>64.0	nd
2α,3β,19α,23-Tetrahydroxy-11-oxoolean-12-en-28-oic acid 28- <i>O</i> -β-D-glucopyranosyl ester ( <b>1</b> )	>64.0	>64.0	13.9	>64.0	>4.6
Albidanoside A ( <b>2</b> )	>64.0	>64.0	11.3	>64.0	>5.7
Ivorenoside C ( <b>3</b> )	>64.0	>64.0	9.1	>64.0	>7.0
Albidic acid A ( <b>4</b> )	>64.0	>64.0	10.1	>64.0	>6.3
Albidic acid B ( <b>6</b> )	>64.0	>64.0	6.1	>64.0	>10.5
Albidic acid C ( <b>7</b> )	>64.0	>64.0	6.1	>64.0	>10.5
Albidienic acid ( <b>8</b> )	>64.0	>64.0	6.9	>64.0	>9.27
Albidiolic acid ( <b>10</b> )	>64.0	>64.0	48.5	>64.0	>1.31
Chloroquine			0.15 ± 0.1 μM		
Doxycycline	0.28 ± 0.2 μM				
Flucytosine		0.70 ± 0.01 μM			
Tamoxifen				10.0 ± 1.5 μM	

TaRBuT  
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1: TOF MS ES-  
BPI  
1.34e7



**Figure 3.** Total ion chromatogram (BPI) of the *n*-BuOH fraction with peaks labelled with compound number (C1-C10 isolated compounds), Ar (arjunglucoside I), Aj (arjungenin), Cb (Chebuloside II), Se (sericoside), Sa (sericic acid), and Ta (Terminolic acid).



## ASSOCIATED CONTENT

### Supporting information

The Supporting Information is available free of charge

Summary of dereplicated compounds from the *n*-BuOH fraction, molecular networks (clusters corresponding to the oleanane triterpenoid compounds of the *n*-BuOH fraction), NMR and HR-ESIMS spectra of compounds (1-10) are available

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#### **Notes**

The authors declare no competing financial interest.

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## REFERENCES

- (1) Zhang, X. R.; Kaunda, J. S.; Zhu, H. T.; Wang, D.; Yang, C. R.; Zhang, Y. J. *Nat. Prod. Bioprospect.* **2019**, *9*, 357–392.
- (2) Cock, I. E. *Inflammopharmacology* **2015**, *23*, 203–229.
- (3) Silva, O.; Serrano, R. *Battle Against Microb. Pathog. Basic Sci. Technol. Adv. Educ. Programs* **2015**, No. December 2015, 236–245.
- (4) Balde, M. A.; Traore, M. S.; Diane, S.; Diallo, M. S. T.; Tounkara, T. M.; Camara, A.; Baldé, E. S.; Bah, F.; Ouedraogo, U.; Drame, H.; Diallo, H.; Balde, A. M. *J. plant Sci.* **2015**, *3*, 32–39.
- (5) Traore, M. S.; Baldé, M. A.; Diallo, M. S. T.; Baldé, E. S.; Diané, S.; Camara, A.; Diallo, A.; Balde, A.; Keita, A.; Keita, S. M.; Oularé, K.; Magassouba, F. B.; Diakité, I.; Diallo, A.; Pieters, L.; Baldé, A. M. *J. Ethnopharmacol.* **2013**, *150*, 1145–1153.
- (6) Diallo, A.; Traore, M. S.; Keita, S. M.; Balde, M. A.; Keita, A.; Camara, M.; Miert, S. V.; Pieters, L.; Balde, A. M. *J. Ethnopharmacol.* **2012**, *144*, 353–361
- (7) Magassouba, Diallo, A Kouyaté, M Mara, F.; Mara, O.; Bangoura, O.; Camara, A.; Traor, S.; Diallo, A. K.; Zaoro, M.; Lamah, K.; Diallo, S.; Camara, G.; Traor, S.; Oular, K.; Barry, M. S.; Donzo, M.; Camara, K.; Tot, K. *J. Ethnopharmacol.* **2007**, *114*, 44–53.
- (8) Baldé, M.A., Tuenter, E., Traoré, M.S., Matheussen, A., Cos, P., Maes, L., Camara, A., Haba, N.L., Gomou, K., Telly Diallo, M.S., Baldé, E.S., Pieters, L., Balde, A.M., Foubert, K. *J. Ethnopharmacol.* **2020**, *263*, 113232.
- (9) Camara, A.; Haddad, M.; Reybier, K.; Traoré, M. S.; Baldé, M. A.; Royo, J.; Baldé, A. O.; Batigne, P.; Haidara, M.; Baldé, E. S.; Coste, A.; Baldé, A. M.; Aubouy, A. *Malar. J.* **2019**, *18*, 1–15.
- (10) Salem, M. A.; De Souza, L. P.; Serag, A.; Fernie, A. R.; Farag, M. A.; Ezzat, S. M.; Alseekh, S. *Metabolites* **2020**, *10*, 1–30.
- (11) Allard, P. M.; Péresse, T.; Bisson, J.; Gindro, K.; Marcourt, L.; Pham, V. C.; Roussi, F.; Litaudon, M.; Wolfender, J. L. *Anal. Chem.* **2016**, *88*, 3317–3323.
- (12) Baldé, M. A.; Tuenter, E.; Matheussen, A.; Traoré, M. S.; Cos, P.; Maes, L.; Camara, A.; Telly Diallo, M. S.; Baldé, E. S.; Balde, A. M.; Pieters, L.; Foubert, K. *J. Ethnopharmacol.* **2021**, *267*, 113624.
- (13) Rivera-Mondragón, A.; Peeters, L.; Van, A. A.; Breynaert, A.; Caballero-George, C.; Pieters, L.; Hermans, N.; Foubert, K. *Planta Med.* **2020**. DOI:10.1055/a-1258-4383
- (14) Liu, F. J.; Jiang, Y.; Li, P.; Liu, Y. D.; Xin, G. Z.; Yao, Z. P.; Li, H. J. *J. Mass Spectrom.*

- 2020**, *55*, 1–10.
- (15) Ponou, B. K.; Teponno, R. B.; Ricciutelli, M.; Quassinti, L.; Bramucci, M.; Lupidi, G.; Barboni, L.; Tapondjou, L. A. *Phytochemistry* **2010**, *71*, 2108–2115.
- (16) Leo, M. De; Tommasi, N. De; Sanogo, R.; D'Angelo, V.; Germanò, M. P.; Bisignano, G.; Braca, A. Triterpenoid Saponins from *Pteleopsis Suberosa* Stem Bark. *Phytochemistry* **2006**, *67*, 2623–2629.
- (17) Yi, Y. H.; Dai, F. B. A New Triterpenoid and Its Glycoside from *Phytolacca Esculenta*. *Planta Med.* **1991**, *57*, 162–164.
- (18) Dou, H.; Zhou, Y.; Chen, C.; Peng, S.; Liao, X.; Ding, L. *J. Nat. Prod.* **2002**, *65*, 1777–1781.
- (19) Tsugawa, H.; Cajka, T.; Kind, T.; Ma, Y.; Higgins, B.; Ikeda, K.; Kanazawa, M.; Vanderghenst, J.; Fiehn, O.; Arita, M. *Nat. Methods* **2015**, *12*, 523–526.
- (20) Tsugawa, H.; Kind, T.; Nakabayashi, R.; Yukihira, D.; Tanaka, W.; Cajka, T.; Saito, K.; Fiehn, O.; Arita, M. *Anal. Chem.* **2016**, *88*, 7946–7958.
- (21) Wang, M.; Carver, J. J.; Phelan, V. V.; Sanchez, L. M.; Garg, N.; Peng, Y.; Nguyen, D. D.; Watrous, J. *Nat. Biotechnol.* **2016**, *34*, 828–837.
- (22) Cos, P.; Vlietinck, A. J.; Vanden, D.; Maes, L. *J. Ethnopharmacol.* **2006**, *106*, 290–302.
- (23) Baldé, E. S.; Megalizzi, V.; Traoré, M. S.; Cos, P.; Maes, L.; Decaestecker, C.; Pieters, L.; Baldé, A. M. *J. Ethnopharmacol.* **2010**, *130*, 529–535.
- (24) Tuenter, E.; Exarchou, V.; Balde, A.; Cos, P.; Maes, L.; Apers, S. *J. Nat. Prod.* **2016**, *79*, 1746–1751.