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TETRANORTRITERPENES FROM *TURRAEA ROBUSTA*

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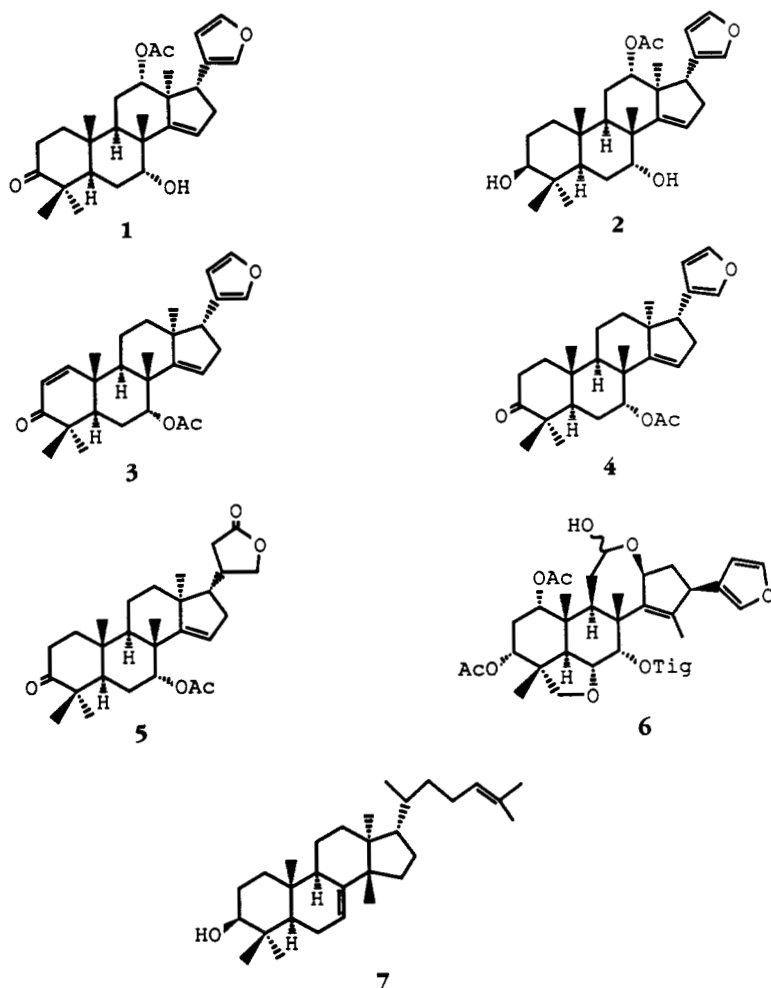
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ABSTRACT.—A new limonoid, mzikonol [2], in addition to the known limonoids mzikonone [1], azadirone [3], 1,2-dihydroazadirone [4], and nimbolin B [6], was isolated from the root bark of *Turraea robusta*. In addition, a new tetranortriterpene lactone, turranolide [5], and the known triterpene, buryospermol [7], both possible protolimonoids, were isolated. Compounds were identified by chemical and spectroscopic methods.

Turraea robusta Guerke (Meliaceae) is a small tree found in East Africa. The Zaramo tribe of Tanzania utilizes a tea prepared from the root bark of this tree, called mzikoziko in the Zaramo language, as a traditional medicine for the treatment of stomach pains and diarrhea. The leaves are used as an antidote for poisoning (1). We reported earlier the isolation and identification of a new compound, mzikonone [1], as the major tetranortriterpene (limonoid) from the MeOH extract of the root bark (2). Limonoids from two other members of this genus, *Turraea floribunda* and *Turraea obtusifolia*, have been reported (3). The latter plant was shown to contain prieurianin, while the former contained simpler limonoids of the havanensin type. Study of a third species, *Turraea nilotica*, revealed the presence of protolimonoids, but no limonoids were found (4). Further exploration will be required to elucidate chemotaxonomic patterns in this scantily studied genus. In this report, we present the results of further examination of the MeOH extract of *T. robusta* root bark and demonstrate the presence of four additional limonoids and two possible limonoid precursors.

Chromatography of a portion of the MeOH extract on Si gel using a hexane/Me₂CO gradient, followed by preparative Si gel tlc, led to isolation of compounds 2–5. The ¹H-nmr spectrum of 2 was similar to that of 1, with a major difference being the presence of a broad one-proton multiplet at 3.27 ppm, typical of the α-H of a 3β-ol; the ir spectrum also indicated absence of a keto function. The molecular formula, C₂₈H₄₀O₅, derived from hrms, was consistent with a limonoid differing from 1 by reduction of the 3-keto function. The structure of mzikonol [2], a new limonoid, was verified by conversion of 1 into 2 by reduction with NaBH₄. Compounds 3 and 4, also isolated by preparative tlc of fractions from the above cc, were shown to be the known compounds azadirone [3] (5,6) and 1,2-dihydroazadirone [4] (7,8) by comparison of spectral data with those previously published. Compound 4 has been reported as a semi-synthetic (7,8) but was not previously known as a natural product. Turranolide [5], a new compound isolated by preparative tlc of a fraction from the gradient cc described above, had molecular formula C₂₈H₄₀O₅ and ir absorptions indicating the presence of a γ-lactone, an ester, and a ketone. The ¹H-nmr spectrum exhibited some similarities with that of dihydroazadirone, including the probable presence of a 14,15-double bond and a 7-α-acetate but, significantly, demonstrated the absence of the H-17β and furan absorptions characteristic of limonoids of this class. Present instead were a doublet of doublets pair at 3.92 and 4.46 ppm, very similar to the 21-α and 21-β absorptions reported for related compounds (9,10) bearing a γ-lactone at the 17 position. The ¹³C-nmr spectrum was also consistent with the lactone structure, displaying no furan absorptions but exhibiting a carbonyl absorption at 176.4 ppm and two carbons each attached to two protons (APT) at 37.5 and 72.4 ppm, as well as a quaternary carbon at 37.5 ppm. Com-



pounds **6** and **7** displayed spectral properties consistent with those reported for nimbolinin B (11) and butyrospermol (12), respectively. The structure of nimbolinin B was further confirmed by oxidation to the lactone, ochinolide B, and comparison of the spectral properties of that product with those previously reported (11). We were rather surprised to find the highly oxidized **6**, because we were unable to find other limonoids having intermediate degrees of oxidation. We have also been unable to isolate any priurianin-type limonoids and must conclude that these will not prove diagnostic for this genus. Compounds **5** and **7** are possible protolimonoids, although in the absence of rigorous studies of the biosynthetic pathway, this must be considered tentative. It is of interest that another possible protolimonoid closely related to **7**, kulinone, differing from **7** only by oxidation at C-1 and hydroxylation at C-16, has been isolated from *Melia azadirach* (Meliaceae) (12) but, as far as we know, **7** has not been previously observed in Meliaceae.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.— ^1H - and ^{13}C -nmr spectra were obtained on a Varian XL200 nmr spectrometer. Multiplicities of the ^{13}C -nmr spectra were determined using the attached proton test (APT). Ir spectra were recorded on a Biorad FTS-60 FTIR system. Medium resolution mass spectra were obtained on a HP-5985-B system and hrms on a VG-70E system by Dr. George Goodloe at Auburn University.

PLANT MATERIAL.—Root bark of *T. robusta* was collected in Awasi, Kisumu District, Kenya in September 1985. The plant was identified by Mr. S. G. Mathenge of the Department of Botany herbarium at the University of Nairobi. A voucher specimen is deposited in that department.

EXTRACTION AND ISOLATION.—Root bark (2.0 kg) of *T. robusta* was air-dried, powdered, and allowed to stand in MeOH (4 liters) at room temperature for 1 week. The extract was filtered and evaporated to dryness under vacuum to yield an oil (40 g). A portion of the oil (5 g) was chromatographed on Si gel (50 × 3.5 cm; 70–130 mesh) using a hexane-Me₂CO (1:4)→Me₂CO gradient (HA). A second portion of the oil (9.8 g) was chromatographed on a Si gel column (75 × 4.5 cm, 230–400 mesh) using a hexane/EtOAc gradient (HEA).

Mzikonol [2].—Preparative tlc on Si gel [toluene-MeCOEt (7:3)] of fractions from HA led to the isolation of 10 mg of **2** as a white solid: mp 195–197°, ir (KBr) 3420 (hydroxyl), 1730 (ester); eims *m/z* [M]⁺ 456.2892 (C₂₈H₄₀O₅ requires 456.2875); ¹H nmr (CDCl₃) δ 0.79 (s, 3H, Me-29), 0.91 (s, 3H, Me-28), 1.00 (s, 3H, Me-18 or -19), 1.04 (s, 3H, Me-18 or -19), 1.11 (s, 3H Me-30), 1.45 (m, 1H, H-11β), 1.51 (m, 1H, H-1β), 1.76–1.85 (m, 3H, H-1α and H-6), 2.55 (m, 2H, H-16), 3.03 (dd, *J* = 8.5, 8.6, 1H, H-17), 3.27 (m, 1H, H-3), 3.97 (t, 1H, *J* = 2.4, 2.5, H-7), 5.09 (dd, *J* = 7.5, 6.8, 1H, H-12), 5.65 (dd, *J* = 1.7, 1.9, 1H, H-15), 6.28 (m, 1H, H-22), 7.24 (m, 1H, H-23), 7.35 (m, 1H, H-21); ¹³C nmr (CDCl₃) δ 170.9 (Ac C=O), 159.3 (C-14), 141.2 (C-23), 140.3 (C-21), 124.7 (C-20), 122.3 (C-15), 111.7 (C-22), 78.6 (C-3), 77.9 (C-12), 72.2 (C-7), 51.7 (C-13), 50.2 (C-17), 46.3 (C-5), 44.3 (C-8), 43.5 (C-9), 38.3 (C-4), 37.8 (C-1 or C-16), 37.0 (C-10), 36.9 (C-16 or C-1), 28.0 (C-28), 27.9 (C-30), 27.1 (C-2), 25.4 (C-11), 23.8 (C-6), 22.3 (C-18), 21.3 (Ac Me), 15.8 (C-19), 15.4 (C-29).

Mzikonone (100 mg) was treated with 33 mg of NaBH₄ in 10 ml of dioxane under reflux for 1 h. Addition of H₂O, extraction with CHCl₃, and preparative tlc led to isolation of a compound having ir, eims, and ¹H-nmr spectra identical with those of **2**.

Azadirone [3].—Preparative tlc [toluene-MeCOEt (7:3)] of fractions from HA led to the isolation of 57 mg of **3** as an oil, eims *m/z* [M]⁺ 436, ir (KBr) 1730 (ester), 1665 (α,β-unsaturated ketone); ¹H nmr (CDCl₃) δ 0.80 (s, 3H, Me-18), 1.08 (s, 6H, Me-28 and -29), 1.20 (s, 3H, Me-19), 1.25 (s, 3H, Me-30), 1.96 (s, 3H, Ac), 2.82 (dd, *J* = 8, 7.8, 1H, H-17), 5.39 (dd, *J* = 1.8, 1.8, 1H, H-15), 6.28 (m, 1H, H-22), 7.24 (m, 1H, H-23), 7.38 (m, 1H, H-21).

1,2-Dihydroazadirone [4].—Preparative tlc [toluene-MeCOEt (7:3)] of further HA fractions led to the isolation of 8 mg of **4**: mp 108–110°, eims *m/z* [M]⁺ 438, ir (KBr) 1732 (ester), 1706 (ketone); ¹H nmr (CDCl₃) δ 0.78 (s, 3H, Me-18), 1.02 (s, 3H, Me-28 or -29), 1.04 (s, 3H, Me-28 or -29), 1.06 (s, 3H, Me-19), 1.19 (s, 3H, Me-30), 1.97 (s, 3H, Ac), 2.78 (dd, *J* = 8, 8, 1H, H-17), 5.27 (dd, *J* = 2.6, 2.0, 1H, H-7), 5.36 (dd, *J* = 1.8, 1.9, 1H, H-15), 6.28 (m, 1H, H-22), 7.24 (m, 1H, H-23), 7.35 (m, 1H, H-21).

Turranolide [5].—Preparative tlc [toluene-MeCOEt (7:3)] of fractions from HA resulted in isolation of **5** (20 mg) as a white solid: mp 197–201°; ir (KBr) 1784 (γ-lactone), 1726 (ester), 1701 (ketone); eims *m/z* [M]⁺ 456.2906 (C₂₈H₄₀O₅ requires 456.2875); ¹H nmr (CDCl₃) δ 1.01 (s, 6H, Me-28 and -29), 1.03 (s, 3H, Me-18 or -19), 1.04 (s, 3H, Me-18 or -19), 1.14 (s, 3H, Me-30), 1.96 (s, 3H, Ac), 3.92 (dd, *J* = 9, 9, 1H, H-21), 4.46 (dd, *J* = 9, 9, 1H, H-21), 5.21 (dd, *J* = 2.5, 1.8, 1H, H-7), 5.29 (dd, *J* = 1.5, 1.6, 1H, H-15); ¹³C nmr (CDCl₃) δ 216.2 (C-3), 176.4 (C-23), 169.9 (Ac), 158.7 (C-14), 118.6 (C-15), 74.8 (C-7), 72.4 (C-21), 58.1 (C-17), 48.2 (C-5), 46.9 (C-13), 46.6 (C-10), 42.7 (C-9), 41.9 (C-8), 38.8 (C-1), 37.5 (C-20), 37.0 (C-4), 34.8 (C-22), 33.92 (C-12 or C-16), 33.9 (C-12 or C-16), 33.8 (C-2), 26.9 (C-18), 26.3 (C-28), 24.2 (C-6), 21.3 (C-29 or Ac Me), 21.0 (C-29 or Ac Me), 19.9 (C-30), 16.3 (C-11), 15.5 (C-19).

Nimbolin B [6].—Preparative tlc [toluene-MeCOEt (1:1)] of further HEA fraction led to the isolation of **6** (94 mg): mp; ir (KBr) 3471 (hydroxyl), 1740 (ester), 1718, 1662 (conjugated ester); eims *m/z* [M]⁺ 626; ¹H nmr (CDCl₃) δ 1.01 (s, 3H, Me-19), 1.18 (s, 3H, Me-29), 1.45 (s, 3H, Me-30), 1.78 (s, 3H, Me-18), 1.83 (s, 3H, Me-4'), 1.93 (s, 3H, Me-5'), 2.01 (s, 3H, Me-7' or -9'), 2.09 (s, 3H, Me-7' or -9'), 2.86 (d, *J* = 12.8, 1H, H-5), 3.26 (dd, *J* = 8.4, 8.7, 1H, H-17), 3.52 (m, 2H, H-28), 4.12 (dd, *J* = 12.9, 2.7, 1H, H-6), 4.78 (t, *J* = 2.8, 1H, H-1), 4.95 (t, *J* = 2.8, 1H, H-3), 5.12 (dd, *J* = 7.9, 1H, H-15), 5.27 (m, 1H, H-12), 5.78 (d, *J* = 2.6, 1H, H-7), 6.34 (m, 1H, H-22), 6.94 (qq, *J* = 1.3, 7, 1H, H-3'), 7.23 (m, 1H, H-23), 7.35 (m, 1H, H-21). Treatment of 8.8 mg of **6** with 6.0 mg of CrO₃ in 0.2 ml of pyridine at room temperature led, after preparative Si gel tlc [EtOAc-toluene (1:1)] to the isolation of ohchinolide B. The structure of that product was confirmed by comparison of the ¹H-nmr spectrum with that reported by Kraus and Bokel (11).

Butyrospermol [7].—Preparative Si gel tlc [MeCOEt-toluene (1:8)] of HEA fractions led to the isolation of **7** (28.7 mg) as a white solid: mp 108–110°; eims *m/z* [M]⁺ 425; ir (KBr) 3384 (hydroxyl), 1660 (double bond); ¹H nmr (CDCl₃) δ 0.74 (s, 3H, Me-19), 0.80 (s, 3H, Me-18), 0.86 (s, 3H, Me-29), 0.97

(s, 6H, Me-28 and Me-30), 1.60 (s, 3H, Me-26 or -27), 1.69 (s, 3H, Me-26 or -27), 3.25 (m, 1H, H-3), 5.10 (m, 1H, H-24), 5.26 (dd, $J = 3.1, 3.2$, H-7).

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