International Journal of Physical Sciences Vol. 3 (6), pp. 156-158, June 2008
Available online at http://www.academicjournals.org/IJPS
ISSN 1992 - 1950 © 2008 Academic Journals

Short Communication

Friedelanone and other triterpenoids from *Hymenocardia acida*

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Accepted 10 June, 2008

The stem barks of the plant *Hymenocardia acida* Tul. (Hymenocardiaceae) has yielded five triterpenoids which were identified by spectroscopic methods as friedelan-3-one, betulinic acid, lupeol, β-sitosterol, stigmasterol and the fatty acid, oleic acid. These compounds are being reported for this plant material for the first time.

Key words: *Hymenocardia acida*, hymenocardiaceae, Nigeria, friedelanone, betulinic acid, lupeol, oleic acid.

INTRODUCTION

Hymenocardia acida Tul. (Hymenocardiaceae) is a well known medicinal plant in Nigeria (Adjanahoun et al., 1991) and it is associated with the treatment of skin diseases (Igoli et al., 2003) and diabetes (Igoli et al., 2005) in the traditional medicinal practices of the Igede people of Nigeria. The plant has been screened for anti-drepanocytary or anti-sickle cell (Mpiana et al., 2007), anti-trypanosomal (Hoet et al., 2004), antidiarrhoeal (Tona et al., 1999), anti-plasmodial (Vonthron-Senecheau et al., 2003), antitumor and anti-HIV activities (Muanza et al., 1995) with certain levels of activity recorded in each case. The plant's stem bark is also reportedly used for bone setting or as an anti-inflammatory agent by traditional bone healers and in the treatment of chest pains (Muanza et al., 1994). Earlier phytochemical screening indicated the presence of steroids and or triterpenes in its stem bark (Tona et al., 1998).This has prompted a further investigation of the plant with a view to isolating the steroidal compounds or compounds possessing any of the activities for which it has been screened.

MATERIALS AND METHODS

General

Melting points (mp) are uncorrected. The ^{1}H NMR and ^{13}CNMR (400 MHz) spectra were run in a Bruker DPX 400 spectrometers using $CDCl_3$ as solvent and TMS as internal standard. ESI-MS were run using Bruker Esquire 3000 while GC and GC-MS were run using Shimadzu GC-17A/MS QP5050. Exact masses were measured using an Autospec X magnetic sector mass spectrometer with EBE geometry (Vacuum Generators, now Micromass, Manchester, UK). IR with Perkin-Elmer 841. Column chromatographic separations were performed on glass columns using silica gel MN-60 (Macherey-Nagel GmbH & Co. KG).

Plant Material

The barks of the plant were collected from mature trees growing around the University of Agriculture Makurdi. The plant was identified by the Forestry and Wildlife Department of the University of Agriculture, Makurdi where a voucher specimen has been deposited.

Extraction and isolation of constituents

Dried and ground barks (1kg) were placed in a Soxhlet apparatus and extracted (72 h) successively with hexane, ethyl acetate and thereafter with methanol (2.5L each). The hexane extract (2.46 g) was subjected to column chromatography over silica gel. The column was eluted with hexane and then gradient wise with ethyl acetate in hexane to yield friedelan-3-one (1) 35.4 mg, oleic acid, 13.3 mg, lupeol (3), 23.3mg, a mixture of β-sitosterol and stigmasterol, 33.6 mg and betulinic acid (2), 32.5 mg.

RESULTS AND DISCUSSION

The hexane extract of the bark gave friedelanone 1. Exact mass measurement (HR EI-MS) of the molecular

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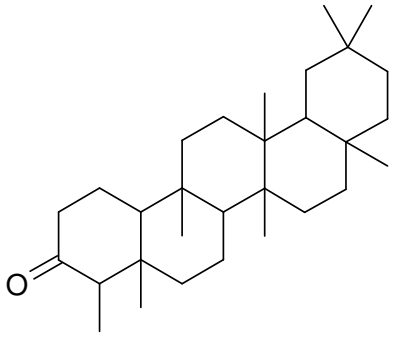

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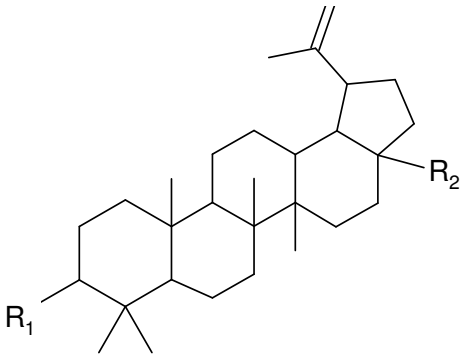

2: R_1 = OH, R_2 = COOH
3: R_1 = OH, R_2 = CH_3

Figure 1. Structure of isolated triterpenoids.

ion of the compound (M^+: *m/z* 426) gave the molecular formula $C_{30}H_{50}0$. It gave carbonyl absorption at 1715 cm^{-1} in its IR spectra indicative of a saturated ketone. This was confirmed by the absorption at δ 213 ppm in its ^{13}C NMR spectra. Its ^1H NMR and mass spectra were typical of a pentacyclic triterpene. The absence of unsaturated protons in its ^1H NMR indicates the compound must be wholly saturated. Its structure was confirmed by comparison of its spectral data with literature reports (Hisham et al., 1995).

Exact mass measurement (HR EI-MS) of the molecular ion of compound 2 (M^+: *m/z* 456) gave the molecular formula $C_{30}H_{48}0_3$. Its mass spectrum was characteristic of a pentacyclic triterpene of the lupane series (Budzikiewicz et al., 1963). It was found to be identical to the mass spectra of betulinic acid (Budzikiewicz et al., 1963, Robinson and Martel 1970, Herz et al., 1972). The ^1H NMR and ^{13}C NMR data were also consistent with the earlier reported ones (Herz et al., 1972; Sholichin et al., 1980; Bhattacharya and Cymone, 1986). 2D NMR experiments gave correlation for all the C-H bonds/groups and identified the quaternary carbons in the structure.

Exact mass measurement (HR EI-MS) of the molecular ion of compound 3 (M^+: *m/z* 426) gave the molecular formula $C_{30}H_{50}0$. Its mass spectrum was also characteristic of a pentacyclic triterpene of the lupane series (Budzikiewicz et al., 1963). It was found to be identical to the mass spectra of lupeol. A comparison of its spectral properties (MS, NMR and IR) with those of compound **2** showed they were analog with slight differences resulting from the absence of a carboxylic acid unit in compound 3. This was confirmed by the absence of carbonyl absorption in the ^{13}C NMR and IR for the compound and the presence of an additional methyl group at 18.23ppm in its ^{13}C NMR. The characteristic peaks in its EI-MS spectrum coupled with the other spectral data confirm its structure when compared to literature reports (Sholichin et al., 1980; Promsattha et al., 1987). β-sitosterol**,** stigmasterol and oleic acid were also isolated. Their spectral data confirmed their structures when compared with authentic samples and literature/database reports (Aldrich NMR Lib. 1992, NIST 2006 and SDBS, 2006).The presence of triterpenoids in the plant extracts as reported earlier (Tona et al., 1998) has been confirmed. These triterpenoids may be responsible or do contribute significantly to the observed bioactivity of the plant extracts. Betulinic acid and lupeol have been identified in the fractions of the extracts of *Caesalpinia paraguariensis* found to posses antibacterial activity (Woldemichael et al., 2003) while Betulinic acid and its derivatives have been shown to posses anti-HIV activity (Yogeeswari and Sriram, 2005, Singh et al., 2005; Fujioka and Kashiwada, 1994). Oleic acid has been shown to possess anti-diabetic properties (Soriguer et al., 2004).

Analytical data

Compound 1 Friedelan-3-one

White crystals from *n*-pentane, mp 262 - 264 °C; Tlc: R_f 0.78 (hexane-ethyl acetate (6:4)); UV $\lambda^{CH_3OH}_{max}$ (nm) 205,EI-MS *m/z* (rel. int.): 426.5 (10) $[M]^+$, 411 (8), 302 (10), 273 (15), 218 (12), 205 (15), 163 (12), 123 (25), 95 (40), 69 (52) 44 (100); Exact Mass (HR EI-MS) *m/z* 426.3860 $[M]^+$, $C_{30}H_{50}O$ requires 426.3862; IR ν^{KBr}_{max} (cm^{-1}): 2925 (C-H alkane), 2848 (C-H alkane), 1715 (C=O ketone), 1472, 1389, 1176; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.74 (3H, s, H-24), 0.88 (3H, s, H-25), 0.89 (3H, d, *J* = 2.7 Hz, H-23), 0.96 (3H, s, H-30), 1.01 (3H, s, H-26), 1.02 (3H, s, H-27), 1.06 (3H, s, H-28), 1.19 (3H, s, H-29), 1.26 (3H, s, H-30), 1.97 (1H, m, H-1a), 2.28 (2H, m, H-2b, H-4), 2.40 (1H, m, H-2a), 1.29-1.78 (m, rest of the

protons); ^{13}C NMR (400 MHz, $CDCl_3$) δ (ppm): (C-1-C-30): 22.51, 41.76, 213.00, 58.48, 42.70, 41.55, 18.48, 53.36, 37.70, 59.75, 35.88, 30.75, 39.95, 38.55, 32.68, 36.26, 29.93, 43.06, 35.59, 28.40, 32.33, 39.49, 7.04, 14.32, 18.17, 20.48, 18.88, 32.16, 32.01, 35.24

Compound 2 betulinic acid (3-Hydroxy-20(29)-lupen-28-oic acid)

White crystals from n-pentane, mp 279 - 280°C; $TlcR_f$ 0.41 in *n* pentane/dichloromethane/ethylacetate/formic acid (2:3:4:1). UV $\lambda^{CH_3CN}{}_{max}$: 283.5; ESI-MS *m/z*: 455.3 $[M-H]^-$. EI-MS *m/z* (rel. int.): 456 (22) $[M]^+$, 438 (17), 423 (14), 395 (15), 259 (7), 248 (27), 207 (42), 189 (89), 175 (33), 161 (23), 135 (48), 43 (100); Exact Mass (HR EI-MS) *m/z* 456.3600 $[M]^+$, $C_{30}H_{48}O_3$ requires 456.3603. IR $\nu^{KBr}{}_{max}$ (cm^{-1}): 3461 (OH), 2945 (C–H), 1688 (C=O), 1561 (C=C) 1189 (C–O). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 4.68 (2H, d, *J* = 32 Hz, H-29), 3.17 (m), 3.00 (m), 2.29 (q), 1.96 (d), 1.69 (s, 3H, H-30), 0.75-1.61 (m, rest of protons); ^{13}C NMR: (400 MHz, $CDCl_3$ δ (ppm) (C-1-C-30): 38.77, 27.44, 79.05, 38.90, 55.41, 18.33, 34.38, 40.76, 50.58, 37.26, 20.90, 25.56, 38.45, 42.49, 30.61, 32.20, 57.23, 46.93, 49.34, 150.41, 29.74, 37.06, 28.02, 15.36, 16.06, 16.15, 14.73, 180.40, 109.71, 19.41

Compound 3, Lupeol (20 (29)-lupen-3-ol)

White needles, mp 210 - 211°C; tlc: R_f 0.80 in ethyl acetate/hexane (4:6). UV $\lambda_{max\ (MeOH)}$ (nm): 210; EI-MS *m/z* (rel. int.): 426 (70) $[M]^+$, 411 (20), 302 (100), 286 (31), 189 (64), 135 (62), 69 (98) 55 (96); Exact Mass (HR EI-MS) *m/z* 426.3868 $[M]^+$, $C_{30}H_{50}O$ requires 426.3862; IR $\nu_{max\ (KBr)}$ (cm^{-1}): 3400 (OH), 2944 (C–H), 1458 (C=C) 1379 (CH_3-C) 1037 (C–O) 881 (C-H). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 4.68 (1H, d, *J* = 2.20 Hz, H-29a) and 4.56 (1H, d, *J* = 1.32, H-29b), 3.17 (1H, dd, *J* = 11.4, 4.8 Hz, H-3ax), 2.36 (ddd, *J* = 5.3, 11.0, 11.0 Hz, H-19), 1.90 (m), 1.67 (3H, s, H-30), 0.75-1.64 (m, rest of protons); ^{13}C NMR (400 MHz, $CDCl_3$) δ (ppm) (C-1-C-30): 38.94, 27.65, 79.24, 39.09, 55.53, 18.55, 34.52, 41.07, 50.68, 37.40, 21.16, 25.38, 38.29, 43.06, 27.68, 35.81, 43.23, 48.54, 48.21, 151.20, 30.08, 40.23, 28.21, 15.59, 16.34, 16.20, 14.78, 18.23, 109.54, 19.53

ACKNOWLEDGEMENTS

Igoli J.O is grateful for a research visit to the University of Strathclyde, Glasgow, UK and NAPRALERT for the use of their database.

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