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A NEW PHTHALIDE AND XANTHONES FROM *ANTHOCLEISTA DJALONENSIS* AND *ANTHOCLEISTA VOGELLI*

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Key Word Index—*Anthocleista djalonensis*; *A. vogelli*; Loganiaceae; phthalide; djalonensin; lichexanthone; triterpenoids; xanthone decussatin; alkaloid fagaramide; triterpenes.

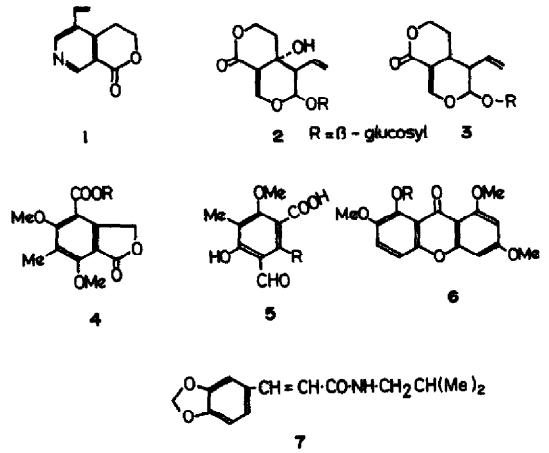
INTRODUCTION

Anthocleista djalonensis (A. Chev.) and *Anthocleista vogelli* (Planch), Loganiaceae, are small trees which grow in the tropical rain forest areas of West Africa [1,2]. The stem bark is used in local medicine for curing fever, stomach ache and as a purgative [2]. Early work reported on the genus *Anthocleista* were on *A. procera* which yielded the alkaloid gentianine (**1**) [3], the heteroside swertiamarin (**2**) [4] and anthocleistin [5], an α-amyrin type of triterpene; on *A. rhizophoroides* which afforded gentianine [6] and on *A. zambesiaca*, from which erthocentaurine and sweroside (**3**) were obtained [7]. Recently, pharmaceuticals were reported [8] from *A. rhizophoroides* and *A. nobilis*, the latter is said to be identical [1] with *A. djalonensis*. We now report on the chemical examination of the stem bark of *A. djalonensis* which gave a new phthalide, djalonensin (**4**, R = Me), lichexanthone, two triterpenes and some compounds whose structures have not been fully determined. The stem bark of *A. vogelli* yielded a xanthone decussatin, an alkaloid fagaramide and a triterpene.

RESULTS

Column chromatography on silica gel of the resultant gummy solid from hot hexane extraction of the stem bark of a young tree of *A. djalonensis* furnished seven crystalline compounds (A to G.).

Compound B was yellow crystals mp 178–180°. The presence of a xanthone nucleus was indicated [9] by the UV data and it was identified as lichexanthone [10] (1-hydroxy-3, 6-dimethoxy-8-methylxanthone) by the IR, NMR, UV and MS data. This identification was further confirmed by both the spectral data [10] and mp 190°–191° of the monoacetate.



Compound G, mp 137–139°, formed white silky crystals and was named djalonensin. The presence of phthalide ring was demonstrated by heating djalonensin with resorcinol and H_2SO_4 when flourescence developed [11]. Djalonensin was identified as 4-carbomethoxy-5, 7-dimethoxy-6-methyl phthalide (**4**, R = Me) by detailed study of the IR, NMR and MS data and those of its hydrolysis product djalonensic acid. This compound was produced [12] when either cyclopolic acid (**5**, R = CH_2OH) or cyclopaldic acid (**5**, R = CHO), both mould metabolic products of *Penicillium cyclopium* were heated with KOH, the former at 150° in air for a long time and the latter for a short time in aqueous solution followed by methylation with dimethyl sulphate in ME_2CO and K_2CO_3. It was named methyl isocyclopaldate monomethyl ether. Although the synthesis has also been reported [12], no spectroscopic data or authentic sample were available for comparison. But since the mp 138–139° of djalonensin was clearly the same as that reported (139–139.5°) for methylisocyclopaldate monomethyl ether prepared by three different methods, we suggest they are the same. Moreover the mp 197°–199° of djalonensic acid (**4**, R = H) was similar to that reported (198°–199°) for isocyclopaldic acid methyl ether [12] prepared from different sources, further confirming the identity. This is the first report of the isolation of djalonensin from natural sources.

Examination of the stem bark of older trees of *A. djalonensis* yielded only triterpene compound A and lichexanthone.

Examination of the stem bark of *Anthocleista vogelli* afforded three crystalline compounds. The first one, mp 132–134°, MW 414, was shown by spectroscopic data to be a triterpene. The IR and UV spectral data of the second compound, mp 152–154°, were consistent with the presence of a xanthone nucleus. A study of the NMR and MS revealed that the compound was the xanthone decussatin (**6**, R = H) mp 151° first isolated from the flowers and roots of *Swertia decussata* [13]. Production of the monoacetate (**6**, R = OCOMe) whose mp and spectral data were identical with those reported for decussatin monoacetate [13] confirmed the identification.

The third compound, mp 116–118°, had MW 247 indicating the presence of nitrogen. Detailed NMR study led to the conclusion that the compound was fagaramide (**7**) [14]. Complete identity was confirmed by a comparison of the spectral data and mp with an authentic sample.

Examination of the wood of *A. vogelli* furnished decussatin, and two triterpenes.

The isolation of xanthones and phthalide from the genus *Anthocleista* is reported for the first time. It is significant that none of the compounds isolated from the four species *A. nobilis*, *A. procera*, *A. rhizophoroides* and *A. zambesiaca* so far reported in the literature was found in the two species which were the subject of this paper.

EXPERIMENTAL

Unless otherwise specified UV spectra were taken in MeOH and IR spectra were in Nujol. Si gel refers to Merck Kieselgel 60 (70–230 mesh ASTM). NMR spectra were recorded at 60 MHz in $CDCl_3$ with TMS as internal standard.

Extraction of Anthocleista djalonensis. The dried powdered stem bark (4.5 kg) of a young tree from Ile-Ife in Western Nigeria was extracted with refluxing hexane. The concentrate gave a gummy solid (32.0 g) which was dissolved in C_6H_6 and chromatographed on a column of Si gel (130.0 g) eluting with Et_2O–petrol (60–80°). Petrol–Et_2O (19:1) eluted triterpene compound A as white crystals mp 156–159°, MS:*m/e* 424(M^+) (0.65 g). Petrol–Et_2O (9:1) fractions afforded Compound B, lichexanthone as yellow crystals mp 178–180° (2.6 g), UV λ_{max} nm (log ϵ):257 (3.8), 270 (3.78), 307 (3.90), 340 (36.5); IR ν_{max} cm^{-1}: 1665, 1642, 1601, 1550, 1460, 1375, 1310, 1275, 1200, 1160, 1130, 1040, 1035, 960, 900, 870, 840, 825. NMR: δ 13.4 (1H, *s*, disappearing with D_2O, Ar OH), 6.67 (2H, *s*, ArH), 6.3 (2H, *s*, ArH), 3.90 (3H, *s*, OMe), 3.88 (3H, *s*, OMe), 2.84 (3H, *s*, ArMe); MS:*m/e* 286 (M^+). (Found: C, 67.00, H, 4.85; $C_{16}H_{14}O_5$ requires: C, 67.12; H, 4.93%). Petrol–Et_2O (4:1) eluates furnished compound C mp 180–182° (0.018); MS:*m/e* 402(M^+) and compound D mp 191–194° (decomp. 0.012 g) MS:*m/e* 354 (M^+). Petrol–Et_2O (2.3) fractions gave compound E mp 255° (decomp. 0.014 g), MS:*m/e* 438 (M^+) and a triterpene F, mp 120–122° (0.40 g), MS:*m/e* 414 (M^+). Petrol–Et_2O (1:1) eluted compound G, djalonensin (**4**, R = Me) white silky crystals; mp 137–139°. IR ν_{max} cm^{-1}: 1750 (phthalide lactone), 1700 (aryl ester), 1595 (aromatic ring) 1450, 1430, 1370, 1350, 1300, 1240, 1130, 1115, 1075, 1020, 990, 943, 837, 800; NMR: δ4.15 (3H, *s*, OMe), 3.93 (3H, *s*, OMe) 3.85 (3H, *s*, COOMe, lost on hydrolysis), 5.4 (2H, *s*, Ar–CH_2–O), 2.20 (3H, *s*, Ar–Me); MS:*m/e* 266 (M^+, 100%). (Found: C, 58.7; H, 5.3; $C_{13}H_{14}O_6$ requires C, 58.6; H, 5.3%). A batch of stem bark (4.0 kg) of an old tree was similarly treated. Petrol–Et_2O (19:1) afforded compound A above (0.80 g) while petrol–Et_2O (9:1) furnished lichexanthone (2.2 g).

Extraction of Anthocleista vogelli. *Stem bark.* Powdered stem bark (6.3 kg) of the tree from Apomu Forest Reserve in Western Nigeria were similarly extracted with refluxing hexane to give a gum (45.0 g). This was dissolved in C_6H_6 and chromatographed on Si gel (180.0 g) eluting with increasing percentages of Et_2O–petrol (60–80°). Petrol–Et_2O (19:1) eluates gave a triterpene mp 132–134° (0.45 g) Petrol–Et_2O (9:1) fractions afforded decussatin mp 152–154° (6.8 g) (lit [13] mp 151°) IR ν_{max} cm^{-1}: 1660, 1601, 1475, 1450, 1350, 1300, 1275, 1152, 1088, 1057, 972, 956, 806, 760; NMR: δ 13.22 (1H, *s*, disappeared on deuteration, ArOH) 7.3 (1H, *d*, *J* 10.0 Hz, ArH), 7.08 (1H, *d*, *J* 10.0 Hz, ArH), 3.98 (3H, *s*, OMe), 3.90 (3H, *s*, OMe) 3.82 (3H, *s*, OMe); MS:*m/e* 302 (M^+). (Found: C, 63.49; H, 4.61; $C_{16}H_{14}O_6$ requires: C, 63.57; H, 4.67%). Petrol–Et_2O (1:1) furnished yellowish-white crystals of fagaramide mp 116–118° (lit. [14] mp 119.5°). IR ν_{max} cm^{-1}: 3300, 1640, 1600, 1550, 1442, 1365, 1245, 1030, 980, 920, 852; NMR: δ6.0 (2H, *s*, O–CH_2–O), 6.3 (1H, *d*, *J* 16Hz, ArCH=C), 7.6 (1H, *d*, *J* 16Hz, ArC=CH), 7.0 (2H, *m*, ArH), 6.82 (1H, *s*, ArH), 3.25 (2H, *t*, *J* 6Hz, N–CH_2–C) 3.95 (1H, *m*, C=CH–Me_2), 1.0 (6H, *d*, *J* 6Hz, sec.Me); MS:*m/e* 247 (M^+). (Found: C, 67.9, H, 6.9; N, 5.9; $C_{14}H_{17}O_3N$ requires: C, 68.0; H, 6.93; N, 5.7%). This compound was identical by direct comparison (IR, NMR, MS, mp and mmp with an authentic sample.

Extraction of A. vogelli *wood.* Hot hexane extraction of the wood (9.2 Kg) and concentration of the extract gave a copious yellow ppt. (11.6 g) and some gum (35.0 g). Recrystallisation of the yellow ppt. from $CHCl_3$ furnished yellow needles of decussatin (10.5 g). Column chromatographic separation of the gum as described above gave petrol–Et_2O (19:1) eluates which afforded a triterpene mp 156–159° (1.2 g) identical with compound A from stem bark of *A. djalonensis*. Further petrol–Et_2O (19:1) fractions gave white crystals mp 132–134° (0.90 g) of triterpene identical with that from the stem. Petrol–Et_2O (9:1) furnished crystals of decussatin (2.3 g).

Acetylation of xanthones. (a) Lichexanthone (0.10 g) added to Ac_2O and C_5H_5N was refluxed for 5 hr cooled and poured into cold H_2O when lichexanthone monoacetate was precipitated (0.085 g). Recrystallization from Me_2CO afforded white crystals mp 190–191° (lit. [15] mp 192°). IR ν_{max} cm^{-1}: 1755, 1620, 1550, 1440, 1352, 1260, 1225, 1134, 1050, 823; NMR: δ 6.61 (1H, *d*, *J* 2Hz, ArH), 6.58 (2H, *s*, ArH), 6.46 (1H, *d*, *J* 2Hz, ArH), 3.81 (6H, *s*, OMe), 2.78 (3H, *s*, ArMe), 2.42 (3H, *s*, OCOMe); MS:*m/e* 314 (M^+). (Found: C, 65,75; H, 4.83; $C_{18}H_{16}O_6$ requires: C, 65.85; H, 4.91%). (b) Decussatin (0.20 g) was acetylated as for lichexanthone to give after re-crystallisation (0.16 g) of white crystals mp 167–169° (lit. [13] mp 168–169°). MS:*m/e* 344 (M^+). (Found) C, 62.84; H, 4.65; $C_{18}H_{16}O_7$ requires: C, 62.79; H, 4.68%).

Hydrolysis of djalonensin. Djalonensin (**4**, R = Me) (0.075 g) suspended in 25 ml MeOH and 20 ml 1M NaOH was refluxed for 4 hr cooled, diluted with H_2O and extracted with Et_2O and then $CHCl_3$. Evaporation of both organic fraction yielded no products. The fraction was acidified with 2M HCl and extracted 3 × 30 ml $CHCl_3$. Evaporation of dried combined $CHCl_3$ fractions afforded an oil (0.058 g) which crystallised from Et_2O–petrol to give needle-like crystals of djalonensic acid (**4**, R = H) mp 197–199°. (mp of isocyclopaldic acid methyl ether 198–199° lit. [12]. IR ν_{max} cm^{-1} 3300–2700 (Carboxylic–OH) 1755 (phthalide–C=O), 1675 (Carboxylic–C=O), 1600, 1450, 1360, 1282, 1225, 1120, 1100, 1020, 942, NMR: δ 5.44 (2H, *s*, Ar–CH_2–O), 4.20 (3H, *s*, OMe), 4.0 (3H, *s*, OMe), 2.24 (3H, *s*, ArMe); MS:*m/e* 252 (M^+). (Found: C, 57.3; H, 5.0; $C_{12}H_{12}O_6$ requires: C, 57.1; H, 4.8%). Methylation of djalonensic acid (**4**, R = H) with etheral CH_2N_2 regenerated djalonensin (**4**, R = Me).

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