Journal of Natural Products
Vol. 52, No. 4, pp. 818-821, Jul-Aug 1989

AN INVESTIGATION OF *BONGARDIA CHRYSOGONUM*

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ABSTRACT.—*Bongardia chrysogonum* of Jordanian origin has yielded the phenolic fatty ester bongardol [**1**] and the amidic alkaloid jordanine [**3**].

Bongardia chrysogonum C.A. Mey. (Leonticaceae) is a small plant native to the eastern Mediterranean. In Jordan, it is known as "Uruf-el-Deek" (Rooster's Coxcomb) due to the deep red dots spotted on the leaves. Both the rhizomes and leaves are edible, possessing a taste resembling that of lemons. Additionally, the boiled extracts are used locally in the treatment of epilepsy. The only recorded previous study of *B. chrysogonum* had resulted in the isolation of the stylbenoid base leonticine, which corresponds to the Hofmann product from the tetrahydrobenzylisoquinoline alkaloid petaline (1,2).

With a view to a further investigation of this plant, the aerial parts and the tubers were collected in southern Jordan at Al Karak within sight of the old crusaders' castle.

Alkaloidal as well as neutral and acidic fractions were investigated. Known alkaloids found were the phenethylamine hordenine (3), and the tetrahydrobenzylisoquinolines (+)-reticuline (4), (+)-codamine (5), (±)-*N*-methylcoclaurine (6) and (+)-coclaurine (7). Among the neutral and acidic compounds were methyl 4-hydroxyphenylacetate (8), which was present in large amounts, 4-hydroxyphenylacetamide (9), 4-hydroxyphenethyl alcohol (10), propionamide (11), 4-hydroxy-3-methoxyphenethyl alcohol (12), 4-hydroxy-3-methoxyphenylpropyl alcohol (13), octadecanoic acid (14), hexacosanoic acid (15), triacontanoic acid (16), and the nearly ubiquitous β-sitosterol.

RESULTS AND DISCUSSION

The first new compound obtained was the colorless and crystalline phenolic fatty ester bongardol [**1**], $C_{36}H_{64}O_3$. The 500 MHz nmr spectrum ($CDCl_3$) of this material, summarized around structure **1**, exhibited 2-proton doublets at δ 7.08 and 6.77 (J_o = 8.5 Hz) corresponding to two sets of ortho aromatic protons. The presence of two coupled 2-proton triplets at δ 4.26 and 2.87 denoted two adjacent methylenes, with the downfield signal indicating a methylene next to oxygen, while the upfield signal suggested a benzylic methylene. A fatty ester chain was also present resulting in a strong multiplet at δ 1.29, a 2-proton triplet at δ 2.29 representing the methylene adjacent to the carbonyl, and a 2-proton multiplet at δ 1.61 denoting the methylene hydrogens next in line. Finally, a 3-proton triplet upfield at δ 0.90 described the terminal methyl group.

The ^{13}C-nmr spectrum of bongardol, supplemented by a GASPE analysis, further buttressed the structural assignment. The results have been summarized around structure **1a**. The most salient feature of the spectrum is the short peak at δ 173.9 typical of ester carbonyls (17).

The ei mass spectrum of bongardol did not yield a noticeable molecular ion. Rather, a McLafferty rearrangement resulted in formation of base peak *m/z* 120, C_8H_8O, corresponding to 4-hydroxystyrene (18). The molecular ion, *m/z* 544, could be observed, however, through cims.

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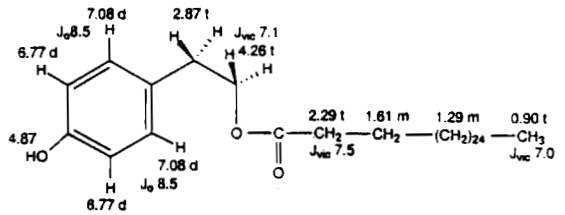
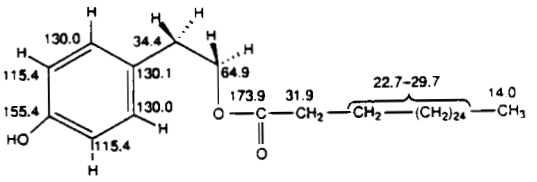
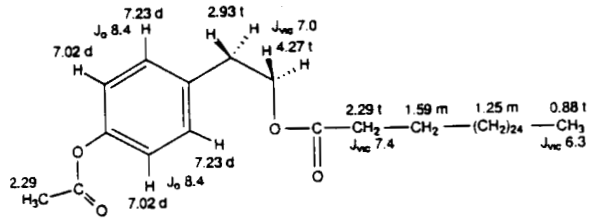

7.08 d
J_o8.5
2.87 t
J_{vic} 7.1
6.77 d
4.26 t
2.29 t
1.61 m
1.29 m
0.90 t
J_{vic} 7.5
J_{vic} 7.0
4.87
HO
7.08 d
J_o 8.5
6.77 d

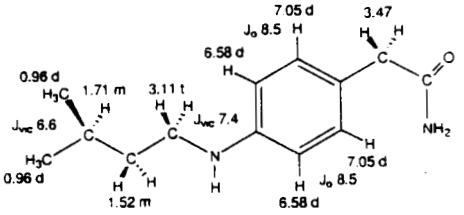
1


130.0
34.4
115.4
130.1
64.9
155.4
130.0
173.9
31.9
22.7–29.7
14.0
HO
115.4

1a


7.23 d
J_o 8.4
2.93 t
J_{vic} 7.0
7.02 d
4.27 t
2.29 t
1.59 m
1.25 m
0.88 t
J_{vic} 7.4
J_{vic} 6.3
7.23 d
2.29
J_o 8.4
7.02 d

2


7.05 d
J_o 8.5
3.47
6.58 d
0.96 d
1.71 m
3.11 t
J_{vic} 6.6
J_{vic} 7.4
NH_2
7.05 d
0.96 d
J_o 8.5
1.52 m
6.58 d

3

Complementing the above data was the ir spectrum, which exhibited a strong ester carbonyl band at 1720 cm^{-1} and a phenolic hydroxyl absorption at 3550 cm^{-1}.

Acetylation of bongardol with Ac_2O in pyridine provided bongardol acetate, $C_{38}H_{66}O_4$, whose nmr spectrum has been indicated around structure **2**. Significantly, the acetoxyl methyl singlet appeared at δ 2.29, while the aromatic doublets were now shifted further downfield to δ 7.02 and 7.23. The mass spectrum of bongardol acetate displayed small molecular ion *m/z* 586, and larger peak *m/z* 162, $C_{10}H_{10}O_2$, corresponding to 4-acetoxystyrene, again generated through a McLafferty rearrangement. As with the mass spectrum of bongardol itself, the base peak was *m/z* 120 and represented 4-hydroxystyrene.

Conclusive proof of structure was provided by synthesis. Acid-catalyzed condensation of octacosanoic acid with 4-hydroxyphenethyl alcohol led to material identical in all respects (nmr, ir, ms, tlc) with the natural product.

The second new compound from *B. chrysogonum* was the colorless, crystalline amidic alkaloid jordanine [**3**], $C_{13}H_{20}N_2O$. The 360 MHz nmr spectrum of this monocyclic compound is quoted around structure **3**. In a pattern reminiscent of that for bongardol [**1**], two sets of aromatic ortho coupled protons were in evidence at δ 7.05 and 6.58. A sharp 2-proton singlet at δ 3.47 pointed to the presence of benzylic protons adjacent to a carbonyl. Finally, peaks and multiplicities characteristic of an isoprene unit attached to an amine function were in evidence at δ 3.11, 1.52, 1.71, and 0.96. In particular, the δ 0.96 signal appeared as a clean 6-proton doublet with $J_{vic} = 6.6$ Hz.

The presence of the amide function in jordanine [**3**] was also suggested by the ir spectrum, which showed a strong carbonyl absorption at 1670 cm^{-1} and NH stretching bands at 3510 and 3400 cm^{-1}.

The mass spectrum of jordanine [**3**] included molecular ion *m/z* 220 (27%) and base peak *m/z* 176, $C_{12}H_{18}N$, due to loss of $CONH_2$ from the molecular ion. Another strong peak was *m/z* 163, $C_9H_{11}N_2O$, caused by alternate loss of $(Me)_2CHCH_2$ from the molecular ion.

Synthesis was again used as final proof of structure. Condensation of ethyl 4-aminophenylacetate with 1-bromo-3-methylbutane in the presence of K_2CO_3 and diisopropylamine led to the ethyl ester corresponding to **3**. Treatment of this ethyl ester with NH_3 then generated material identical (nmr, ir, ms, tlc) with jordanine [**3**].

It should be pointed out that bongardol [**1**] is the first known naturally occurring ester of 4-hydroxyphenethyl alcohol and a fatty acid, specifically octacosanoic acid. Furthermore, no alkaloids structurally related to jordanine [**3**] are known, although it is quite possible that 4-hydroxyphenylacetic acid may act as one of the biogenetic precursors. Interestingly enough, no leonticine or petaline was found in the course of the present work.

EXPERIMENTAL

PLANT COLLECTION AND EXTRACTION.—The tubers and aerial parts of *B. chrysogonum* were collected in April 1986, from a cultivated field at Al Karak near the Wadi Al Mojeb in southern Jordan. A sample specimen was deposited in the Herbarium of the University of Jordan. The dried ground plant (10.5 kg) was defatted with petroleum ether and extracted with cold MeOH. Evaporation of the solvent left a residue which was treated with 5% HCl and filtered. The insoluble residue was dissolved in $CHCl_3$ and fractionated on a Si gel column. Elution was with $CHCl_3$ gradually enriched with MeOH. The different fractions were further purified by tlc on Si gel glass plates to provide bongardol [**1**] (120 mg), octadecanoic acid (57 mg), hexacosanoic acid (60 mg), triacontanoic acid (85 mg), and β-sitosterol (161 mg).

The fraction soluble in HCl was basified with NH_4OH and extracted with $CHCl_3$. The organic solvent was evaporated and the residue chromatographed on a Si gel column. The eluent was again $CHCl_3$ slowly enriched with MeOH. Compounds thus obtained were jordanine (3 mg), (+)-reticuline (16 mg), (+)-codamine (6 mg), (±)-*N*-methylcoclaurine (7 mg), (+)-coclaurine (44 mg), hordenine (100 mg), methyl 4-hydroxyphenylacetate (5.5 g), 4-hydroxyphenylacetamide (823 mg), 4-hydroxyphenethyl al-

cohol (123 mg), propionamide (15 mg), 4-hydroxy-3-methoxyphenethyl alcohol, and 4-hydroxy-3-methoxyphenylpropyl alcohol (9 mg). All the known compounds were characterized spectroscopically (nmr, ir, ms) or by comparison with known samples.

BONGARDOL [**1**].—Mp 81–82° (MeOH); uv λ max (hexane) 220, 276, 368, 422 nm (log ε 3.85, 3.43, 2.94, 2.96); ir ν max ($CHCl_3$) 1410, 1500, 1720, 2810, 3550 cm^{-1}; eims *m/z* 424 (0.1), 407 (0.1), 396 (0.03), 379 (0.04), 120 (100), 57 (7), 43 (9); cims in isobutane *m/z* 545 for mol wt 544.

BONGARDOL ACETATE [**2**].—Acetylation of **1** with Ac_2O in pyridine at room temperature afforded **2**; mp 66–67° (MeOH); ir ν max ($CHCl_3$) 1450, 1500, 1720, 1750, 2820, 2910, 2920; uv λ max (hexane) 216, 264, 270 nm (log ε 3.75, 3.55, 2.48); eims *m/z* $[M]^+$ 586 (0.01), 544 (0.01), 424 (0.01), 407 (0.1), 379 (0.1), 162 (18), 120 (100); cims *m/z* 587 for mol wt 586.

SYNTHESIS OF **1**.—Octacosanoic acid (150 mg) was mixed with 4-hydroxyphenethyl alcohol (350 mg) in anhydrous Et_2O (10 ml), and a small amount of dry HBr gas was added. The solution was refluxed very gently overnight, using an efficient condenser. Workup provided **1** (15 mg) identical with the natural product.

JORDANINE [**3**].—Mp 167–170° (MeOH); uv λ max (MeOH) 253, 368, 402, 424 nm (log ε 3.51, 1.92, 1.97, 1.92); ir ν max ($CHCl_3$) 1300, 1510, 1570, 1610, 1670, 2910, 2930, 3000, 3400, 3510 cm^{-1}; eims *m/z* $[M]^+$ 220 (27), 176 (100), 163 (69), 119 (23), 106 (33), 57 (2), 43 (21); hrms calcd for $C_{13}H_{20}N_2O$, 220.1576, found 220.1560.

SYNTHESIS OF **3**.—A mixture of ethyl 4-aminophenylacetate (0.68 g), 1-bromo-3-methylbutane (3 g), and K_2CO_3 (0.5 g) in diisopropylamine (3.5 ml) was refluxed with stirring overnight. Workup supplied the crude oily ethyl ester corresponding to jordanine. This material was dissolved in EtOH, and NH_3 gas was added. The mixture was refluxed gently for 3 days under an efficient condenser. Additional amounts of NH_3 gas were added intermittently. Workup supplied jordanine [**3**] (66 mg) identical with the natural product.

ACKNOWLEDGMENTS

This research was supported by National Science Foundation grant INT-8805184.

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Received 23 February 1989