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ALKALOIDS AND OLEFINIC ACIDS FROM *CRYPTOCARYA AMYGDALINA*

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Key Word Index—*Cryptocarya amygdalina*; Lauraceae; novel olefinic acids; benzylisoquinoline alkaloids.

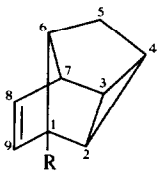
Abstract—From the bark of *Cryptocarya amygdalina* two new olefinic acids with a tetracyclo(4.3.$0^{2,4}$.$0^{3,7}$) non-8-ene moiety are reported. From the same source the benzylisoquinoline alkaloids orientaline and laudanidine are also reported.

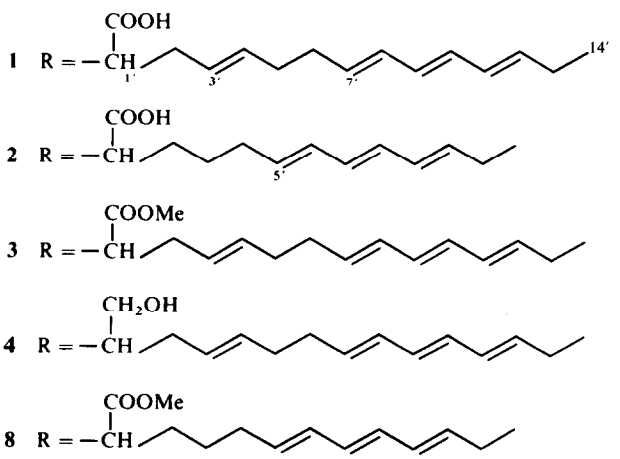
In the course of our phytochemical investigation on Lauraceae plants we isolated two new olefinic acids, cryptocaryic acid (**1**) and amygdalinic acid (**2**), in addition to two known benzylisquinoline alkaloids, (+)-orientaline (**10**) and laudanidine (**11**). The isolation and structure elucidation of **1** and **2** are reported here.

Cryptocaryic acid (**1**), $C_{24}H_{30}O_2$, M^+ 350, mp 112°, IR (KBr) 1700 (>C=O) cm^{-1}, exhibits a UV spectrum in EtOH at 258 (4.54), 268 (4.66) and 278 (4.54) nm, respectively, for a conjugated triene system. The presence of a carboxylic acid group was confirmed by preparing the Me ester **3** [NMR δ 3.65 (*s*, 3H,-COOMe)]. The presence of a >CH—COOH group was also confirmed by reducing **3** with $LiAlH_4$ to the corresponding >CH—CH_2OH compound **4** [NMR δ 3.47 (*d*, 2H, J = 6–7 Hz, CH_2 of $CHCH_2OH$ system)].

Although the hydrogenation of **1** over Pd–C or Pt_2O gave decahydrocryptocaryic acid (**5**), the hydrogenation of the last double bond was difficult, which suggested that out of the five double bonds of **1** one was in the ring and remaining four were outside it. The NMR of the partially reduced compound **6** exhibited two ring olefinic protons at δ 5.3 and 5.4 respectively. The presence of a long side chain was confirmed from the high resolution mass spectrum of **5** and its Me ester **7** which gave base peaks at *m/e* 178 and 192, respectively, due to McLafferty rearrangement (Table 1).

The ^{1}H NMR spectrum of **1** showed a Me triplet at δ 1.0 (*s*, 3H, J = 7 Hz) and a methylene quartet at 2.05 (1, 2H, J = 7 Hz) for a terminal Et group. A prominent peak at *m/e* 121 appeared in the mass spectrum of **1** but was absent in those of **5** and **7**, suggesting that this peak arises from the β-cleavage to the double bond. Therefore, from spectral data of **1** and biogenetic considerations, the triene was placed at the Et end. The position of the fourth double bond was fixed primarily from mass spectrometry, but was also supported by NMR data. It is known that if the only γ-hydrogen available is attached to a double bond, transfer of such a hydrogen and elimination of a neutral allene molecule is an unfavourable process. As in the mass





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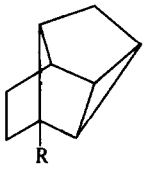
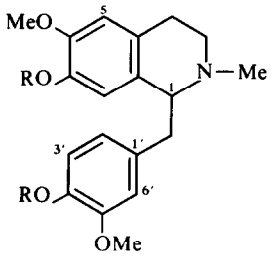


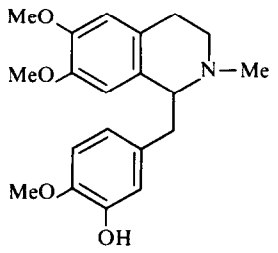
5 R = —CH(COOH)—CH_2—$(CH_2)_{11}$—Me

7 R = —CH(COOMe)—CH_2—$(CH_2)_{11}$—Me

9 R = —CH(COOH)—CH_2—$(CH_2)_9$—Me



10 R = H
12 R = Ac



11

spectrum of cryptocaryic acid (**1**) no McLafferty rearrangement was observed so that the double bond is located at the γ-carbon to the carboxylic acid group.

To accommodate four rings and a ring double bond in the C_9H_9 part of **1**, we examined the Dreiding model and found that the tetracyclo(4.3.$0^{2,4}$.$0^{3,7}$)non-8-ene [1] skeleton was free from strain, and also that the 6H methine proton which remained above the plane of the ring double bond appeared in the NMR at higher field, i.e. δ 1.26 (*m*, 1H).

The second olefinic acid, amygdalinic acid (**2**), $C_{22}H_{28}O_2$, M^+ 324, IR(KBr) 1700 (>C=O) cm^{-1} exhibited peaks in the UV spectrum in EtOH at 258 (4.78), 269 (4.90) and 278 (4.79) nm, respectively, for a triene system. The presence of a carboxylic acid group was confirmed by preparing the corresponding Me ester **8**, NMR δ 3.78 (*s*, 3H, COOMe). The presence of four double bonds was confirmed by hydrogenation of **2** over Pd–C in MeOH to obtain octahydroamygdalinic acid (**9**), $C_{24}H_{36}O_2$, mp 56–62°. The appearance of a *m/e* 117 (C_9H_9) peak in the mass spectrum of **2**, as in **1**, and a high field methinine proton at δ 1.35 (*m*, 1H) suggested a tetracyclo(4.3.$0^{2,4}$.$0^{3,7}$)non-8-ene (**1**) moiety for **2** also. The close similarity of UV, NMR and mass spectral data of **2** with that of **1** and their isolation from the same source suggested almost identical structure of **2** with that of cryptocaryic acid (**1**).

It is important to observe that (+)-orientaline (**10**), which was isolated along with another benzylisoquinoline alkaloid, laudanidine (**11**), was for the first time isolated from a Lauraceae plant, the first natural source being a Menispermaceae plant [2–4]. (+)-Orientaline was identified from its mp, UV, mass spectral data and comparison of its NMR with that of its *O,O*-diacetyl derivative **12**. Compound **11** was identified from its mp, UV, mass spectrum and comparison of IR spectrum with that of an authentic sample.

Table 1. High resolution mass fragmentation of **5** and **7**

Compound	MS peak for *m/e* (rel. int.)						
	McLafferty (a)	$M^+ - CO_2R$	$M^+ - C_{10}H_{20}$	$M^+ - C_{11}H_{23}$	(a) $- CO_2R$ (b)	(b) − 2H	(c)
5, $C_{24}H_{40}O_2$ M^+ 360.3008 (18)	178.0990 (100)	315.3037 (13)	220.1432 (10)	205.1235 (10)	133.1004 (47)	131.0849 (15)	119
7, $C_{25}H_{42}O_2$ M^+ 374.3153 (27)	192.1148 (100)	315.2994 (37)	234.1579 (11)	—	133.1003 (68)	131.0855	119

Table 2. ^{1}H NMR data of compounds **1** and **2**

Protons	**1**		**2**	
	Signal position (δ)	Splitting, J, No. of protons	Signal position (δ)	Splitting, J, No. of protons
Olefinic	6.3–7.3	*m*, 10H	5.6–6.4	*m*, 8H
1′CH	3.0	*s*, 1H	3.07	*m*, 1H
7CH	3.0	*s*, 1H	2.87	*d*, 4 Hz, 1H
2′CH	2.52	*m*, 2H	2.54–2.77	*m*, 2H
2CH, 3H, 4H and 5CH_2	1.42–1.73	*br. m*, 5H	1.54–1.86	*brm*, 5H
6H	1.26	*m*, 1H	1.35	*m*, 1H
5′CH_2 6′CH_2	1.9–2.38	*m*, 4H	—	—
11′CH_2, 3′CH_2 and 4′CH_2	—	—	2.0–2.43	*m*, 6H
13′CH_2	2.05	*q*, 7 Hz, 2H	—	—
14′Me	1.0	*t*, 7 Hz, 3H	—	—
12′Me	—	—	1.03	*t*, 7 Hz, 3H

EXPERIMENTAL

Olefinic acids. Air-dried, crushed bark (collected from the Sibsagar district of Assam) of *C. amygdalina* (500 g) was extracted with petrol (40–60°) for 96 hr, concd and kept overnight at 0° to obtain pale yellow flakes of **1** (200 mg) which was further recrystallized from petrol (40–60°). Mp 112°; MS: M^+ 350, *m/e* (321, 268, 121, 117, 93, 91, etc.); UV λ_{max}^{EtOH} (log ε) nm: 258 (4.54), 268 (4.66) and 278 (4.54); IR(KBr) cm^{-1}: 1700 (>C=O); ^{1}H NMR ($CDCl_3$, 100 MHz): see Table 2.

After separation, 180 mg of **2** separated out from the mother liquor, which was further crystallized from petrol (40–60°). Mp 115°; MS: M^+ 324, *m/e* (264, 131, 121, 117, 93, 91, etc.); UV λ_{max}^{EtOH} (log ε) nm: 258 (4.78), 269 (4.90) and 278 (4.79); IR(KBr) cm^{-1}: 1700 (>C=O); ^{1}H NMR: see Table 2. *Preparation of* **3**. 50 mg of **1** was treated 18 hr with CH_2N_2–Et_2O to obtain 40 mg of **3**. ^{1}H NMR (CCl_4, 60 MHz): δ 1.01 (*t*, 3H, J = 7 Hz, Me of $MeCH_2$), 3.65 (*s*, 3H, COOMe), 5.5–6.1 (*m*, 10H, olefinic protons) along with methylene and methine protons between 1.3–3.0. *Preparation of* **4**. 30 mg of **3** was reduced with $LiAlH_4$ in dry Et_2O to obtain *ca* 20 mg of **4**. ^{1}H NMR (CCl_4): δ 1.0 (*t*, 3H, J = 7 Hz, Me of $MeCH_2$), 2.07 (*q*, 2H, J = 7 Hz, CH_2 of $MeCH_2$), 3.47 (*d*, 2H, J = 6–7 Hz, CH_2 of R-CH-CH_2OH), 5.3–6.05 (*m*, 10H, olefinic protons) along with other aliphatic protons between 2.7 and 1.2. *Preparation of* **5**. 100 mg of **1** was hydrogenated over Pd/C in EtOH to obtain 48 mg of **5**. Mp 61–62°; MS: M^+ 360 (Table 1); ^{1}H NMR ($CDCl_3$, 100 MHz): 0.8–2.5 broad envelope of protons. *Preparation of* **7**. 30 mg **3** was hydrogenated over Pt_2O in MeOH to obtain 26 mg of **7**. MS: M^+ 374 (Table 1); ^{1}H NMR: δ 3.73 (*s*, 3H, –COOMe). *Preparation of* **8**. 45 mg of **2** treated with CH_2N_2–Et_2O yielded 18 mg of **8**. ^{1}H NMR (CCl_4, 60 MHz): δ 1·05 (*t*, 3H, J = 7 Hz, Me of $MeCH_2$), 1.32 (*s*, 1H, methine proton above the plane of a double bond), 2.17 (*q*, 2H, J = 7 Hz, CH_2 of $MeCH_2$), 2.85 (*d*, J = 3 Hz), 3.05 (*t*, J = 4 Hz, 1H, methine proton of CH-COOH), 3.78 (*s*, 3H, —COOMe), 6.0–6.3 (*m*, 8H, olefinic protons) and other aliphatic protons between 2.7 and 1.5. *Preparation of* **9**. 80 mg of **2** was hydrogenated over Pd/C in 10 ml EtOH at ambient pres. and temp. to obtain **9**. Mp 58–62° (Found: C = 79%, H = 10.2%, Calc. 79.51%, H = 10.58%). ^{1}H NMR ($CDCl_3$) a broad envelope of peaks between δ 0.9 and 2.6.

Alkaloids. The above de-fatted bark was worked up for phenolic tertiary N compounds to obtain 260 mg crude phenolic alkaloid which was passed through a neutral Al_2O_3 column and eluted with petrol, C_6H_6, EtOAC and MeOH in different proportions. From MeOH–EtOAc (1:9) 40 mg crude (on TLC) along with 7 mg pure (TLC one spot) **10** was obtained. Mp 80–87°; MS *m/e* (rel. int.): 192 (100), 177 (35) and 137; IR(KBr) cm^{-1}: 3500–3400 for —OH band; UV λ_{max}^{EtOH} nm: 283 (3.7).

Optical rotation

$$[\alpha]^{25} = (+)\frac{\begin{matrix}589 & 578 & 546 & 436\\ 69^\circ & 75^\circ & 87^\circ & 95^\circ\end{matrix}}{} \quad (c = 0.2, CHCl_3).$$

Table 3. ^{1}H NMR data of compounds **10** and **12**

Compound	Position of protons (δ)							
	5	8	2	3	6	N Me	O Me	OAc
10 in $CDCl_3$	6.55 (*s*)	6.36 (*s*)	6.742 *d*, J = 1–2 Hz	6.61 *dd*, J = 1–2 and 7–8 Hz	6.74*d*, J = 7–8 Hz	2.50 (*s*)	3.86 (*s*) and 3.87 (*s*)	—
12 in CCL_4	6.41 (*s*)	6.66 (*s*)	6.74 *d*, J = 1–2 Hz	6.92 *dd*, J = 1·2 and 7–8 Hz	6.825 *d*, J = 7–8 Hz	2.56 (*s*)	3.80 (*s*) and 3.80 (*s*)	2.27 (*s*) and 2.30 (*s*)

^{1}H NMR ($CDCl_3$, 270 MHz): see Table 3. After separation of **10** all the fractions from the column were collected and subjected to repeated prep. TLC on Si gel in MeOH–$CHCl_3$ (3:17) to obtain 4 mg of **11**. Mp 179–180°; MS: M^+ 345 for $C_{19}H_{25}NO_4$, *m/e* 206 (100), UV λ_{max}^{EtOH} nm: 282. *Preparation of* **12**. 35 mg of crude **10** was treated 18 hr with Ac_2O–pyridine, the product passed through a neutral Al_2O_3 column and 18 mg *O,O*-diacetate of **10** (or **12**) was collected from the EtOAc eluent. MS *m/e* (rel. int.): 234 (100), 192, 177 and 137. UV λ_{max}^{EtOH} nm: 230 and 277. IR (CCl_4) cm^{-1}: two OAc bands at 1765 and 1740 respectively.

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REFERENCES

1. Freeman, P. K., Balls, D. M. and Blazevich, J. N. (1970) *J. Am. Chem. Soc.* **92,** 205.
2. Freeman, P. K., and Balls, D. M. (1967) *J. Org. Chem.* **32,** 2354.
3. Fukuda, F. (1953) *Pharm. Bull. (Jpn.)* **1,** 189.
4. Tomita, M. and Yamaguchi, H. (1965) *Pharm. Bull. (Tokyo)* **4,** 225.