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PHENOLIC CONSTITUENTS OF ELM WOOD

2-NAPHTHOIC ACID DERIVATIVES FROM *ULMUS THOMASII*

CHEN-LOUNG CHEN and F. D. HOSTETTLER

Forest Products Laboratory,* Forest Service, U.S. Department of Agriculture, Madison, Wisconsin 53705

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Abstract—Two new 2-naphthoic acid derivatives have been isolated from the aqueous extract of the heartwood of *Ulmus thomasii* Sarg. They have been shown to be 6-hydroxy-5,7-dimethoxy-2-naphthoic acid (I) and 6-hydroxy-3-hydroxymethyl-5,7-dimethoxy-2-naphthoic acid lactone (IV). The NMR spectra of several related naphthols and naphthoic acids and their derivatives have been examined. Acetylation of naphthol derivatives produces a characteristic downfield shift of naphthalene protons *ortho* to OH groups in their NMR spectra.

THOMASIC ACID, three other related lignans including a glycoside, and 2,6-dimethoxy-*p*-benzoquinone were previously isolated from aqueous extracts of the heartwood of *Ulmus thomasii* Sarg.[1,2] These lignans are biogenetically interesting because they can be regarded as *in vivo* dehydrogenative condensation products of either sinapic acid or sinapyl alcohol. In this communication we report the proof of structure of two minor constituents isolated from the same aqueous extracts, the 2-naphthoic acid derivatives (I and IV).

Compound I was found to have the molecular formula $C_{13}H_{12}O_5$ and to possess two OMe groups. The presence of an aromatic OH and a carboxyl group were indicated by IR spectroscopy and by the bathochromic and hypsochromic shifts[2] observed respectively in the UV spectrum when sodium ethoxide solution and sodium acetate were added. The UV spectrum also indicated the presence of a naphthalene nucleus and the aromatic region of the NMR spectrum corresponded to four protons (Table 1). Three of these constituted a characteristic ABX system with coupling constants $J_{AB} = 8{\cdot}4$ MHz and $J_{BX} = 1{\cdot}5$ MHz, indicative of an *ortho* and a *meta* relationship of the protons, hence a 1,3,4-relationship of three hydrogens. Furthermore, the deshielding of these protons was also evidence for a 2-naphthoic acid derivative[3] with the remaining functional groups substituted on ring A.

Compound I afforded a trimethoxy methyl ester $C_{15}H_{16}O_5$ (II) on treatment with dimethylsulfate in presence of K_2CO_3 and a monoacetoxy-dimethoxy-carboxylic acid (III) by acetylation. NMR spectra for the derivatives may be found in Table 1.

The mass spectrum of compound II showed two fragmentation sequences (Fig. 1 and Scheme 1). Loss of $\dot{O}Me$ from the molecular ion (*m/e* 276), caused by methyl ester cleavage, produced the ion at *m/e* 245. The molecular ion also lost successively $\dot{C}H_3$, CO, and $\dot{C}H_3$, which is characteristic of a 1,2,3-trimethoxybenzenoid compound.[4] Of the two possible structures, only that of methyl 5,6,7-trimethoxy-2-naphthoate (II) was compatible with the NMR spectrum. In comparison with the

* Maintained at Madison, Wis., in cooperation with the University of Wisconsin.

TABLE 1. NMR SPECTRA[a,b,c] of β-NAPHTHOIC ACID DERIVATIVES

Compound	H-1	H-3	H-4	H-5	H-8	Methoxy		Miscellaneous
I	8·51 d (1) J = 1·5	7·89 m (1) J = 8·4; 1·5	8·06 d (1) J = 8·4		7·30 s (1)	4·02 s (6)		
II	8·42 d (1) J^d = 1·5	7·83 m (1) J^d = 9·0; 1·5	8·04 d (1) J^d = 9·0		7·25 s (1)	4·00 s (3), 3·90 s (3),	3·96 s (3) 3·88 s (3)	
III[b]	8·58 d (1) J = 1·5	7·93 m (1) J = 8·8; 1·5	8·15 d (1) J = 8·8		7·40 s (1)	4·00 s (3),	3·96 s (3)	2·37 s (3) (acetyl)
IV[b]	8·28 s (1)		8·10 t (1) J^d = 1·3		7·48 s (1)	4·02 s (3)	3·99 s (3)	5·47 d (2) J^d = 1·3 (C—CH_2—O—)
VII[c]	8·03 d (1) J = 1·5	7·36 d (1) J = 1·5		7·58 s (1)	7·38 s (1)	3·91 s (6)		
VIII	8·31 d (1) J = 1·5	7·70 d (1) J = 1·5		7·18 s (1)	7·07 s (1)	3·98 s (3)	3·92 s (3)	2·41 s (3) (acetyl)
IX	8·03 d (1) J = 1·5	7·26 d (1) J = 1·5		7·48 s (1)	7·10 s (1)	4·01 s (6) 3·93 s (3)	3·96 s (3)	

[a] δ values in ppm using TMS as internal standard. s = singlet, d = doublet, t = triplet, m = multiplet. Figures in parentheses = number of protons. J values in MHz.

[b] Figures given for a 60 Mc instrument except those for III and IV that were measured by a 100 Mc instrument.

[c] Solvent: d_6 acetone except for VII with $CDCl_3$ as solvent.

[d] Gives singlet on decoupling.

TABLE 2. NMR SPECTRA OF COMPOUNDS V AND VI[a]

Compound	H-1 H-5	H-3 H-7	H-4 H-8	J_{13}	J_{14}	J_{34}	Methoxy
V	8·58	8·08	7·94	1·3	0·3	8·6	3·97
Compound	**H-2 H-3**	**H-5 H-8**	**H-6 H-7**	J_{56}	J_{57}	J_{58}	J_{67}
VI	6·70	8·17	7·45	8·3	1·4	0·3	6·6

[a] W. Brügel, *Nuclear Magnetic Resonance Spectra and Chemical Structure* pp. 128–129. Acad. Press, New York (1967).

NMR spectrum of dimethyl naphthalene 2,6-dicarboxylate (V)[3] (Table 2), it can be observed that the A component (H-4) of the ABX system in the NMR spectrum of compound II is shifted downfield, whereas the B and X components are shifted upfield. The downfield shift of the A component is caused by *peri*-deshielding effect of the α-OMe group, as shown by the NMR spectrum of 1,4-dimethoxynaphthalene (VI)[3] in comparison with that of compound II. The three OMe groups of compound II are therefore substituted at C-5, C-6, and C-7.

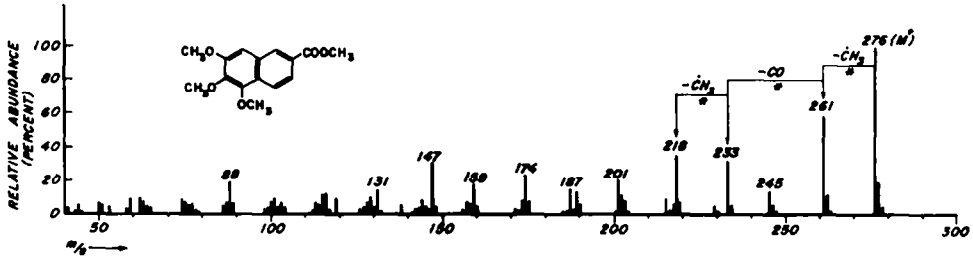
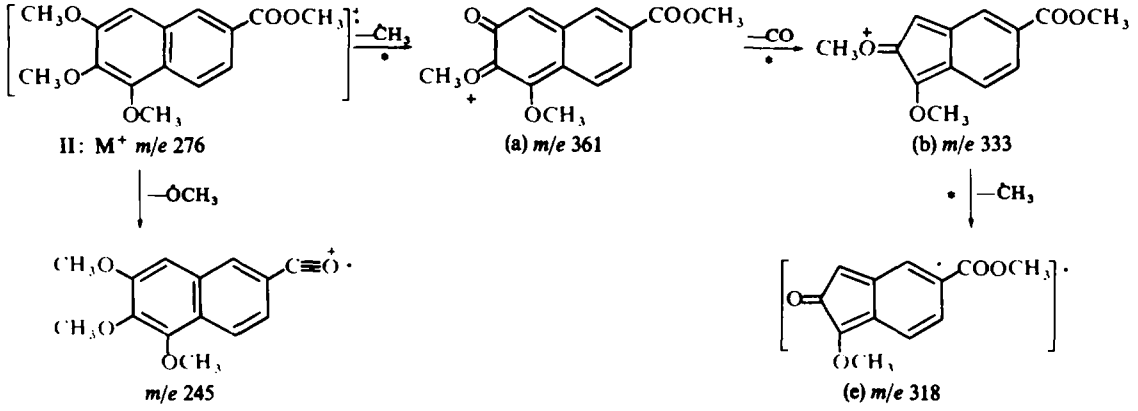


FIG. 1 Mass spectrum of compound II (determined on an AEI MS 12 mass spectrometer).

SCHEME 1. Transitions substantiated by an appropriate metastable peak are indicated by an asterisk.



The mass spectrum of the mono-acetate (III) exhibited ion peaks corresponding to successive loss of $CH_2{=}C{=}O$ and $\dot{C}H_3$ from the molecular ion, which is characteristic of an *o*-acetoxy-methoxybenzenoid compound,[4] as indicated in Scheme 2 and Table 3. Its NMR spectrum showed no marked difference from that of the parent

TABLE 3. MASS SPECTRA OF 2-NAPHTHOIC ACID DERIVATIVES[a]

Compound	*m/e*	43	89	105	133	201	233	234	248	249	290			
III	I (%)	21	5	5	9	10	45	7	100	13	17			
Compound	*m/e*	40	41	43	44	51	55	57	77	89	105	117	145	156
IV	I (%)	11	8	11	9	5	7	9	5	5	5	5	5	6
		173	213	216	217	231	245	246	260	261				
		7	6	6	7	15	59	8	100	16				

[a] All peaks with a relative abundance greater than 5% of the base peak are recorded.

TABLE 4. NMR SPECTRA OF 2,3-DIHYDROXY NAPHTHALENE AND DERIVATIVES[a]

Compound	H-1 H-4	H-7[b] H-6	H-8[b] H-5	Miscellaneous
X	7·29 s (2)	7·23 m (2)	7·65 m (2)	8·74 (hydroxy) Br (2)
XI	7·80 s (2)	7·53 m (2)	7·94 m (2)	2·33 (acetyl) s (6)
XIII	7·27 s (2)	7·32 m (2)	7·76 m (2)	3·93 (methoxy) s (6)

[a] See Table 1, footnotes *a*, *b*, *c*.

[b] H-5, H-6, H-7, and H-8 constitute an AA'BB' system. No accurate K, L, M, and N parameters could be calculated because of merging lines; chemical shifts are therefore approximate values.

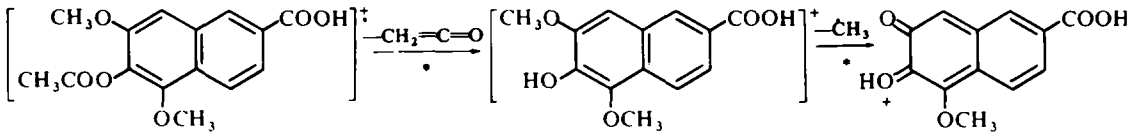
TABLE 5. NMR SPECTRA OF 2,7-DIHYDROXY NAPHTHALENE AND DERIVATIVES[a]

Compound	H-1 H-8	H-3 H-6	H-4 H-5	J_{13}	J_{14}	J_{34}	Miscellaneous
XIII	7·13 s (2)	7·00 m (2)	7·70 m (2)	2·7	0·3	8·6	8·92 (hydroxy) Br (2)
XIV	7·58 s (2)	7·28 m (2)	7·89 m (2)	2·6	0·3	8·6	2·24 (acetyl) s (6)
XV	7·17 s (2)	6·94 m (2)	7·66 m (2)	2·6	0·3	8·6	3·85 (methoxy) s (6)

[a] See Table 1, footnotes *a*, *b*, and *c*.

compound I, except a slight downfield shift (~0·10 ppm) of all aromatic protons. In contrast, after acetylation of 4-hydroxy-6,7-dimethoxy-2-naphthoic acid (VII), 2,3-dihydroxynaphthalene (X), and 2,7-dihydroxynaphthalene (XIII), the protons *ortho* to OH groups showed a characteristic downfield shift in their NMR spectra caused by the deshielding effect of the acetyl group (Tables 4 and 5). Compound I therefore has no hydrogen atom *ortho* to its OH group. Furthermore, the A component in the NMR spectrum of compound III like that of compound I was apparently deshielded indicative of the presence of a C-5 OMe group. The compound I is therefore 6-hydroxy-5,7-dimethoxy-2-naphthoic acid.

SCHEME 2. Transitions substantiated by an appropriate metastable peak are indicated by an asterisk.



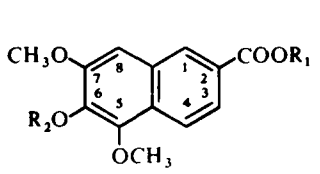
III: M^+ *m/e* 290 (d), *m/e* 248 (e), *m/e* 233

Compound IV isolated only in small amounts, was shown by mass spectrometry to have the molecular formula $C_{14}H_{12}O_5$. Its IR and NMR spectra showed the presence of an OH, two OMe, and a γ-lactone groups. The UV spectrum and the characteristic bathochromic shift observed on the addition of sodium ethoxide solution revealed the naphthol nature of the compound.

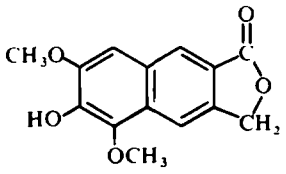
In its NMR spectrum, the application of double-irradiation technique resulted in decoupling of the two-proton doublet at δ 5·47 (Ar—X)—C<u>H</u>$_2$—O—) and the one-proton triplet at δ 8·10 (Ar—<u>H</u>) to give singlets. This could be rationalized by assuming a four-bond long-range σ-π-spin–spin interaction[5] between those protons. This required that the methylene group of the lactone be situated at β-position on a naphthalene nucleus. The large deshielding of the aromatic proton singlet at δ 8·28 was evidence of an α-proton *ortho* to a deshielding group such as the >C=O. The compound (IV) therefore is a derivative of 3-hydroxymethyl-2-naphthoic acid lactone with the remaining three functional groups substituted at ring A. The one-proton singlet at δ 7·48 was apparently caused by the α-proton of a naphthalene nucleus. The deshielding of H-4 was evidence of a C-5 methoxyl group (see discussion of *peri*-deshielding effect of the α-methoxyl group). The mass spectrum of the compound (Table 3) exhibited a stable molecular ion and an (M-15) ion, indicative of an *o*-hydroxymethoxybenzenoid compound.[4] Two possible structures for compound IV are therefore apparent. However, because of the structure of thomasic acid and compound I, we believe the compound is 6-hydroxy-3-hydroxymethyl-5,7-dimethoxy-2-naphthoic acid lactone (IV).

Compounds I and IV have a skeleton that could be formed by aromatization of thomasic acid with the elimination of the pendant hydroxydimethoxyphenyl group. This together with the presence of 2,6-dimethoxy-*p*-benzoquinone[2] indicates that the formation of these phenolic constituents *in vivo* are biogenetically interrelated to thomasic acid and its homologs.

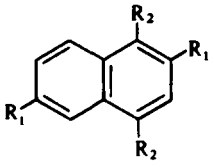
Recently, other naphthols and related compounds, 3-hydroxy-8-isopropyl-5-methyl-2-naphthaldehyde, its 7-methoxy and 5,6,7,8-tetrahydro derivatives, and 7-hydroxycadalene, were isolated from the heartwoods of *Ulmus rubra* Mühl.,[6] *U. glabra* Huds. and *U. carpinifolia* Gled.[7] However, no trace of these compounds could be detected in the extracts of *U. thomasii* Sarg. Thus, a clear-cut chemical difference exists between several woods of different species of the genus *Ulmus*.



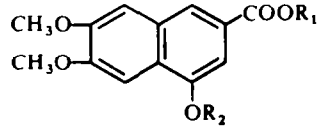
I: $R_1 = R_2 = H$
II: $R_1 = R_2 = CH_3$
III: $R_1 = H$; $R_2 = CH_3CO—$



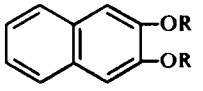
IV



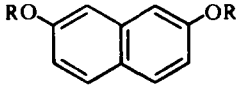
V: $R_1 = —COOCH_3$; $R_2 = H$
VI: $R_1 = H$; $R_2 = —OCH_3$



VII: $R_1 = R_2 = H$
VIII: $R_1 = CH_3$; $R_2 = CH_3CO—$
IX: $R_1 = R_2 = —CH_3$



X: R = H
XI: $R = CH_3CO—$
XII: $R = CH_3$



XIII: R = H
XIV: $R = CH_3CO—$
XV: $R = CH_3$

EXPERIMENTAL

M.ps are uncorrected. UV spectra were determined on a Beckman DK recording spectrophotometer in 95% EtOH with diagnostic shifts obtained by adding (1) 1 drop/ml of 1N NaOEt in EtOH and (2) excess solid NaOAc to the alcohol soln. IR spectra were determined on a Baird infrared recording spectrophotometer in KBr pellets.

NMR spectra were determined in d_6-acetone, unless otherwise specified, on a Varian A-60A or 100 Mc instrument. To some solns D_2O was added to check on exchangeable protons.

Mass spectra were determined on an Altas CH-4 mass spectrometer unless otherwise specified.

Isolation. Compounds I and IV were isolated from aqueous extracts of finely ground heartwood of *Ulmus thomasii* Sarg. The isolation and physical constants of compound I including UV and IR spectral data have been previously reported.[2] On paper chromatography, both of these compounds fluoresce vividly under UV light. Compound I gave a white color that brightened to a fluorescent lavender on fuming with ammonia; compound IV, a white that brightened to fluorescent yellow-orange.

Methyl 5,6,7-trimethoxy-2-naphthoate (II). Compound I was methylated in acetone with Me_2SO_4 in presence of K_2CO_3; the product was purified by preparative TLC (1% MeOH in $CHCl_3$) and recrystallized from EtOH–water. It yielded white needles, m.p. 98–99°; IR, 1710 (Ar ester C=O), 1625, 1608, 1480 (all Ar), 1260 and 1247 (C—O—, Ar ether and ester), 1108 (—OMe), 1092, 1033, and 756 cm^{-1}.

6-Acetoxy-5,7-dimethoxy-2-naphthoic acid (III). Compound I was acetylated by refluxing it in Ac_2O. The product was recrystallized from MeOH–water, m.p. 219–220°; IR, 2970 (OH), 2600 (Ar COOH), 1770 (acetyl C=O), 1686 (Ar acid C=O), 1626, 1608, 1473 (all Ar), 1400, 1325, 1266 (Ar ether), 1212 and 1192 (Ar acetate and COOH), 1120 (OMe), 1024, 910, and 825 cm^{-1}.

6-Hydroxy-3-hydroxymethyl-5,7-dimethoxy-2-naphthoic acid *lactone* (IV). This compound was eluted from polyamide column in the same fraction as compound I.[2] It was separated from I by preparative PC

(banding in isopropyl alcohol–2N ammonia (3:1), R_f 0·55), then purified by preparative TLC (solvent: 2% MeOH in $CHCl_3$), and recrystallized from MeOH–water. It yielded pale tan needles (6 mg), m.p. 188·5–189·5°. It gave a negative test with monochloroquinonimide. UV spectra, λ_{max}^{EtOH} 261 nm ($\varepsilon = 4{\cdot}7 \times 10^4$), 322 nm ($\varepsilon = 9{\cdot}3 \times 10^3$); λ_{max}^{EtONa} 250, 287, and 380 nm; λ_{max}^{NaOAc} 259, 288, 326, and 380 nm; IR, 3460 (OH), 1761 and 1736 (γ-lactone C=O), 1626, 1508, 1484, 1464 (all Ar), 1427, 1311 (Ar—OH), 1276 and 1020 (Ar ether), 1085 (—OMe), and 906 cm^{-1}.

4-Hydroxy-6,7-dimethoxy-2-naphthoic acid (VII). This compound was prepared according to the method of El-Assal and El-Wahhab.[8] It gives m.p 245–246° (recorded, 245°). Compounds VIII, m.p. 141–142°, and IX, m.p. 125–126° were prepared and purified by the methods described for II and III.

2,3-Dihydroxynaphthalene (X) *and 2,7-dihydroxynaphthalene* (XIII) were used as purchased (Eastman Organic Chemicals): Compound X, m.p. 160–161°;[9] diacetate XI, m.p. 104–105°; dimethyl ether XII, m.p. 115–116°; compound XIII, m.p. 189–190°;[10] diacetate XIV, m.p. 135–136°; dimethyl ether XV, m.p. 138–139°.

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