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Components of Podophyllin. VII. Absorption Spectra and Reaction with Iodine of the Dihydro-β-naphthoic Acids[1]

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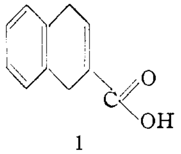
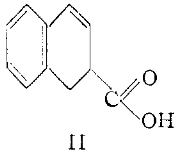
The ultraviolet and infrared absorption spectra of the dihydro-β-naphthoic acids are reported. The reaction of these acids with iodine in aqueous bicarbonate has been studied.

In connection with the investigation of the structure of the apopicropodophyllins,[2] it was desired to compare the absorption spectra of simple model compounds, and the readily prepared[3-5] dihydro-β-naphthoic acids were selected for this purpose.

The ultraviolet absorption spectra of these acids do not appear to have been published previously. However, related data have been presented by v. Auwers and Möller,[5] who studied the molecular refractions and dispersions of the corresponding ethyl esters and found that the exaltations increased in the order: 1,4-dihydro-2-naphthoic acid (I), 1,2-dihydro-2-naphthoic acid (II) and 3,4-dihydro-2-naphthoic acid (III). This was explained by v. Auwers as follows: In I, which is analogous to an α-alkyl-α,β-unsaturated fatty acid, there exists only a single conjugation between the carboxyl group and the ethylenic double bond. II is analogous to styrene, with the double bond conjugated with the aromatic ring. Finally, there exists a "cumulated" conjugation (ring-double bond-carboxyl group) in III, which is analogous to an α-alkyl cinnamic acid. Comparison of III with β-naphthoic acid (IV) showed that the exaltation of the refraction was somewhat lower in the former, and the exaltation of dispersion higher.


I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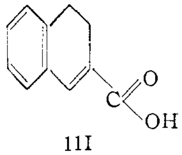
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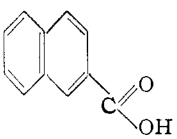
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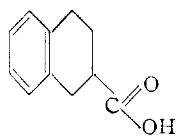
V

The ultraviolet absorption spectra (Fig. 1) are consistent with the observations of v. Auwers. 1,4-Dihydro-2-naphthoic acid (I) does not show any absorption maximum down to 205 $m\mu$, with the exception of the low intensity peak at 273 $m\mu$, which is also present in 1,2,3,4-tetrahydro-2-naphthoic acid (V).[6] Since the α,β-unsaturated carboxyl is not in conjugation with the benzene ring, the spectrum results roughly from an additive combination of the absorptions of tetralin[6] and of an α,β-unsaturated acid.[7] On the other hand, 1,2-dihydro-2-naphthoic acid (II) has a high intensity maximum at 260.5 $m\mu$, resulting from the conjugation between the double bond and the aromatic ring, and which is also present in 1,2-dihydronaphthalene[8] (max. 262 $m\mu$, log ϵ 4.01). Finally, absorption is greatly shifted toward the visible in the 3,4-dihydro-2-naphthoic acid (III), in which the conjugated system includes the benzene ring, the double bond and the carboxyl group. The main feature of the spectrum of this acid is the broad band at 290 $m\mu$. This might be contrasted with the much more detailed spectrum of β-naphthoic acid (IV).[9]

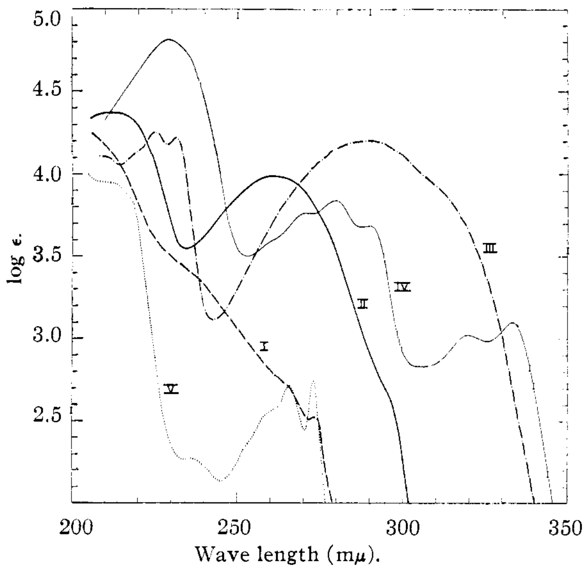

Fig. 1.—Ultraviolet absorption spectra in 95% ethanol of: — — —, 1,4-dihydro-2-naphthoic acid (I); ———, 1,2-dihydro-2-naphthoic acid (II); —·—·—, 3,4-dihydro-2-naphthoic acid (III); ———, β-naphthoic acid (IV); ...., 1,2,3,4-tetrahydro-2-naphthoic acid (V).

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[1] Paper VI: M. V. Nadkarni, P. B. Maury and J. L. Hartwell, THIS JOURNAL, **74**, 280 (1952).

[2] A. W. Schrecker and J. L. Hartwell, *ibid.*, **74**, 5676 (1952).

[3] A. Baeyer and E. Besemfelder, *Ann.*, **266**, 187 (1891).

[4] C. G. Derick and O. Kamm, THIS JOURNAL, **38**, 400 (1916).

[5] K. v. Auwers and K. Möller, *J. prakt. Chem.*, [2] **109**, 124 (1925).

[6] The spectrum of 1,2,3,4-tetrahydro-2-naphthoic acid and the very similar spectrum of tetralin appear in R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1951, which was published after our experiments were completed. Friedel and Orchin also give an excellent general discussion of the effects of substituents on the spectra of aromatic ring systems. A more complete treatment of this subject may be found in R. N. Jones, THIS JOURNAL, **67**, 2127 (1945).

[7] H. Ley and H. Wingchen, *Ber.*, **67**, 501 (1934), found maxima at 208 $m\mu$ (log ϵ 4.15) and at 257.5 $m\mu$ (log ϵ 1.9) for crotonic acid; *cf.* L. J. Haynes and E. R. H. Jones, *J. Chem. Soc.*, 954 (1946), for absorption spectra of α,β-unsaturated lactones and esters.

[8] R. A. Morton and A. J. A. de Gouveia, *ibid.*, 916 (1934); *cf.* T. W. Campbell, *et al.*, THIS JOURNAL, **69**, 880 (1947), for a discussion of benzene derivatives with unsaturated side chains.

[9] Our curve for β-naphthoic acid is nearly identical with the one published by Y. Hirshberg and R. N. Jones, *Can. J. Research*, **27B**, 437 (1949).

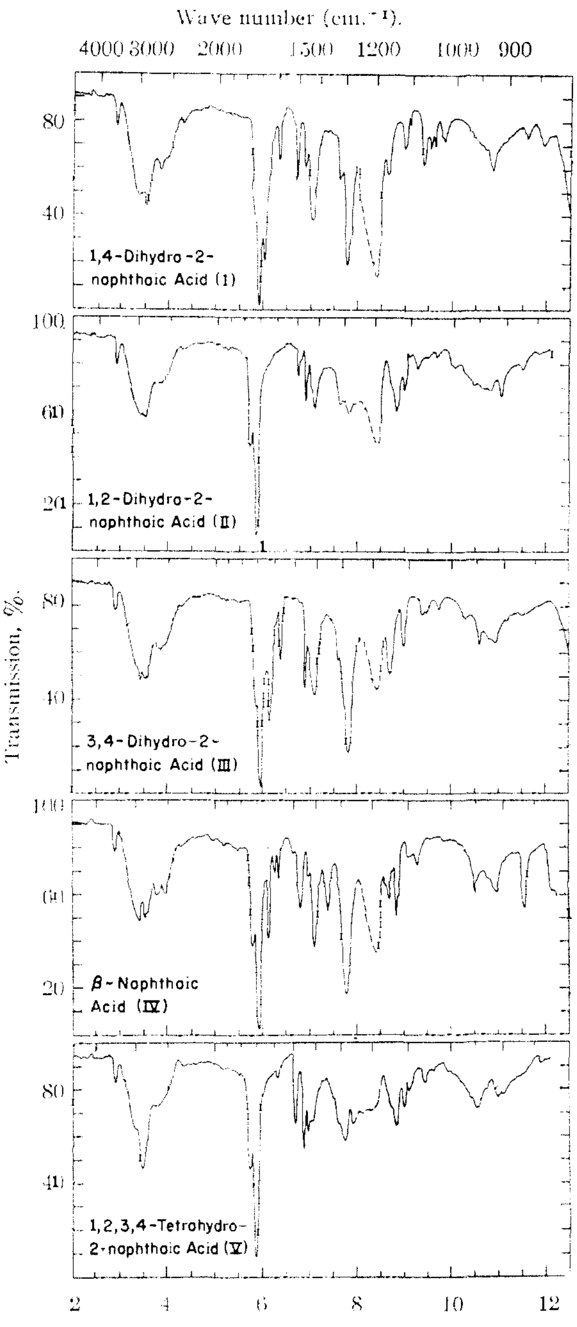
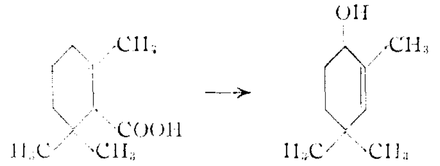


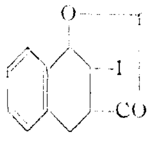
Fig. 2.—Infrared absorption spectra in chloroform.

The infrared absorption spectra of the various acids are shown in Fig. 2. The two maxima corresponding to the unconjugated carboxylic acid function are found at their usual position[10] in V and in II, while conjugation of the carboxyl group with an ethylenic double bond or benzene ring causes the expected shift toward lower frequencies. No C=C stretching vibration[11] could be detected in II, the only acid with the double bond not conjugated with a carboxyl group, whereas I and III showed peaks at 1658 and 1631 cm.$^{-1}$, respectively, corresponding to the ethylenic double bond.

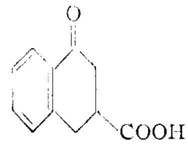
The reaction of the isomeric dihydro-2-naphthoic acids with iodine in aqueous bicarbonate was also studied. Bougault had observed that α,β-unsaturated acids were recovered unchanged from such treatment[12a,13] while β,γ-unsaturated acids gave iodolactones when the double bond formed part of an aliphatic chain.[12a] The only β,γ-unsaturated acid studied by Bougault in which the double bond was situated within a ring, α-cyclogeranic acid (VI), underwent oxidative decarboxylation to 2,4,4-trimethyl-2-cyclohexenol (VII).[12b] In our work,



VI VII



VIII



IX

both α,β-unsaturated dihydro-2-naphthoic acids (I and III) were recovered unchanged from a solution containing iodine and sodium bicarbonate, a result consistent with Bougault's findings. 1,2-Dihydro-2-naphthoic acid (II), on the other hand, yielded the 1,2,3,4-tetrahydro-4-hydroxy-3-iodo-2-naphthoic acid lactone (VIII). Its structure was proven by its conversion with methyl alcoholic potassium hydroxide to 1,2,3,4-tetrahydro-4-keto-2-naphthoic acid (IX), which was identical with the acid obtained by Derick and Kamm[4] from 1,2,3,4-tetrahydro-4-hydroxy-3-bromo-2-naphthoic acid lactone. It was also observed that when the iodolactone was boiled with aqueous potassium hydroxide, it gave β-naphthoic acid rather than the keto acid IX, which was obtained under these conditions from the bromolactone. The oxidative decarboxylation observed with α-cyclogeranic acid in the Bougault reaction, as contrasted with formation of an iodolactone in the case of the acid II, appears to be caused by the presence of the β-methyl group.

Experimental[14,15]

1,4-Dihydro-2-naphthoic Acid (I).—Material melting at 159.6–160.4° (lit.[3,4] 161°), $\lambda_{\max}^{\mathrm{EtOH}}$ 273 mμ (log ε 2.61), was obtained by reduction of β-naphthoic acid and fractional precipitation,[3] followed by repeated crystallizations. Further purification through the dibromide[3,4] yielded glistening

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[10] R. N. Jones, P. Humphries and K. Dobriner, This Journal, **72**, 956 (1950).

[11] R. N. Jones, P. Humphries, E. Packard and K. Dobriner, *ibid.*, **72**, 86 (1950).

[12] J. Bougault, *Ann. chim. phys.*, (a) **14**, 145 (1908); **15**, 296 (1908); (b) **22**, 125 (1911).

[13] R. P. Linstead and C. J. May, *J. Chem. Soc.*, 2565 (1927), showed that some β,β-disubstituted α,β-unsaturated acids did react, although much more slowly and incompletely than the β,γ-isomers.

[14] All melting points are corrected and were determined with the Hershberg apparatus.

[15] Ultraviolet absorption spectra were determined in 95% ethanol with a Beckman model DU spectrophotometer, on at least three different concentrations of each compound. Infrared spectra were measured in chloroform solution with a Perkin–Elmer model 21 spectrometer; the absorption of the solvent between 1180 and 1250 cm.$^{-1}$ has masked any characteristic bands possibly present in that range.

leaflets, m.p. 156.6–157.3° (lit.[3] 156–159°), λ_{max}^{EtOH} 273 mμ (log ε 2.53), $\lambda_{max}^{CHCl_3}$ 1721 and 1695 cm.$^{-1}$ (COOH), 1658 cm.$^{-1}$ (CH═C).

1,2-Dihydro-2-naphthoic Acid (II).—This acid[4] had m.p. 100.4–101.0° (lit.[4] 101.2°), λ_{max}^{EtOH} 260.5 mμ (log ε 3.99), 211.5 mμ (log ε 4.37), $\lambda_{max}^{CHCl_3}$ 1750 and 1712 cm.$^{-1}$ (COOH).

3,4-Dihydro-2-naphthoic Acid (III).—The procedure of v. Auwers and Möller[5] afforded colorless needles, m.p. 119.2–120.2° (lit.[4,5] 118–119°), λ_{max}^{EtOH} 290 mμ (log ε 4.20), 231.5 mμ (log ε 4.22), 225 mμ (log ε 4.25), $\lambda_{max}^{CHCl_3}$ 1710 and 1682 cm.$^{-1}$ (COOH), 1631 cm.$^{-1}$ (CH═C).

β-Naphthoic Acid (IV).—Vacuum sublimation and recrystallization of commercial material[16] gave a product which had m.p. 184.5–185°, λ_{max}^{EtOH} 333 mμ (log ε 3.10), 320 mμ (log ε 3.02), 280 mμ (log ε 3.84), 229 mμ (log ε 4.81), λ_{infl}^{EtOH} 289.5 mμ (log ε 3.69), 271 mμ (log ε 3.76), $\lambda_{max}^{CHCl_3}$ 1733 and 1695 cm.$^{-1}$ (COOH).

1,2,3,4-Tetrahydro-2-naphthoic Acid (V).—This acid was prepared[3] as colorless needles (from dilute ethanol), m.p. 97.6–98.4° (lit.[3] 96°), λ_{max}^{EtOH} 273 mμ (log ε 2.74), 266 mμ (log ε 2.71), λ_{infl}^{EtOH} 236 mμ (log ε 2.27), $\lambda_{max}^{CHCl_3}$ 1748 and 1710 cm.$^{-1}$ (COOH).

1,2,3,4-Tetrahydro-4-hydroxy-3-iodo-2-naphthoic Acid Lactone (VIII).—Solutions of 0.87 g. of II in 30 cc. of 0.5 *N* sodium bicarbonate and of 2.54 g. of iodine and 5.08 g. of potassium iodide in 15 cc. of water were mixed and allowed to stand in the dark for 28 hours. The black tarry solid, which had begun to separate after a few moments, was washed with water and shaken with chloroform and aqueous sodium thiosulfate until two almost colorless layers were obtained. The chloroform solution was separated and the aqueous layer extracted with additional chloroform. The combined chloroform extracts were washed with aqueous sodium bicarbonate, then with water, and dried over sodium sulfate. The yellowish oil remaining after evaporation of the solvent solidified when triturated with hexane to yield 0.87 g. (58%) of nearly colorless crystals, m.p. 117–118° (darkening). Recrystallization from methanol (Darco S-51) gave small colorless needles; the melting point was unchanged. The compound was rather unstable and decomposed slowly on standing, even in the dark.

Anal. Calcd. for $C_{11}H_9O_2I$: C, 44.02; H, 3.02; I, 42.29. Found: C, 44.26; H, 3.21; I, 42.3.

A solution of I, treated with iodine under the same conditions, remained clear after 28 hours. Acidifying with potassium bisulfite, dissolving the precipitate in aqueous ammonia and reacidifying with dilute hydrochloric acid, afforded a 95% recovery of starting material, m.p. 156–159°. Three recrystallizations from aqueous ethanol gave colorless leaflets, m.p. and mixed m.p. 159–161°.

When the reaction was carried out with III, only a trace of dark material separated within 24 hours. The supernatant solution was treated with sodium bisulfite, and the solid dissolved in aqueous potassium carbonate, reprecipitated with dilute hydrochloric acid, and identified as starting material by m.p. (119–120°) and mixed m.p. Recovery was 78%.

1,2,3,4-Tetrahydro-4-keto-2-naphthoic Acid (IX). (a) **From 1,2,3,4-Tetrahydro-4-hydroxy-3-bromo-2-naphthoic Acid Lactone.**[4]—The solution obtained by boiling 1.24 g. of the bromolactone, m.p. 126.2–126.6° (lit.[4] 126.5°), with 6.95 g. of 20% aqueous potassium hydroxide for 10 minutes, was diluted with water to 25 cc., cooled in ice, and acidified with 12.5 cc. of 2 *N* hydrochloric acid. The colorless crystalline solid was washed with a small amount of ice-water. The yield of material, m.p. 134–146°, was 0.69 g. (74%). Recrystallization from water gave small fine needles, m.p. 142–145° (lit.[4] 143–145°). Further recrystallization from benzene yielded material, m.p. 149–150°. The semicarbazone (from ethanol) melted at 266° (dec.) (lit.[4] 266° dec.).

(b) **From 1,2,3,4-Tetrahydro-4-hydroxy-3-iodo-2-naphthoic Acid Lactone** (VIII).—A solution of 110 mg. of the iodolactone in 0.75 cc. of 10% methyl alcoholic potassium hydroxide was allowed to stand at room temperature for 30 minutes, then diluted with 2 cc. of water. Methanol was removed by boiling, and the hot solution acidified with 0.6 cc. of 2 *N* hydrochloric acid. The pale yellow crystalline keto acid was collected after standing in the ice-box and washed with ice-water; yield 60 mg. (86%), m.p. 132–139°. Recrystallization from benzene gave material melting at 144–149°, no depression with the keto acid obtained from the bromolactone. A similar preparation yielded 91% of crude keto acid, m.p. 130–139°. The semicarbazone (from ethanol) had m.p. and mixed m.p. 266° (dec.).

β-Naphthoic acid (0.28 g., 41%), m.p. and mixed m.p. 183–184°, was obtained, but none of the keto acid, when 1.20 g. of the iodolactone was boiled for 0.5 minute with 5.95 g. of 20% aqueous potassium hydroxide, and the solution diluted with 20 cc. of water, cooled in ice and acidified with 11 cc. of 2 *N* hydrochloric acid. Another experiment, in which the iodolactone was boiled for 10 minutes with 20% aqueous potassium hydroxide, gave a 39% yield of β-naphthoic acid (m.p. 182–183.5°) and no keto acid.

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[16] Eastman Kodak Co.

[17] Laboratory of Chemistry, NIAMD, National Institutes of Health.