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SOME DERIVATIVES OF LONCHOCARPIC ACID

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Numerous species of *Derris* and *Lonchocarpus* have been examined for their insecticidal activity and especially for their rotenone content (1, 2). In the course of such studies Jones (3) isolated from an unknown species of *Lonchocarpus* from Venezuela a colorless crystalline compound, which he designated as lonchocarpic acid. More recently Harper (4) has obtained from *Derris robusta* a crystalline substance which in some of its reactions behaves similarly to lonchocarpic acid, and which he has called robustic acid. The latter has been assigned the tentative molecular formula $C_{27}H_{24}O_8$, and the former has been shown to correspond to $C_{26}H_{26}O_6$. The two compounds behave similarly, but in marked contrast to rotenone, in the Durham test (5), a reaction used for the detection of rotenone and some of its closely related compounds.

When lonchocarpic acid was first isolated, it appeared of interest to determine whether or not this compound was related to rotenone, but because it is insecticidally inert, it has been studied only intermittently over a period of several years. Since both of the authors are now engaged in work that will preclude further studies on lonchocarpic acid for some time, and in view of the publication by Harper (4) and one by Clark (6), our findings are recorded in this paper.

In the early experiments it was found difficult to obtain lonchocarpic acid in a pure state. Extraction of the crude crystalline product with hexane removed a small amount of waxy material and gave a product that could be satisfactorily crystallized from ethyl acetate, ethanol, or acetone. Ethyl acetate usually gave a product that melted at 204° (corr.) and did not resolidify, whereas the crystals from ethanol usually melted at 221° (corr.). Acetone, as previously recorded (3), gave sometimes one, sometimes the other form. The molecular weight (434) previously found by titration was confirmed by the Signer method (7). The compound did not reduce Fehling's solution, and the iodoform reaction was negative. Lonchocarpic acid is soluble in carbonate solution. On refluxing in alcoholic alkali, more than 90% of the product may be recovered. Partly on this basis the conclusion was drawn that the product is an acid, but in the light of subsequent experiments it now appears that a strongly acidic hydroxyl group is present instead.

Methylation of lonchocarpic acid with diazomethane in ether solution yielded a monomethyl derivative, but in methanol a dimethyl derivative was obtained. Both products are insoluble in alkali, and attempts to obtain an alkali-soluble product on saponification with alcoholic potash of either derivative were unsuccessful. Methylation with dimethyl sulfate yielded a product which from its methoxyl content appeared to be a mixture of the mono- and di-methyl derivatives.

Acetylation of lonchocarpic acid yielded a diacetyl derivative which was

insoluble in aqueous alkali. On saponification with alcoholic potash the diacetyl derivative yielded approximately 60% of lonchocarpic acid, about 25% of alkaliinsoluble material, and a small quantity of alkali-soluble resin. The alkaliinsoluble part gave a deep brown-violet color and the resin an intense green color with ferric chloride. Saponification of diacetyllonchocarpic acid with potassium acetate in absolute ethanol yielded a product that has not been satisfactorily purified. Treatment of diacetyllonchocarpic acid with diazomethane both in ether and in methanol produced no effect.

On catalytic hydrogenation of lonchocarpic acid a tetrahydro derivative was formed. Acetylation of this product gave a compound that was identical with the substance obtained on hydrogenation of the diacetyl derivative. With diazomethane the tetrahydro derivative reacted similarly to lonchocarpic acid.

Oxidation of lonchocarpic acid with iodine in alcohol in the presence of potassium acetate gave no recognizable product (*cf.* the formation of dehydrorotenone from rotenone) (8). When lonchocarpic acid was oxidized in alkaline solution with hydrogen peroxide, *p*-hydroxybenzoic acid was obtained in a yield of about 25%. Oxidation of the mono- and di-methyl derivatives have given inconclusive results.

Phosphorus pentachloride and thionyl chloride did not react with lonchocarpic acid.

The foregoing results indicate that, in spite of their closely related origin, no close relationship between lonchocarpic acid and rotenone exists. Furthermore, it is quite probable that the characteristic chromane-chromanone (9) system present in rotenone and the rotenoids is absent in lonchocarpic acid.

EXPERIMENTAL

Lonchocarpic acid. The compound used in these experiments was obtained from a second lot of the same species of Lonchocarpus that was used in the earlier experiments (3). The crude product obtained from the root as previously described was extracted with hexane and then recrystallized from either ethyl acetate or ethanol. The former solvent usually gave a compound that melted at $203-204^{\circ}$ (corr.); the product from the latter solvent usually melted at $220-221^{\circ}$ (corr.).

Anal. Calc'd for C₂₆H₂₆O₆: C, 71.86; H, 6.03; OCH₃, 7.14; Mol. wt., 434.

Found: C, 71.87, 71.87; H, 6.01, 5.98; OCH₃, 7.19, 7.25; Mol. wt. (Signer), 429.

Diacetyllonchocarpic acid. Five grams of lonchocarpic acid was refluxed for 2 hours in 50 cc. of acetic anhydride and 2.5 grams of anhydrous sodium acetate. The solution was cooled and poured into 250 cc. of methanol. Most of the solvent was removed on the steambath and water was added. The product that separated was washed with water and dried. The yield of crude product was 5.8 grams. After recrystallization from ethanol the product melted at 154°. The compound was insoluble in boiling 5% potassium hydroxide solution. Anal. Calc'd for $C_{30}H_{30}O_8$: C, 69.45; H, 5.83; OCH₃, 5.98; CH₃CO, 16.6.

Found: C, 69.60, 69.20; H, 5.81, 5.82; OCH₃, 5.99; CH₃CO, 17.0.

Dimethyllonchocarpic acid. To 1 gram of lonchocarpic acid in 40 cc. of dry methanol was added 40 cc. of an ether solution of diazomethane $(10 \text{ cc.} = 0.118 \text{ g. CH}_2\text{N}_2)$. A vigorous reaction took place. The slightly yellow solution was allowed to stand overnight, filtered, and then concentrated on the steam-bath. The crystalline product was recrystallized from methanol. It melted at 150–151°. The yield was 0.6 gram.

Anal. Calc'd for C₂₈H₃₀O₆: C, 72.70; H, 6.54; OCH₃, 20.12.

Found: C, 72.24, 72.16; H, 6.49, 6.45; OCH₃, 19.64, 19.9.

Monomethyllonchocarpic acid. When 2 grams of lonchocarpic acid was dissolved in dry ether and treated with diazomethane in a manner similar to that described above, a product was obtained that melted at 208-211°. After recrystallization from ethanol it melted at 210-212°. The yield was 1.7 grams.

Anal. Calc'd for C₂₇H₂₈O₆: C, 72.29; H, 6.30; OCH₃, 13.83.

Found: C, 71.97; H, 6.30; OCH₃, 14.22.

Tetrahydrolonchocarpic acid. Two and one-half grams of lonchocarpic acid in 100 cc. of ethanol was shaken with reduced platinum oxide in an atmosphere of hydrogen. Reduction took place rapidly and ceased when 300 cc. (uncorr.) of hydrogen had been absorbed (theory for 2 moles = 280 cc.). The solution was filtered, and concentrated, and the separated product was recrystallized from ethanol. It melted at 239-240°. The yield was 2.2 grams. Anal. Calc'd for $C_{28}H_{30}O_6$: C, 71.20; H, 6.90; OCH₃, 7.07.

Found: C, 70.92, 71.36; H, 6.77, 6.89; OCH₃, 7.00.

Diacetyltetrahydrolonchocarpic acid. Acetylation of tetrahydrolonchocarpic acid with acetic anhydride and sodium acetate according to the procedure described above for lonchocarpic acid yielded the same product as that obtained on reduction of diacetyllonchocarpic acid by the hydrogenation procedure described for lonchocarpic acid. When recrystallized from ethanol it melted at 192-192.5°.

Anal. Calc'd for C30H34O8: C, 68.94; H, 6.56; OCH3, 5.93; CH3CO, 16.46.

Found: C, 68.74; H, 6.50; OCH₃, 5.86; CH₃CO, 16.99.

Monomethyltetrahydrolonchocarpic acid. This compound was prepared by treatment of tetrahydrolonchocarpic acid in dry ether with diazomethane according to the procedure given for monomethyllonchocarpic acid. The product purified by recrystallization from ethanol melted at $211-212.5^{\circ}$.

Anal. Calc'd for C₂₇H₃₂O₆: C, 71.65; H, 7.13; OCH₃, 13.71.

Found: C, 71.49, 71.69; H, 7.21, 7.31; OCH₃, 13.88.

Dimethyltetrahydrolonchocarpic acid. This compound was obtained on methylation of tetrahydrolonchocarpic acid with diazomethane in methanol according to the procedure described for dimethyllonchocarpic acid. When recrystallized from ethanol it melted at $166-167^{\circ}$.

Anal. Calc'd for C23H34O6: C, 72.07; H, 7.35; OCH3, 19.95.

Found: C, 71.65, 71.53; H, 7.26, 7.23; OCH₃, 19.30.

Oxidation of lonchocarpic acid with hydrogen peroxide. Two grams of lonchocarpic acid was dissolved in 25 cc. of 5% potassium hydroxide, and to the solution 8 cc. of 30% hydrogen peroxide was added in small portions. The solution was heated on the steam-bath, boiled for a few minutes, and then cooled and saturated with carbon dioxide. The small amount of tarry material that had formed was extracted with ether. The aqueous solution was acidified to Congo red and then concentrated to a small volume under reduced pressure. On standing for several days the concentrated solution deposited brown nodules. These were removed by filtration and recrystallized from water with the aid of Norit. The recrystallized product melted at 209-210°. The yield was 0.2 gram. It was identified as p-hydroxybenzoic acid by titration, by mixture melting point determination with an authentic sample of this acid, and by a similar comparison of their acetates.

SUMMARY

Catalytic hydrogenation of lonchocarpic acid produces a tetrahydro derivative and acetylation yields a diacetyl derivative.

In ether solution lonchocarpic acid with diazomethane yields a monomethyl derivative, in methanol with the same reagent a dimethyl compound. On oxidation with hydrogen peroxide lonchocarpic acid yields p-hydroxybenzoic acid. Lonchocarpic acid is probably an acidic phenol.

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