was inactive. (Found in material dried *in vacuo* over P_2O_5 at 50°: C, 60.0; H, 6.1; N, 2.0%. Average value for corresponding product from tomatoes: C, 56.4; H, 6.1; N, 1.8%.)

CONCLUSIONS

The growing of *Solanum nigrum* out of doors with the minimum amount of attention yielded a root excretion which was highly active in hatching larvae of the potato eelworm from their cysts. Unfortunately, the rapid growth and short growing period of the plants did not permit more than about 9 weeks' leachings to be collected. The active principle from *S. nigrum* root excretion could be concentrated by the same procedure as was used for tomato root excretion, but the limited number of analyses on the brucine salt and free acid did not justify the deduction that the active principle from *S. nigrum* was identical with that obtained from tomatoes. Nevertheless, making allowance for the

non-crystalline character of the products, the great similarity in general properties would make it appear probable that the *S. nigrum* factor is either identical with that obtained from tomatoes or some very closely related substance.

SUMMARY

1. *Solanum nigrum* grown out of doors yielded a root excretion which was highly active in hatching potato eelworm cysts.

2. Concentration of the active material in this excretion gave a product which was closely similar to the corresponding product from tomato root excretion in its properties. The active principle in the two cases may well be identical.

We are grateful to Imperial Chemical Industries Ltd., and to the Agricultural Research Council, for grants in aid of this work. We wish to thank Sir E. J. Salisbury, F.R.S., for his interest and advice.

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The Potato Eelworm Hatching Factor

5. ATTEMPTS TO PREPARE ARTIFICIAL HATCHING AGENTS.

PART I. SOME FURAN DERIVATIVES

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(Received 8 April 1949)

From the time when it became clear that highly active concentrates of the potato eelworm hatching factor prepared from tomato root excretion possesses both acidic and lactonic properties (Calam, Todd & Waring, 1949), synthetic experiments have been carried out alongside work on the natural factor in the hope that simpler substances might be prepared which would show hatching activity and which might be of practical interest in controlling eelworm infestation in potato crops. The examination of a number of tetrone acid derivatives has been described in a previous paper (Calam, Todd & Waring, 1949); the present communication deals with experiments on the synthesis of a number of lactones containing furan nuclei, such compounds being of interest, since it seemed probable that the natural hatching factor contained heterocyclic oxygen.

In commencing studies in the furan series an attempt was made to oxidize furitaconic acid (furfurylidenesuccinic acid) to β -hydroxy- β -carboxy- γ -2-furylbutanolide by means of potassium permanganate or monoperphthalic acid without result; this was unexpected in view of the ease with which itaconic acid yields hydroxyparaconic acid on similar treatment. Condensation of furfural with laevulinic acid in presence of sodium acetate gives a 10% yield of β -furfurylidene-laevulinic acid (Kehrer & Kleberg, 1893). Replacement of sodium acetate by piperidine failed to give any condensation and sodium hydroxide gave sticky products; with potassium acetate, however, yields of about 30% were obtained. No condensation occurred between furfural and ethyl laevulinate in presence of piperidine, but with sodium hydroxide β -furfurylidene-

laevulinic acid was produced in moderate yield. Reduction of β -furfurylidene-laevulinic acid with sodium amalgam gave, according to conditions, β -furfuryl-laevulinic acid (I) or β -furfuryl- γ -methylbutanolide (II). Attempts to prepare analogous compounds by condensing ethyl 5-methyl-2-formylfuran-4-carboxylate with laevulinic acid failed.

shows hatching activity had suggested other possible lines of development.

EXPERIMENTAL

β -Furfuryl-laevulinic acid. β -Furfurylidene-laevulinic acid (2 g.) was dissolved in aqueous NaOH (10 ml. of 3N), diluted

(I)

(II)

(III)

(IV)

(V)

Condensation of furfural with $\Delta^{\beta:\gamma}$ -angelicalactone gave α -furfurylidene- γ -methyl- $\Delta^{\beta:\gamma}$ -butanolide (III), hydrolysed to α -furfurylidene-laevulinic acid and reduced by sodium amalgam to α -furfuryl- γ -methylbutanolide. On refluxing α -furfurylidene-laevulinic acid with acetic anhydride it was reconverted to (III) in good yield. In similar fashion ethyl 5-methyl-2-formylfuran-4-carboxylate and $\Delta^{\beta:\gamma}$ -angelicalactone gave α -(5-methyl-4-carbethoxyfurfurylidene)- γ -methyl- $\Delta^{\beta:\gamma}$ -butanolide (IV). This lactone was readily hydrolysed to α -(5-methyl-4-carboxyfurfurylidene)-laevulinic acid, which gave α -(5-methyl-4-carboxyfurfurylidene)- γ -methyl- $\Delta^{\beta:\gamma}$ -butanolide on refluxing with acetic anhydride. On reduction with sodium amalgam the original lactone (IV) gave as the only pure product α -(5-methyl-4-carboxyfurfuryl)-laevulinic acid. Attempts to condense furfural with ethyl sodio-oxaloacetate gave only resinous products, although benzaldehyde condensed readily enough, yielding the crystalline α -hydroxy- β -carbethoxy- γ -phenyl- $\Delta^{\alpha:\beta}$ -butanolide (V; cf. Gault & Durand, 1943).

All the above lactones and the corresponding laevulinic acid derivatives were tested for hatching activity on potato eelworm cysts by the technique described elsewhere (Calam, Raistrick & Todd, 1949), but in no case was any activity detected. Further synthetic work in this series was therefore abandoned, especially as the discovery that anhydrotetrone acid

with water (200 ml.) and Na amalgam (50 g. of 4%; 2 mol.) added with shaking. After a time the solution became colourless and it was then acidified, extracted with ether and the extract dried and evaporated. The crystalline product was purified by sublimation at 70°/10⁻⁴ mm. (bath temp.). Colourless needles, m.p. 98–99°. (Found: C, 60.8; H, 6.2. C₁₀H₁₂O₄ requires C, 61.2; H, 6.1%.)

β -Furfuryl- γ -methylbutanolide. β -Furfurylidene-laevulinic acid was dissolved in aqueous NaOH (50 ml. of 3N) and excess Na amalgam (150 g. of 4%; 6 mol.) added. The mixture, which became colourless in 1 hr., was shaken overnight and then acidified and extracted with ether. The ethereal extract was thoroughly washed with NaHCO₃ and water, dried and evaporated. The residual lactone (1.8 g.), a colourless oil, was purified by distillation and had b.p. 70–75°/10⁻¹ mm. (bath temp.); at atmospheric pressure it had b.p. 230°. (Found: C, 66.2; H, 6.7; equiv. (lactone), 183. C₁₀H₁₂O₃ requires C, 66.7; H, 6.7%; equiv. (lactone), 180.) On refluxing the lactone with hydrazine hydrate in ethanol it yielded the hydrazide of γ -hydroxy- β -furfurylvaleric acid, crystallizing from ethyl acetate as colourless plates, m.p. 153–154°. (Found: N, 13.5. C₁₀H₁₆O₃N₂ requires N, 13.2%.)

α -Furfurylidene- γ -methyl- $\Delta^{\beta:\gamma}$ -butanolide. A mixture of furfural (1 g.), $\Delta^{\beta:\gamma}$ -angelicalactone (1 g.) and piperidine (5 drops) was warmed on the steam bath for 1 hr. and then allowed to cool. The yellow solid was washed with a little ether and recrystallized from methanol. The yellow needles, m.p. 78–79°, had a slight brownish tinge which could be removed by sublimation *in vacuo*. (Found: C, 68.0; H, 4.7. C₁₀H₈O₃ requires C, 68.1; H, 4.5%.)

α -Furfurylidene-laevulinic acid. The above lactone (1g.) was refluxed with excess methanolic KOH (3%) during 3 hr. Most of the methanol was then distilled off and the residue diluted with water and acidified. The yellow oil which separated was dissolved in a minimum of hot aqueous ethanol. On cooling α -furfurylidene-laevulinic acid separated as colourless needles, m.p. 125–126°. (Found: C, 62.3; H, 5.4. $C_{10}H_{10}O_4$ requires C, 61.8; H, 5.1%.) On refluxing with acetic anhydride (3 ml.) for 2 hr. the acid (0.1 g.) was reconverted to the above butenolide (0.09 g.), m.p. 78–79°.

α -Furfuryl- γ -methylbutanolide. The above unsaturated lactone (2 g.) was dissolved in aqueous ethanol (50 ml. of 90%) and Na amalgam (150 g. of 4%; 6 mol.) added. The mixture was shaken until colourless (about 1 hr.) then acidified and ethanol removed by evaporation under reduced pressure. The residual solution was extracted with ether and the extract washed with $NaHCO_3$, dried and evaporated. The pale yellow residual oil distilled at 85°/10⁻¹ mm. (bath temp.). (Found: C, 66.4; H, 6.5; equiv. (lactone), 180. $C_{10}H_{12}O_3$ requires C, 66.7; H, 6.7%; equiv. (lactone), 180.)

Refluxed with hydrazine hydrate in ethanol the product gave the hydrazide of γ -hydroxy- α -furfurylvaleric acid as colourless needles (ethyl acetate), m.p. 138–139°. (Found: C, 56.6; H, 7.5; N, 13.6. $C_{10}H_{16}O_3N_2$ requires C, 56.6; H, 7.5; N, 13.2%.)

Ethyl 5-methyl-2-formylfuran-4-carboxylate. Prepared by oxidation of ethyl 5-methyl-2-(*d*-arabotetrahydroxybutyl)-furan-4-carboxylate (West, 1925; Gonzalez, 1934), the aldehyde had m.p. 56° and gave a 2:4-dinitrophenylhydrazone, m.p. 220–221°. Unknown to us at the time this work was carried out, it had also been prepared by Müller & Varga (1939), and was subsequently described by Jones (1945).

α -(5-Methyl-4-carbethoxyfurfurylidene)- γ -methyl- $\Delta^{\beta:\gamma}$ -butenolide. Prepared in similar fashion to the analogous α -furfurylidene lactone by condensing $\Delta^{\beta:\gamma}$ -angelicalactone with ethyl 5-methyl-2-formylfuran-4-carboxylate. Yellow needles, m.p. 143–144° from methanol. (Found: C, 63.8; H, 5.4. $C_{14}H_{14}O_6$ requires C, 64.1; H, 5.3%.) Reduction in aqueous ethanol with Na amalgam in the usual manner gave α -(5-Methyl-4-carboxyfurfuryl)-laevulinic acid crystallizing from water in colourless needles, m.p. 126–129°. (Found: C, 56.4; H, 5.6. $C_{12}H_{14}O_6$ requires C, 56.7; H, 5.5%.) Treatment of the gummy neutral fraction (which gave a positive Legal reaction) from the reduction mixture with hydrazine

gave a colourless product, m.p. 218–219°, which from analysis appeared to be the pyridazine corresponding to α -(5-methyl-4-carboxyfurfuryl)-laevulinic acid. (Found: C, 57.7; H, 5.5; N, 11.0. $C_{12}H_{14}O_4N_2$ requires C, 57.6; H, 5.6; N, 11.2%.)

α -(5-Methyl-4-carboxyfurfurylidene)-laevulinic acid. The foregoing ester lactone (0.5 g.) was refluxed with methanolic KOH (3%) for 3 hr., the bulk of the methanol removed under reduced pressure and the residue diluted with water and acidified. The acid separated from aqueous ethanol as a yellow microcrystalline powder, m.p. 225–226°. (Found: C, 57.4; H, 5.0; equiv., 125. $C_{12}H_{12}O_6$ requires C, 57.1; H, 4.8%; equiv., 126.)

α -(5-Methyl-4-carboxyfurfurylidene)- γ -methyl- $\Delta^{\beta:\gamma}$ -butenolide. The above acid (0.5 g.) was refluxed with acetic anhydride (3 ml.) during 4 hr. The mixture was poured into ice water and the brown solid product crystallized several times from methanol. Small yellow needles, m.p. 219–220°. (Found: C, 61.5; H, 4.1. $C_{12}H_{10}O_6$ requires C, 61.5; H, 4.3%.)

α -Hydroxy- β -carbethoxy- γ -phenyl- $\Delta^{\alpha:\beta}$ -butenolide. Ethyl sodio-oxaloacetate (4.36 g.; 1 mol.) was ground to a paste with ethanol (7 ml.) and water (20 ml.), the mixture cooled in ice and a solution of freshly distilled benzaldehyde (2.12 g.; 1 mol.) in ethanol (5 ml.) added. After 30 min. the reaction mixture was removed from the ice bath and left overnight at room temperature. Acidification with HCl gave an oil which was taken up in ether, the extract freed from any unchanged benzaldehyde with $NaHSO_3$, washed and evaporated. The solid residue crystallized from aqueous methanol in colourless needles, m.p. 104–105°. (Found: C, 62.7; H, 4.8. $C_{13}H_{14}O_5$ requires C, 62.9; H, 4.8%.) The compound gave a positive reaction with $FeCl_3$, but had no ketonic properties.

SUMMARY

A number of substituted lactones and laevulinic acid derivatives containing furan nuclei have been synthesized. None of the compounds showed any activity when tested as hatching agents for the potato eelworm.

The authors' thanks are due to the Agricultural Research Council and Imperial Chemical Industries Ltd. for their support of this investigation.

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