143. *Constituents of the Bark of* Zanthoxylum americanum (*Mill*). *Part I. Xanthoxyletin.*

By (Miss) Janet C. Bell, Alexander Robertson, and T. S. Subramaniam.

The crystalline substance which, according to Gordin (*J. Amer. Chem. Soc.*, 1906, **28**, 1649), was first isolated from the bark of the prickly ash, *Zanthoxylum americanum* (Mill), by Staples and named xanthoxyline (*Amer. J. Pharm.*, 1829, **163**), has been studied by Witte (*Arch. Pharm.*, 1878, **212**, 283), Maffet (*Amer. J. Pharm.*, 1886, 672), Lloyd (*ibid.*, 1890, 229), Eberhardt (*ibid.*, 1890, 5, 230), and Gordin (*loc. cit.*). Witte, who named his material xanthoxyloin, proposed the empirical formula $C_{14}H_{14}O_4$, but Gordin, to whom we owe the first detailed examination of the compound, m. p. 132·5°, found the formula to be $C_{15}H_{14}O_4$ and suggested the name xanthoxylin N to distinguish this substance from other natural products which had been previously isolated from related genera and to which the name xanthoxylin had been applied (compare Stenhouse, *Annalen*, 1854, **89**, 251; 1857, **104**, 237; Eberhardt, *loc. cit.*; Colton, *Amer. J. Pharm.*, 1890, 191). Gordin found that the compound contained a methoxyl group, was devoid of hydroxyl or keto-groups, gave a hydrated dibromide, and yielded a dihydro-derivative on treatment with hydrogen iodide. Though unable to determine the function of the three remaining oxygen atoms, this author suggested that a lactone or acid anhydride group might be present.

In the course of an examination of the complex mixture of substances present in the bark of prickly ash we have isolated by an improved method the compound, m. p. 133°, described by Gordin (*loc. cit.*) and have confirmed the empirical formula $C_{14}H_{11}O_3(OMe)$ and general properties ascribed to it by this author. In order to avoid confusion with other well-defined compounds bearing the name xanthoxylin (compare Gordin, *loc. cit.*;

Bocquillon, *Rep. Pharm.*, 1917, **28**, 66; Dieterle and co-workers, *Arch. Pharm.*, 1931, **269**, 384) we have re-named the substance, m. p. 133°, xanthoxyletin.*

Although xanthoxyletin does not contain a phenolic hydroxyl group and is almost insoluble in water (dilution of an alcoholic solution with water precipitates the compound), it cannot be precipitated by addition of excess of water to a solution in a little alcohol containing an equivalent of sodium hydroxide. Saturation of this alkaline aqueous-alcoholic solution with carbon dioxide, however, slowly but almost completely precipitates xanthoxyletin. This property, which is shared by some coumarins, together with the fact that the usual tests indicated the presence of at least one ethylenic linkage, led us to believe that xanthoxyletin contained an α-pyrone ring system and had in all probability the skeleton C_5–(C_6·C:C·CO·O), in which, by analogy with the rotenone series, the C_5 residue was probably present as an isoprene unit. In accordance with the coumarin hypothesis it was found that xanthoxyletin is readily converted into the unsaturated monobasic acid, O-*methylxanthoxyletinic acid*, by application of Canter and Robertson's standard procedure for converting a coumarin into the *O*-methyl ether of the corresponding cinnamic acid. Further, hydrolytic fission with boiling 25% aqueous sodium hydroxide gives rise to acetone and a comparatively good yield of phloroglucinol monomethyl ether, which is conveniently characterised by conversion into the *di*-p-*nitrobenzoate*. The isolation of a phloroglucinol derivative in this manner clearly defines the nature of the C_6 residue.

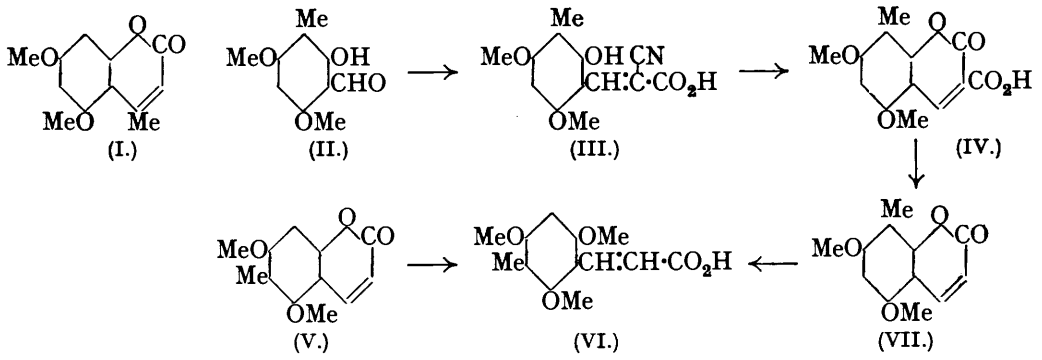
Hydrogenation of xanthoxyletin with the aid of a palladium catalyst furnished dihydroxanthoxyletin, m. p. 145—146°, which appears to be identical with Gordin's dihydroderivative, m. p. 142—143° (*loc. cit.*), and is converted by the standard procedure into O-*methyldihydroxanthoxyletinic acid*. The latter compound is readily hydrogenated with a palladium catalyst, forming O-*methyltetrahydroxanthoxyletinic acid*, identical with a specimen prepared directly in the same manner from *O*-methylxanthoxyletinic acid.

Degradation of xanthoxyletin by the usual oxidising agents appears to be difficult to control. With neutral permanganate solution a complex oxidation mixture was obtained which has not yet been completely investigated, but oxidation in alkaline solution with an excess of aqueous potassium permanganate gave rise to α-hydroxy*iso*butyric acid, which in conjunction with the production of acetone by hydrolytic fission definitely establishes the presence of the group $Me_2\dot{C}$—C: in the molecule, a result in keeping with the assumption that the C_5 residue has the isoprene skeleton. Ozonolysis under strictly controlled conditions produced a mixture from which a small yield of a product $C_{10}H_5O_4(OMe)$ was readily isolated. This compound, which we have named apo*xanthoxyletin*, has the properties of an *o*-hydroxy-aldehyde, giving a ferric chloride reaction and forming a *phenylhydrazone* and a *triacetyl* derivative which is presumably a benzylidene diacetate. On reduction under conditions whereby phenolic aldehydes are converted into *C*-methyl phenols (Asahina and Tukamoto, *Ber.*, 1933, **66**, 897) *apo*xanthoxyletin yielded a phenolic compound, *deoxy*apo*xanthoxyletin*, which is easily soluble in alkalis but is devoid of aldehydic properties and does not give a ferric reaction. This phenol was readily methylated by the methyl iodide–potassium carbonate method, forming O-*methyldeoxy*apo*xanthoxyletin*, which, on the basis of the α-pyrone hypothesis (see above) together with the foregoing analytical results, was considered to be a *C*-methyl derivative of 5 : 7-dimethoxycoumarin (Type I, V, or VII).

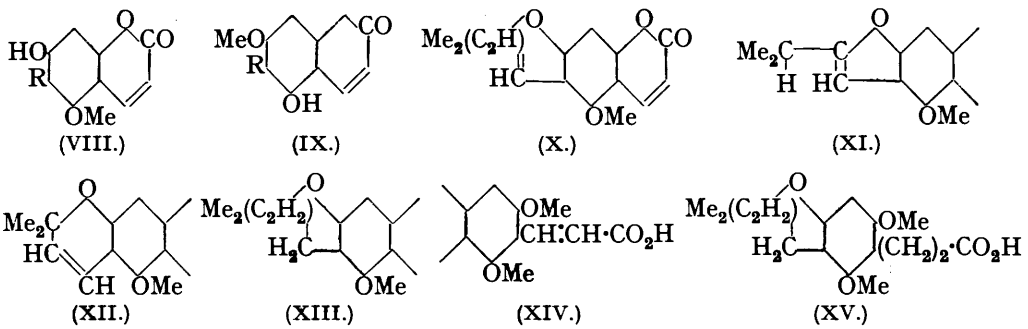
In order to test this view 5 : 7-*dimethoxy*-8-*methylcoumarin* (VII) was synthesised by the following procedure: Interaction of the aldehyde (II) and cyanoacetic acid in the presence of aqueous sodium hydroxide gave rise to the salicylidenecyanoacetic acid (III), which, on simultaneous hydrolysis and ring closure, followed by decarboxylation of the resulting coumarin-3-carboxylic acid (IV), furnished the *coumarin* (VII). Direct comparison, however, showed that the methyl ether of deoxy*apo*xanthoxyletin was not identical with the coumarin (VII) or with 5 : 7-dimethoxy-4-methylcoumarin (I) (Robertson and co-workers, J., 1931, 1255) and therefore it seemed likely that the methyl ether of deoxy*apo*xanthoxyletin had the structure (V). This was conclusively established by the fact that by the

* As we have now shown the compound to be an α-pyrone, this designation is in accordance with the names skimetin, fraxetin, etc., applied to other natural coumarins.

usual procedure the latter compound was almost quantitatively converted into 2 : 4 : 6-*trimethoxy-3-methylcinnamic acid* (VI), identical with a specimen obtained in the same



manner from the synthetic coumarin (VII). It follows, therefore, that deoxy*apo*-xanthoxyletin must be either 7-hydroxy-5-methoxy- (VIII, R = Me) or 5-hydroxy-7-methoxy-6-methylcoumarin (IX, R = Me) and hence *apo*xanthoxyletin must have structure (VIII, R = CHO) or (IX, R = CHO). The evidence at our disposal does not enable us to distinguish between the two pairs of formulæ.



The formation of a tetrahydro-derivative of *O*-methylxanthoxyletinic acid together with the results of ozonolysis clearly shows that, in addition to the double bond in the α-pyrone ring, a second double bond must be present in the C_5 residue of xanthoxyletin. This conclusion is not invalidated by the fact that xanthoxyletin itself forms only a dihydro-compound, because under the conditions employed for hydrogenation the ethylenic linkage of an α-pyrone is not usually attacked. That the fission of the second double bond by ozone is accompanied by the loss of four carbon atoms, giving rise to a 6-formylcoumarin, affords clear proof that (a) xanthoxyletin contains a C_5 unit which is attached to the coumarin residue at the 6-position, and (b) the double bond in this unit, on the assumption that it does not migrate during ozonolysis, is in the αβ-position to the coumarin residue, *i.e.*, there is present the skeleton (A), C_3·Ċ:CH·C_6·CH:CH·CO·O·. Further, since the function of three of the four oxygen atoms in xanthoxyletin has now been clearly defined—one in a methoxyl group and two in the α-pyrone ring—and since the absence of hydroxyl or keto-groups has been confirmed (compare Gordin, *loc. cit.*), the fourth oxygen atom must form an ether system with the C_5 unit in agreement with the existence of one and not two double bonds in the C_5 unit. Moreover, when the presence of the group (C_3·Ċ:CH·) in A, the production of acetone, and the formation of α-hydroxy*iso*butyric acid by oxidation with alkaline permanganate are taken into account, it is obvious that the C_5 unit must possess an isoprene skeleton and (A) can be written $Me_2(C_2H)$:CH·C_6·CH:CH·CO·O·, *i.e.*, xanthoxyletin may be represented by a structure of the type (X). Consequently it follows that the C_5 unit must be present either as in an α-*iso*propylfurano- or in an αα-dimethyl-Δ^3-chromeno-system and hence xanthoxyletin has either formula type (XI) or (XII).

Definite experimental evidence to enable a choice to be made between the two types (XI) and (XII) is lacking. Ozonisation of (XI) would be expected to give rise to *iso*butyric acid in addition to the 6-formylcoumarin (VIII, R = CHO), but so far we have been unable to detect the former in the mixture resulting from ozonolysis. On the other hand, the production of (VIII, R = CHO) from a structure of the chromene type (XII) by means of ozone clearly involves the assumption that the degradation proceeds further than would be normally expected. Regarding the formation of acetone by the hydrolytic fission of xanthoxyletin, the remarks of Heyes and Robertson (J., 1935, 683) on the same topic in the case of the " second half " of toxicarol clearly apply here and further comment at this stage is unnecessary.

The structures (XIII), (XIV), and (XV) for dihydroxanthoxyletin, *O*-methylxanthoxyletinic acid, and *O*-methyltetrahydroxanthoxyletinic acid, respectively, follow from the partial formula (X) for xanthoxyletin.

Experimental.

Xanthoxyletin.—Finely powdered bark of *Zanthoxylum americanum* (Mill) (4 kg.) was extracted in a large Soxhlet apparatus with ether for 4—6 days. After evaporation of the solvent the green extract partly crystallised on being kept for 5—6 days and was then triturated with light petroleum (b. p. 40—60°) (3 l.). 3 Days later the green solid (150 g.) was collected, washed with light petroleum until the washings were colourless, and dried. From this material xanthoxyletin can be conveniently isolated by two methods.

(A) A solution of the green product (85 g.) in boiling alcohol (300 c.c.) was cooled to about 40°, gradually treated with 20% aqueous sodium hydroxide (90 c.c.), cooled, diluted with water (approx. 2 l.), mixed with charcoal, and filtered. Carbon dioxide was passed into the filtrate for 2 days; crystalline material began to separate in the course of 24 hours and 3 days later the solid was collected, well washed, and recrystallised from 80% methyl alcohol (charcoal). Pure xanthoxyletin was isolated from the resulting material by crystallisation from methyl alcohol (3—4 times) and then from ethyl alcohol (6—8 times), being finally obtained in glistening thick prisms, m. p. 133°, which had the solubilities in organic solvents and water given by Gordin (*loc. cit.*). For analysis the substance was recrystallised from light petroleum (b. p. 60—80°), in which it is sparingly soluble, forming flat prisms [Found: C, 69·9, 69·8; H, 5·5, 5·5; OMe, 12·7, 12·7; *M*, 267, 270. Calc. for $C_{14}H_{11}O_3(OMe)$: C, 69·8; H, 5·4; OMe, 12·0%; *M*, 258].

(B) Repeated crystallisation of the green solid first from methyl and then from ethyl alcohol with the aid of charcoal gave xanthoxyletin, m. p. 131·5—132·5°, but the process is more tedious than method (A) and the final product is apt to be slightly coloured.

The main difficulty of obtaining pure xanthoxyletin is due to the presence of another substance having approximately the same solubilities. This compound will be the subject of a future communication.

Xanthoxyletin readily decolorises bromine water and aqueous potassium permanganate and forms a non-fluorescent orange-red solution in concentrated sulphuric acid which becomes red and then dark brown on warming. It does not react with phenylhydrazine or semicarbazide acetate, does not form an *O*-acyl derivative by any of the standard methods, and is optically inactive.

Hydrolytic Fission of Xanthoxyletin.—(A) Well-powdered xanthoxyletin (3 g.) was boiled with 25% aqueous sodium hydroxide (100 c.c.) for 4 hours; the solid dissolved in ½—1 hour and the resulting brownish-yellow solution gradually became dark brown. The mixture was cooled to about 60°, acidified with hydrochloric acid (Congo-red), cleared with the aid of charcoal, filtered, cooled, saturated with ammonium sulphate, and extracted 8—10 times with ether. The extracts were twice washed with saturated ammonium sulphate solution, dried, and evaporated, and the resulting brown oil, which partly solidified, was treated with aqueous sodium bicarbonate to remove traces of acidic material. Phloroglucinol monomethyl ether (1·1 g.) was isolated from the aqueous bicarbonate mixture by means of ether (8 extractions) and purified by distillation in a vacuum and then by crystallisation from benzene, forming clusters of prisms, m. p. 78—79°, identified by comparison with an authentic specimen [Found: OMe, 21·5. Calc. for $C_6H_5O_2(OMe)$: OMe, 22·1%]. A mixture of the ether (0·25 g.), *p*-nitrobenzoyl chloride (1 g.), and pyridine (4 c.c.) was kept at 90° for ½ hour, cooled, and mixed with excess of dilute hydrochloric acid. The well-washed solid was ground with aqueous sodium bicarbonate to remove *p*-nitrobenzoic acid, washed, and dried. Crystallised from acetic acid and then from

benzene–alcohol, the *di*-p-*nitrobenzoate* of phloroglucinol monomethyl ether was obtained in almost colourless needles, m. p. 199—200°, identical in every way with authentic material (Found : C, 57·8; H, 3·4; N, 6·9. $C_{21}H_{14}O_9N_2$ requires C, 57·5; H, 3·2; N, 6·4%).

An authentic specimen of the di-*p*-nitrobenzoate was prepared in good yield from synthetic phloroglucinol monomethyl ether in the same manner and formed needles, m. p. 199—200°, from acetic acid or benzene–alcohol, sparingly soluble in hot alcohol, moderately soluble in benzene, and having a negative ferric reaction (Found : C, 57·7; H, 3·2; N, 6·7%).

(B) The foregoing fission of xanthoxyletin (5 g.) with 25% aqueous sodium hydroxide (150 c.c.) was repeated and after 1 hour the solution was distilled with the gradual addition of water so as to keep the volume of the alkaline mixture constant. In this way 200 c.c. of distillate were collected which on treatment with 2 : 4-dinitrophenylhydrazine hydrochloride in hydrochloric acid gave a yellow precipitate (1—1·2 g.), consisting mainly of acetone-2 : 4-dinitrophenylhydrazone. After being once recrystallised from a little alcohol, this material had m. p. about 105° and under the microscope the yellow crystals of the acetone-hydrazone were seen to be contaminated with a small amount of orange-red prisms. Repeated purification from alcohol finally gave the acetone-2 : 4-dinitrophenylhydrazone in yellow flat prisms, m. p. 126—127°, undepressed by an authentic specimen (Found : C, 45·7; H, 4·5. Calc. for $C_9H_{10}O_4N_4$: C, 45·4; H, 4·2%).

Oxidation of Xanthoxyletin with Potassium Permanganate.—The powdered compound (3 g.) was refluxed (agitate) with 1% aqueous sodium hydroxide (250 c.c.) until a clear solution was obtained, which was then cooled to room temperature; acidification of a test portion with mineral acid precipitated unchanged xanthoxyletin. Potassium permanganate (15 g.), dissolved in water (350 c.c.), was then introduced in the course of 24 hours until the aqueous liquor retained a permanent permanganate colour. The mixture was cleared and neutralised with sulphur dioxide, extracted several times with ether to remove traces of neutral products, acidified with hydrochloric acid, and again extracted (8 times) with ether. Evaporation of the latter extracts, which had been washed and dried, gave a brown acidic residue, from which α-hydroxy*iso*butyric acid was isolated by means of boiling light petroleum (b. p. 60—80°). The acid separated from the concentrated solution in colourless needles, which, after having been twice crystallised from the same solvent, had m. p. 77—78°, undepressed by an authentic specimen, m. p. 78—79° (Hepworth, J., 1919, **115**, 1203) (Found : C, 46·3; H, 7·7. Calc. for $C_4H_8O_3$: C, 46·2; H, 7·7%).

O-Methylxanthoxyletinic Acid.—20% Aqueous sodium hydroxide (72 c.c.) was added to a warm solution of xanthoxyletin (15 g.) in methyl alcohol (150 c.c.), and the mixture warmed on the steam-bath for 5 minutes. After the addition of more aqueous sodium hydroxide (100 c.c.) methyl sulphate was gradually introduced with very vigorous agitation until the mixture was neutral. Further portions of alkali and methyl sulphate were then added alternately and after this process had been repeated 2 or 3 times the reaction mixture was basified, kept at room temperature for 1 hour, and extracted with ether. The solid left on removal of the solvent consisted of the *methyl* ester of the acid. Extraction of the aqueous liquors which had been acidified with mineral acid (Congo-red) gave a small amount of the *acid*. Generally the acid and the ester were isolated together from the reaction mixture which had been acidified with hydrochloric acid and a solution of the product was boiled with 70% alcohol (100 c.c.) containing potassium hydroxide (7 g.) for 1 hour, cooled, diluted with water (100 c.c.), and acidified with excess of hydrochloric acid. 24 Hours later the precipitated *O*-methylxanthoxyletinic acid was collected, purified from traces of non-acidic material by means of aqueous sodium carbonate, dried, and crystallised from methyl alcohol and then from benzene or benzene–light petroleum (b. p. 60—80°), forming colourless prisms (13 g.), m. p. 179·5—180·5° with sintering at 178° [Found : C, 66·2; H, 6·2; OMe, 20·8. $C_{14}H_{16}O_3(OMe)_2$ requires C, 66·2; H, 6·2; OMe, 21·4%]. The compound is considerably less soluble in organic solvents, except alcohol, than xanthoxyletin. It does not give a ferric reaction and dissolves remarkably slowly in aqueous sodium bicarbonate.

The methyl ester separated from light petroleum in colourless, thick, short prisms, m. p. 78·5—79·5° (Found : C, 67·2; H, 6·5. $C_{17}H_{20}O_5$ requires C, 67·1; H, 6·6%).

Dihydroxanthoxyletin.—Hydrogen (approx. 1 mol.) was rapidly absorbed at atmospheric pressure by xanthoxyletin (2 g.), dissolved in acetic acid (50 c.c.) containing 1% palladium chloride solution (10 c.c.). Evaporation of the filtered liquid in a vacuum left an almost pure *product*, which formed colourless rhombic prisms (1·9 g.), m. p. 144·5—145·5°, from benzene and then from benzene–light petroleum (b. p. 80—100°), considerably more soluble in organic solvents than xanthoxyletin [Found : C, 69·3; H, 6·2; OMe, 11·8; *M*, 233. $C_{14}H_{13}O_3(OMe)$ requires C, 69·2; H, 6·2; OMe, 11·9%; *M*, 260]. The same compound was obtained by hydro-

genation of xanthoxyletin (1 g.) in alcohol (150 c.c.) with a palladium catalyst (from 0·1 g. of palladium chloride).

O-*Methyltetrahydroxanthoxyletinic Acid.*—Reduction of *O*-methylxanthoxyletinic acid (1 g.) in acetic acid (50 c.c.) with hydrogen (approx. 2 mols. absorbed) and a palladium–charcoal catalyst (from 1 g. of activated charcoal and 0·05 g. of palladium chloride) was complete in about 10 minutes. Evaporation of the filtered solution in a vacuum left the *tetrahydro-acid*, which separated from benzene and then light petroleum (b. p. 80—100°) in colourless prisms (0·95 g.), m. p. 150·5—151·5° [Found : C, 65·3; H, 7·5; OMe, 22·9. $C_{14}H_{16}O_3(OMe)_2$ requires C, 65·3; H, 7·5; OMe, 21·1%].

When the hydrogenation was carried out in alcohol containing palladium chloride, the product consisted mainly of the ethyl ester, which on hydrolysis with 5% alcoholic sodium hydroxide for 1½ hours gave the tetrahydro-acid, forming colourless needles, m. p. and mixed m. p. 150—151°, from 50% alcohol.

O-*Methyldihydroxanthoxyletinic acid* was prepared from dihydroxanthoxyletin (1 g.) by the procedure used for the preparation of xanthoxyletinic acid and the product was hydrolysed by being boiled with 7% alcoholic potassium hydroxide for 1 hour. The resulting acid separated from benzene in small prisms, m. p. 171—172° (Found : C, 65·9; H, 7·0. $C_{16}H_{20}O_5$ requires C, 65·8; H, 6·9%). Mixed with the tetrahydro-acid, it melted at 135—140°.

Hydrogenation of the dihydro-acid (1 g.) in acetic acid (50 c.c.) with hydrogen and a palladium–charcoal catalyst gave rise to *O*-methyltetrahydroxanthoxyletinic acid, forming colourless prisms, m. p. 150·5—151·5°, from warm light petroleum (b. p. 80—100°), identical with a specimen prepared from *O*-methylxanthoxyletinic acid.

apo*Xanthoxyletin.*—A stream of ozone and oxygen was led into a solution of xanthoxyletin (1 g.) in chloroform (150 c.c.) until the yellow colour, which the solution gradually assumed, appeared to have maximum intensity (¾—1 hour). The residue left on evaporation of the solvent was digested with water (50 c.c.) at room temperature for 12 hours and then on the water-bath for 10 minutes. On cooling, a solution of the solid product in hot alcohol deposited apo*xanthoxyletin* (0·12—0·15 g.), which, after recrystallisation from the same solvent, was obtained in colourless slender needles, m. p. 217—218° [Found : C, 59·9; H, 3·8; OMe, 14·1. $C_{10}H_5O_4(OMe)$ requires C, 60·0; H, 3·6; OMe, 14·1%]. Concentration of the alcoholic mother-liquors from the crude product gave unchanged xanthoxyletin.

Treatment with ozone for shorter periods gave comparatively little *apo*xanthoxyletin with much unchanged material, and prolonged treatment resulted in mixtures from which little or no crystalline material could be isolated.

*apo*Xanthoxyletin is sparingly soluble in cold alcohol, acetic acid, or benzene, moderately easily soluble in hot alcohol, and insoluble in light petroleum or aqueous sodium bicarbonate. With aqueous sodium hydroxide the compound forms a yellow solution, from which it is precipitated unchanged. It gives a deep port-wine coloration with alcoholic ferric chloride and a silver mirror with ammoniacal silver nitrate at 55—60°, reduces Fehling's solution, and gives (slowly) a faint coloration with Schiff's reagent and a yellow solution in concentrated sulphuric acid which is unchanged on warming.

A solution of *apo*xanthoxyletin and excess of phenylhydrazine in acetic acid was gently warmed for several hours; the *phenylhydrazone*, which had gradually separated, was collected 24 hours later and recrystallised from alcohol, forming slender needles, m. p. 251° (decomp.) (Found : C, 65·7; H, 4·5; N, 9·4. $C_{17}H_{14}O_4N_2$ requires C, 65·8; H, 4·5; N, 9·0%).

Acetylation of *apo*xanthoxyletin (0·1 g.) with acetic anhydride (2 c.c.) and pyridine (1 c.c.) on the water-bath for 2½ hours and then under reflux for ½ hour gave rise to the *triacetyl* derivative, which formed colourless prisms, m. p. 151—152°, from alcohol, having a negative ferric reaction [Found : C, 56·2; H, 4·5; OMe, 8·3. $C_{16}H_{13}O_8(OMe)$ requires C, 56·0; H, 4·4; OMe, 8·5%]. Acetylation under less drastic conditions gave unchanged material or a mixture.

*Deoxy*apo*xanthoxyletin.*—The foregoing aldehydo-compound (0·3 g.) was reduced in acetic acid (50 c.c.) with hydrogen and a palladium–charcoal catalyst (from 0·05 g. of palladium chloride and 1 g. of activated charcoal); the absorption (approx. 2 mols.) was complete in about 10 minutes. After having been diluted with water (500 c.c.), the filtered solution was neutralised with sodium bicarbonate, and the *product* isolated with ether (8 extractions) and crystallised from benzene, forming slender needles (0·2 g.), m. p. 197—198°, readily soluble in alcohol and having a negative ferric reaction (Found : C, 64·2; H, 5·2. $C_{11}H_{10}O_4$ requires C, 64·1; H, 4·9%). This compound gives a yellow solution with aqueous sodium hydroxide and does not exhibit reducing properties. A solution of the substance in aqueous alcohol has a blue fluorescence.

The *methyl* ether of deoxy*apo*xanthoxyletin (V) was prepared by methylation of the aforementioned substance (0·7 g.) with methyl iodide (6 c.c.) and excess of potassium carbonate in boiling acetone during 1½ hours. After the addition of more acetone (75 c.c.) the solution was filtered, acidified with acetic acid (0·5 c.c.), and evaporated, and the residual *methyl* ether was well washed with water to remove traces of potassium salts, dried, and crystallised from benzene–light petroleum (b. p. 60—80°), forming colourless slender needles (0·52 g.), m. p. 138—139°, readily soluble in hot benzene or alcohol and insoluble in aqueous sodium hydroxide [Found : C, 65·5; H, 5·5; OMe, 27·7. $C_{10}H_6O_2(OMe)_2$ requires C, 65·5; H, 5·5; OMe, 28·2%]. An aqueous-alcoholic solution of the compound exhibited a blue fluorescence.

2 : 4 : 6-*Trimethoxy*-3-*methylcinnamic Acid* (VI).—By means of methyl sulphate and 20% aqueous sodium hydroxide according to the standard procedure the foregoing methyl ether was converted into the *cinnamic acid* (only traces of the ester were formed during alkylation), which was purified by the aid of 1% aqueous sodium hydroxide and then by crystallisation from benzene, forming colourless prisms, m. p. 163—164°, readily soluble in alcohol or acetic acid and reacting very slowly with aqueous sodium bicarbonate [Found : C, 62·0; H, 6·4; OMe, 36·3. $C_{10}H_7O_2(OMe)_3$ requires C, 61·9; H, 6·4; OMe, 36·9%].

Reduction of this acid (0·2 g.) with hydrogen (1 mol. absorbed) and a palladium catalyst proceeded rapidly in acetic acid (20 c.c.) and gave rise to 2 : 4 : 6-*trimethoxy*-3-*methyldihydrocinnamic acid*, which formed colourless prisms (0·15 g.), m. p. 139—140°, from benzene (Found : C, 61·1; H, 7·2. $C_{13}H_{18}O_5$ requires C, 61·4; H, 7·1%).

5 : 7-*Dimethoxy*-8-*methylcoumarin* (VII).—A mixture of 2-hydroxy-4 : 6-dimethoxy-3-methylbenzaldehyde (Curd and Robertson, J., 1933, 442) (1·5 g.), cyanoacetic acid (8 c.c. of a solution prepared according to the directions of Phelps and Tillotson, *Amer. J. Sci.*, 1908, **26**, 267), and 20% aqueous sodium hydroxide (5 c.c.) was agitated for 4 hours, diluted with water (100 c.c.), and acidified (Congo-red) with 8% hydrochloric acid. The yellow precipitate of 4 : 6-dimethoxy-3-methylsalicylidenecyanoacetic acid (III) (1·5 g.), m. p. 221—222° (decomp.), was converted into 5 : 7-dimethoxy-8-methylcoumarin-3-carboxylic acid (IV) (1·4 g.), m. p. 244—245° (decomp.), by being boiled with 4% hydrochloric acid (100 c.c.) for ½ hour. Decarboxylation of the latter compound (1·4 g.) was effected by boiling with quinoline (80 c.c.) and Kahlbaum's " Natur Kupfer " (5 g.) for 40 minutes. After cooling, ether (2 l.) was added and the filtered mixture was washed with 8% hydrochloric acid until all the quinoline was removed, then with aqueous sodium bicarbonate, and finally with water. Evaporation of the dried ethereal solution gave the *coumarin*, which separated from dilute alcohol in slender needles, m. p. 187—188°, readily soluble in alcohol or acetic acid and sparingly soluble in ether [Found : C, 65·4; H, 5·4; OMe, 27·6. $C_{10}H_8O_2(OMe)_2$ requires C, 65·5; H, 5·5; OMe, 28·2%]. A solution of this compound in aqueous alcohol exhibited a blue fluorescence. Mixed with the methyl ether of deoxy*apo*xanthoxyletin, it had m. p. 125—130°.

Hydrolysis of this coumarin (0·7 g.) and simultaneous methylation of the resulting acid by the standard method gave rise to 2 : 4 : 6-trimethoxy-3-methylcinnamic acid, m. p. 162—163° after crystallisation from benzene–light petroleum (Found : C, 61·8; H, 6·3; OMe, 36·4%). This compound was identical in every way with a specimen obtained from the methyl ether of deoxy*apo*xanthoxyletin. On reduction with hydrogen and a palladium catalyst it formed 2 : 4 : 6-trimethoxy-3-methyldihydrocinnamic acid, m. p. and mixed m. p. 139—140° after purification.

UNIVERSITY OF LIVERPOOL. [*Received, March 19th,* 1936.]