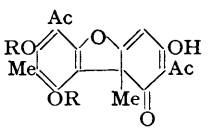
122. *Some Observations on the Constitution of Usnic Acid.*

By D. H. R. Barton and T. Bruun.

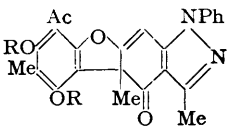
Ozonolysis of usnic acid anhydrophenylhydrazone diacetate affords 3-methyl-1-phenylpyrazole-4 : 5-dicarboxylic acid and a compound $(C_{16}H_{15}O_7)_2$. The latter results from the oxidative coupling of the intermediate 4 : 6-diacetoxy-7-acetyl-5-methylcoumaran-2-one; it is also produced by the oxidation of usnic acid diacetate with potassium permanganate. The degradation of usnic acid anhydrophenylhydrazone by potassium hydroxide in methanol and ethanol is reported. The significance of these results is assessed in terms of Robertson's usnic acid formula.

A number of constitutional formulæ has been suggested for the lichen constituent usnic acid (Dean, *Science Progr.*, 1952, **40**, 635; Mayer and Cook, " Natural Colouring Matters," Reinhold Publ. Corp., 1943, p. 157). Of these (I; R = H) was first proposed by Curd and Robertson (*J.*, 1937, 894). The experiments described in the present paper were designed to test this expression further.

Usnic acid readily affords an anhydrophenylhydrazone (II; R = H), converted by further treatment with phenylhydrazine into the phenylhydrazone anhydrophenylhydrazone (III) (Asahina and Yanagita, *Ber.*, 1938, **71**, 2260). The residual ketonic oxygen in this compound and its equivalent trifunctional derivatives has not hitherto been characterised and it could, *a priori*, be ketonic, oxidic, or ethereal. An attempt to prepare an oxime from (III) proved abortive, the product being the oxime anhydrophenylhydrazone (IV). The latter was also obtained, with concomitant deacetylation, when the anhydrophenylhydrazone diacetate (II; R = Ac) was treated with hydroxylamine hydrochloride in pyridine. Such steric resistance to oximation is not incompatible with structure (III), and indeed the infra-red spectrum showed an intense carbonyl band at 1673 cm.$^{-1}$ ($CHCl_3$ solution) indicative of an unsaturated ketonic function (in a six-membered ring).



(I)



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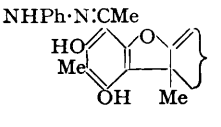

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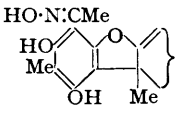
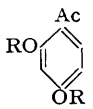


(IV)

The presence of a benzenoid ring in usnic acid was verified in two ways. First, conversion of usnic acid anhydrophenylhydrazone, which shows absorption of relatively low intensity above 300 mμ in the ultra-violet, into the phenylhydrazone anhydrophenylhydrazone (III) produces a characteristic band at 333 mμ of high intensity ($\varepsilon = 25{,}500$). A comparable marked change of absorption spectrum is produced when resacetophenone (V; R = H) is converted into its phenylhydrazone, the latter showing a band at 337 mμ ($\varepsilon = 25{,}500$). Similar arguments in favour of the presence of a system of resacetophenone type, based on ultra-violet measurements, have been adduced by MacKenzie (*J. Amer. Chem. Soc.*, 1952, **74**, 4067). Secondly, the anhydrophenylhydrazone diacetate showed a band at 1783 cm.$^{-1}$ (CCl_4 solution) in the infra-red, characteristic of a phenolic acetate, and of an intensity (cf. Jones, Ramsay, Keir, and Dobriner, *ibid.*, p. 80) corresponding to two such chromophores. Resacetophenone diacetate (V; R = Ac) similarly showed phenolic acetate bands at 1760 and 1775 cm.$^{-1}$ ($CHCl_3$ solution).

Ozonolysis of usnic acid diacetate by Schöpf and Ross (*Annalen*, 1941, **546**, 1; cf. Asahina and Okasaki, *J. Pharm. Soc. Japan*, 1943, **63**, 618) provided strong support for the Robertson formula. They isolated a product, m. p. 130—131°, formulated as 4 : 6-diacetoxy-7-acetyl-3 : 5-dimethylcoumaran-2-one (VI; R = Ac), and 2 : 4-diketopentanoic acid (VII); these account for all but one of the carbon atoms of usnic acid. It seemed to us, however, that there was no definitive evidence that (VII) was formed from (VIII), and indeed that there was only meagre support for the location of the carbon atom lost on ozonolysis within the usnic acid structure (I; R = H). We therefore ozonised usnic acid

anhydrophenylhydrazone diacetate (II; R = Ac). The acid fraction gave 3-methyl-1-phenylpyrazole-4 : 5-dicarboxylic acid (IX), the identity of which was confirmed by thermal decarboxylation to 3-methyl-1-phenylpyrazole-4-carboxylic acid (X). The dicarboxylic acid (X) retains the carbon atom " lost " in the previous ozonolysis, and substantiates its attachment in (I; R = H).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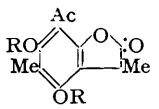
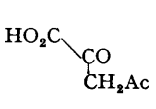

(VI)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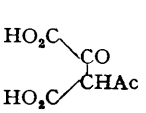
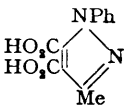

(VIII)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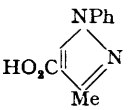
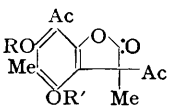

(X)

The neutral fraction from the ozonolysis afforded a compound, m. p. 225—226°, identical with a substance obtained by Takahashi and Shibata (*J. Pharm. Soc. Japan*, 1951, **71**, 1083) by oxidation of usnic acid diacetate with potassium permanganate. These authors had assigned to it the molecular formula $C_{18}H_{18}O_8$ and had regarded it as 4 : 6-diacetoxy-3 : 7-diacetyl-3 : 5-dimethylcoumaran-2-one (XI; R = R′ = Ac). Such a structure for our neutral ozonolysis product would imply that usnic acid had two more carbon atoms than the previously accepted molecular formula, $C_{18}H_{16}O_7$. A search of the earlier usnic acid literature revealed little justification for such a revision and, indeed, a precision molecular-weight determination on usnic acid diacetate gave a value in close agreement with the previously accepted theoretical value. The ozonolysis of usnic acid diacetate was therefore reinvestigated. The neutral fraction gave a compound, m. p. 131—132°, in agreement with previous workers. The constitution (VI; R = Ac) of this substance was confirmed in two ways. First, a precise molecular-weight determination gave a value in excellent agreement with the formula $C_{16}H_{16}O_7$. Secondly, the infra-red spectrum (in $CHCl_3$) showed bands at 1822 (γ-lactone with vinylic conjugation), 1780 (phenolic acetate; intensity corresponding to two acetate residues), and 1698 cm.$^{-1}$. The last band is due to an acetyl group attached to a benzene ring, as in resacetophenone diacetate (V; R = Ac), which shows a carbonyl band at 1690 cm.$^{-1}$ (in $CHCl_3$). The infra-red spectrum of the ozonolysis fragment, m. p. 225—226°, was practically identical with that of (VI; R = Ac), showing, therefore, the presence of identical carbonyl functions. The ultra-violet absorption spectra were also almost identical.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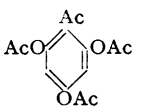
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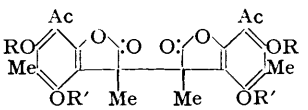
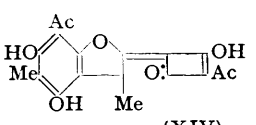

(XIII)

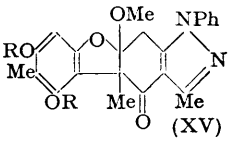
The nature of the compound, m. p. 225—226°, was finally established by its formation in good yield from (VI; R = Ac) by potassium permanganate or ozonolysis. Clearly it is produced by oxidative coupling and has the molecular formula $(C_{16}H_{15}O_7)_2$. A molecular-weight determination supported this conclusion. The analytical data of Takahashi Shibata (*loc. cit.*) are, in fact, in better agreement with the formula $(C_{16}H_{15}O_7)_2$ than with $C_{18}H_{18}O_8$. In so far as phloracetophenone triacetate (XII) shows no tendency to undergo oxidative coupling on treatment with potassium permanganate, and in view of the almost identical infra-red and ultra-violet spectra, with regard to both wave-length and intensity, of (VI; R = Ac) and the compound $(C_{16}H_{15}O_7)_2$, we formulate the latter as (XIII; R = R′ = Ac). There is good analogy for the postulated oxidative coupling (Bernatek and Berner, *Acta Chem. Scand.*, 1949, **3**, 1117).

In reviewing the chemistry of usnic acid as elucidated in this and earlier work it seemed to us that there was at least one other formula (XIV) which, with suitable assumptions, would explain the majority of the facts and would, in addition, afford an acceptable mechanistic explanation for its ready racemisation. In order to differentiate between (I; R = H) and (XIV), the degradation of usnic acid anhydrophenylhydrazone by potassium hydroxide was studied. In methanol this furnished a methoxy-compound, $C_{23}H_{22}O_5N_2$, which on the basis of (II; R = H) should be (XV; R = H). In agreement it afforded a

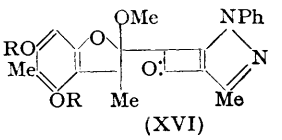
diacetate which showed bands in the infra-red at 1770 (phenol acetate) and at 1672 cm.$^{-1}$ [the sterically hindered ketone group (see above) of the parent anhydrophenylhydrazone], was stable to ozone and, on attempted oximation, gave back the parent phenol. The presence in the phenol of a free aromatic position *ortho* to a hydroxyl group was shown by its ready coupling with diazotised anthranilic acid—usnic acid anhydrophenylhydrazone does not, of course, couple readily with diazonium salts. On the basis of (XIV) the methanolic potassium hydroxide degradation product would be (XVI; R = H). The main objection to this comes from the infra-red spectrum (see above) of the diacetate. *cyclo*Butanones have carbonyl maxima near 1780 cm.$^{-1}$. Conjugation would reduce the frequency of the band, but it would be most unexpected if it were to be reduced to 1672 cm.$^{-1}$ or if the frequency should remain unchanged on going from usnic acid phenylhydrazone anhydrophenylhydrazone (see above) to (XVI; R = Ac).



(XIV)

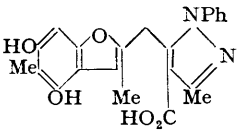


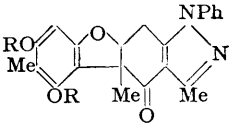
(XV)



(XVI)

(XVII)





(XVIII)

Degradation of usnic acid anhydrophenylhydrazone under more vigorous conditions, with aqueous or (better) ethanolic potassium hydroxide, afforded a high-melting, optically inactive acid, $C_{22}H_{20}O_5N_2$, further characterised as the diacetate methyl ester. The acid coupled at once with diazotised anthranilic acid. This compound may be formulated as (XVII) on the basis of (I; R = H) for usnic acid. It was also obtained in small amount as a by-product in the treatment of the anhydrophenylhydrazone with methanolic potassium hydroxide.

In support of formula (I; R = H) for usnic acid, and against (XIV), dihydrousnic acid diacetate (XVIII; R = Ac) showed bands (in CS_2) at 1780 (phenol acetate), 1690 (acetyl attached to a benzene ring), and 1676 cm.$^{-1}$ (conjugated ketone).

There remains for discussion the mechanism of racemisation of usnic acid. MacKenzie (*loc. cit.*) suggested that this may involve homolysis. It seems to us that this is somewhat improbable, (*a*) because usnic acid anhydrophenylhydrazone is not racemised in boiling xylene solution whereas usnic acid itself is and (*b*) because the racemisation of usnic acid, as in the preparation of racemic usnic acid diacetate from the optically active acid (Asahina and Yanagita, *Ber.*, 1939, **72**, 1140), is acid-catalysed. We conclude that, whilst a plausible mechanism for the racemisation has as yet to be devised, Robertson's structure (I) for usnic acid is probably correct.

Experimental

Unless specified to the contrary rotations were determined in chloroform solution at room temperature (15—25°). Light petroleum refers to the fraction of b. p. 40—60°. Ultra-violet absorption spectra were measured in ethanol solution with a Unicam S.P. 500 Spectrophotometer. Infra-red absorption spectra were kindly determined by Dr. A. R. H. Cole (University of Western Australia) and by Dr. J. E. Page of Messrs. Glaxo Laboratories Ltd. Electrometric titrations were carried out in aqueous solution at room temperature using a Cambridge pH meter; during titrations precautions were taken to prevent ingress of carbon dioxide; a glass electrode was used in the usual way with a calomel cell as reference electrode. Precise molecular weights were kindly determined in benzene solution by Dr. R. C. Mehrotra using a modified Menzies–Wright ebulliometer (Bradley, Mehrotra, and Wardlaw, *J.*, 1952, 2027).

The experiments reported below were carried out with (+)-usnic acid, $[\alpha]_D$ from +445° to +515° (*c*, 2·00 to 3·19) and with (−)-usnic acid, $[\alpha]_D$ −445° to −478° (*c*, 2·00 to 3·08), the rotations varying slightly with the batch of acid supplied.

Usnic Acid Diacetate.—The (+)-diacetate was prepared according to the directions of

Asahina and Yanagita (*Ber.*, 1938, **71**, 2260), care being taken that the temperature did not exceed 50°. Recrystallised from methanol it had m. p. 203—204°, $[\alpha]_D$ +240° (*c*, 2·85), $\lambda_{max.}$ 224 mμ (ε = 26,000), inflexions at 249 and 305 mμ (ε = 17,000 and 9000 respectively) (Found: *M*, 424; Calc. for $C_{22}H_{20}O_9$: *M*, 428). The (−)-diacetate was prepared as for the (+)-compound (see above). It had the same m. p. and $[\alpha]_D$ −235° (*c*, 1·82).

Usnic Acid Anhydrophenylhydrazone (II; R = H).—The (+)-anhydrophenylhydrazone (Asahina and Yanagita, *loc. cit.*; they report m. p. 195°) recrystallised from chloroform–ethanol, had m. p. 199—200°, $[\alpha]_D$ +620° (*c*, 2·13), +624° (*c*, 1·40), $\lambda_{max.}$ 221, 253, 287, and 370 mμ (ε = 37,000, 29,000, 24,000, and 4000 respectively) (Found: C, 68·6; H, 5·05. Calc. for $C_{24}H_{20}O_5N_2$: C, 69·2; H 4·85%). With acetic anhydride in pyridine at room temperature overnight it afforded the *diacetate*, m. p. 225—226° (from methanol containing a little chloroform), $[\alpha]_D$ +426° (*c*, 2·15), $\lambda_{max.}$ 245 and 296 mμ, $\lambda_{inflex.}$ 349 mμ (ε = 34,500, 12,500, and 4000 respectively) (Found: C, 67·4; H, 4·95; N, 5·65, 5·75. $C_{28}H_{24}O_7N_2$ requires C, 67·2; H, 4·85; N, 5·6%).

The anhydrophenylhydrazone diacetate (300 mg.) was refluxed for 6 hours in xylene (25 ml.). The xylene was removed *in vacuo* on the steam-bath and the residue recrystallised from methanol to give unchanged diacetate, identified by m. p., mixed m. p., and $[\alpha]_D$ +411° (*c*, 1·41).

Prepared in analogous ways were (−)-*usnic acid anhydrophenylhydrazone*, m. p. 198—199° $[\alpha]_D$ −604° (*c*, 2·28) (Found: C, 68·6; H, 4·65%), and its *diacetate*, m. p. 222—223°, $[\alpha]_D$ −414° (*c*, 2·12) (Found: C, 67·0; H, 4·35; N, 6·15%).

(+)-*Usnic Acid Phenylhydrazone Anhydrophenylhydrazone* (III).—When prepared according to Widman (*Annalen*, 1900, **310**, 230), this had a wide melting range but was converted in refluxing ethanol into the higher-melting form, m. p. 235—236° (decomp.), $[\alpha]_D$ +512° (*c*, 2·10), $\lambda_{max.}$ 258, 303, and 333 mμ (ε = 33,000, 24,000, and 25,500 respectively). For this compound Asahina and Yanagita (*loc. cit.*) reported m. p. (higher-melting form) 233°, $[\alpha]_D$ +500°.

Treatment of the phenylhydrazone anhydrophenylhydrazone or of the anhydrophenylhydrazone diacetate with excess of hydroxylamine hydrochloride in pyridine on the steam-bath for 1 hour afforded (+)-*usnic acid anhydrophenylhydrazone oxime* (IV), m. p. 279—280° (decomp.) (from chloroform), $[\alpha]_D$ +610° (*c*, 0·48; 2-dm. tube), $\lambda_{max.}$ 223, 257, and 368 mμ (ε = 34,500, 33,500, and 3500 respectively) (Found: N, 9·45. $C_{24}H_{21}O_5N_3$ requires N, 9·75%).

Degradation of Usnic Acid Anhydrophenylhydrazone with Potassium Hydroxide in Methanol.—The anhydrophenylhydrazone (200 mg.) was refluxed with methanolic potassium hydroxide (10 ml. of methanol; 2·0 g. of potassium hydroxide) on the steam-bath for 3 hours. After dilution with water, ether-extraction and working up in the usual way gave the *compound* (XV; R = H). After washing with a little ether and recrystallisation from chloroform–light petroleum the (−)-isomer had m. p. 206—207°, $[\alpha]_D$ −380° (*c*, 0·81), $\lambda_{max.}$ 261 and 326 mμ (ε = 19,500 and 2000 respectively) (Found: C, 67·6; H, 5·4; N, 6·45; OMe, 8·15. $C_{23}H_{22}O_5N_2$ requires C, 67·95; H, 5·45; N, 6·9; OMe, 7·65%). Similarly the (+)-isomer had m. p. 206—207°, $[\alpha]_D$ +376° (*c*, 0·72), $\lambda_{max.}$ 261 and 326 mμ (ε = 18,000 and 2000 respectively) (Found: N, 7·3%). Both isomers coupled readily with diazotised anthranilic acid.

With acetic anhydride in pyridine at room temperature overnight the (−)-isomer gave the *diacetate* (XV; R = Ac). Recrystallised from chloroform–methanol this had m. p. 209—210° (depressed to 170—190° on admixture with starting material), $[\alpha]_D$ −280° (*c*, 2·25), $\lambda_{max.}$ 262 mμ (ε = 17,000) (Found: C, 66·25; H, 5·3; N, 5·8. $C_{27}H_{26}O_7N_2$ requires C, 66·1; H, 5·35; N, 5·7%). Attempted oximation with hydroxylamine hydrochloride in pyridine on the steam-bath for 1·5 hours gave back the parent phenol, m. p. and mixed m. p. 206—207°, $[\alpha]_D$ −380° (*c*, 0·86), $\lambda_{max.}$ 261 and 326 mμ (ε = 19,500 and 2000 respectively). The (−)-diacetate was recovered unchanged on ozonolysis under the conditions applied successfully to usnic acid diacetate and anhydrophenylhydrazone diacetate (see below).

Degradation of Usnic Acid Anhydrophenylhydrazone with Potassium Hydroxide in Water or Ethanol.—The anhydrophenylhydrazone (200 mg.) was heated with water (10 ml.) containing potassium hydroxide (7·5 g.) on the steam-bath for 1 hour in oxygen-free nitrogen. The anhydrophenylhydrazone only partly dissolved. After cooling, dilution with water, acidification with dilute sulphuric acid, and filtration, unchanged starting material (126 mg.), identified by m. p. and mixed m. p., was recovered. The filtrate was extracted with ether and the ethereal layer in turn extracted with 1% aqueous sodium hydrogen carbonate and then with 2% aqueous sodium carbonate. Acidification of these two extracts furnished an *acid* (XVII) (18 and 12 mg. repectively). Recrystallised from chloroform–methanol this had m. p. 306° (decomp.), α 0°, $\lambda_{max.}$ 246, 305, and 352 mμ (ε = 26,500, 12,500, and 4000 respectively) (Found: C, 67·0; H, 4·85; N, 7·2. $C_{22}H_{20}O_5N_2$ requires C, 67·35; H, 5·15; N, 7·15%). From the ethereal extract

(see above) a further 38 mg. of unchanged starting material were recovered (identified by m. p. and mixed m. p.).

The acid (XVII) was prepared in better yield as follows: The anhydrophenylhydrazone (200 mg.) was refluxed with ethanol (10 ml.) containing potassium hydroxide (2·5 g.) for 2 hours. Working up as outlined above gave 150 mg. of the crude acid. The acid, which was obtained from both the (+)- and the (−)-anhydrophenylhydrazone, was also formed in very small amount in the methanolic potassium hydroxide degradations described above. It gave a strongly positive coupling test with diazotised anthranilic acid.

For further characterisation the acid was converted into the *diacetate methyl* ester by acetylation with pyridine–acetic anhydride and methylation of the product with diazomethane. Recrystallised from methanol or acetone the ester had m. p. 157—158°, α 0°, $\lambda_{max.}$ 237 mμ (ε = 30,000), $\lambda_{inflex.}$ 278 and 306 mμ (ε = 8000 and 5000 respectively) (Found: N, 5·55; OMe, 6·75. $C_{27}H_{26}O_7N_2$ requires N, 5·7; OMe, 6·35%).

Ozonolysis of Usnic Acid Anhydrophenylhydrazone Diacetate.—The ozonolyses were carried out on both (+)- and (−)-diacetate with the same results. The diacetate (500 mg.) in carbon tetrachloride (20 ml.) was treated at 0° with ozonised oxygen until the yellow colour of the solution had been discharged. The resulting ozonide was worked up in various ways: (*a*) by addition of ethanol and heating on the steam-bath for 15 minutes, (*b*) by addition of water and either keeping the mixture overnight or refluxing it on the steam-bath for 15 minutes. In all cases the same two crystalline compounds were isolated. After decomposition of the ozonide, 1% aqueous sodium hydrogen carbonate solution was added and the carbon tetrachloride layer extracted. From the neutral fraction (250 mg.) remaining in the carbon tetrachloride the tetra-acetoxy-dilactone (XIII; R = R′ = Ac) was obtained. This was chromatographed over alumina washed with ethyl acetate (see Mancera, Barton, Rosenkranz, and Djerassi, *J.*, 1952, 1025). Elution with benzene gave the dilactone (XIII; R = R′ = Ac) which, after recrystallisation from chloroform–methanol, had m. p. 225—226°, α 0°, $\lambda_{max.}$ 220 and 296 mμ (ε = 19,000 and 2500 respectively) (Found: C, 60·2; H, 4·8%; *M*, 578, not very accurate owing to sparing solubility. Calc. for $C_{32}H_{30}O_{14}$: C, 60·2; H, 4·75%; *M*, 638). Hydrolysis of the tetra-acetate by cold concentrated sulphuric acid (Takahashi and Shibata, *J. Pharm. Soc. Japan*, 1951, **71**, 1083) gave the tetrahydroxy-dilactone (XIII; R = R′ = H); this had m. p. 270—271° (decomp.) (from acetone), α 0°, $\lambda_{max.}$ 240, 286, and 326 mμ (ε = 12,000, 16,000, and 3400 respectively). Re-acetylation gave back the tetra-acetate, identified by m. p., mixed m. p., and ultra-violet spectrum.

The acid fraction from the ozonolysis was isolated by thorough extraction with ether of the acidified sodium hydrogen carbonate solution. It was treated in a little methanol with a concentrated solution of potassium hydroxide in methanol. This precipitated the insoluble potassium salt which was filtered off and washed with methanol. After acidification of the potassium salt, the liberated 3-methyl-1-phenylpyrazole-4 : 5-dicarboxylic acid (IX) was crystallised from ethanol–benzene or ethanol–chloroform. It had m. p. 199—200° (decomp.), α 0°, $\lambda_{max.}$ 255 mμ (ε = 13,000), and behaved as a dicarboxylic acid on electrometric titration: pK_1 = 2·83, pK_2 = 5·89 (Found: Equiv., 123. Calc. for $C_{12}H_{10}O_4N_2$: Equiv., 123). There was no depression in m. p. on admixture with an authentic specimen of 3-methyl-1-phenylpyrazole-4 : 5-dicarboxylic acid, m. p. 202—203° (decomp.), $\lambda_{max.}$ 255 mμ (ε = 11,000), synthesised by Benary's method (*Ber.*, 1910, **43**, 1065) and purified as above.

The acid obtained from the ozonolysis was decarboxylated on melting, to a carboxylic acid (X), m. p. 194—195°, optically inactive, $\lambda_{max.}$ 266 mμ (ε = 21,500). On electrometric titration this behaved as a monobasic acid, pK = 4·58 (Found: Equiv., 200. Calc. for $C_{11}H_{10}O_2N_2$: Equiv., 202). There was no depression in m. p. on admixture with authentic 3-methyl-1-phenylpyrazole-4-carboxylic acid, m. p. 193—194°, $\lambda_{max.}$ 266 mμ (ε = 24,500), prepared by thermal decarboxylation of the authentic 4 : 5-dicarboxylic acid (cf. Benary, *loc. cit.*).

Oxidation of Usnic Acid Diacetate with Potassium Permanganate.—The same results were obtained with (+)- and (−)-usnic acid diacetate. The diacetate (2 g.) in "AnalaR" acetone (100 ml.) was oxidised with potassium permanganate according to Takahashi and Shibata (*loc. cit.*). Recrystallisation of the product from chloroform–methanol or chloroform–acetone afforded the tetra-acetoxy-dilactone (XIII; R = R′ = Ac), m. p. 225—226° (undepressed on admixture with the compound prepared as above), α 0°, $\lambda_{max.}$ 220 and 297 mμ (ε = 17,500 and 2500 respectively). For further comparison this was hydrolysed to the phenol, m. p. 270—271° (decomp.), α 0°, $\lambda_{max.}$ 240, 286, and 325 mμ (ε = 11,500, 15,500, and 3300 respectively), undepressed in m. p. on admixture with the previous sample. Re-acetylation gave back the tetra-acetate (m. p., mixed m. p., and ultra-violet spectrum).

The tetra-acetate obtained by potassium permanganate was further treated with methanolic hydrochloric acid according to the directions of Takahashi and Shibata (*loc. cit.*). The diacetoxy-dilactone (XIII; R = H, R′ = Ac) thus obtained had, after crystallisation from chloroform–methanol, m. p. 194—195°, α 0°, $\lambda_{max.}$ 220, 256, and 336 mμ (ε = 13,000, 12,500, and 3200 respectively.)

Ozonolysis of Usnic Acid Diacetate.—The same results were obtained with (+)- and (−)-usnic acid diacetate. The diacetate (500 mg.) in carbon tetrachloride (20 ml.) at 0° was treated with ozonised oxygen until the yellow colour had been discharged. The ozonide was decomposed by water and either kept overnight or refluxed on the water-bath for 15 minutes. The neutral fraction of the product was recrystallised by Schöpf and Ross's method (*Annalen*, 1941, **546**, 1), to give 4 : 6-diacetoxy-7-acetyl-3 : 5-dimethylcoumaran-2-one (VI; R = Ac), m. p. 130—131°, α 0°, $\lambda_{max.}$ 218 and 297 mμ (ε = 23,000 and 3300 respectively) (Found: *M*, 319. Calc. for $C_{16}H_{16}O_7$: *M*, 320). The mixed m. p. with the tetra-acetoxy-dilactone (XIII; R = R′ = Ac) (m. p. 225—226°) ranged from 130° to 205° even on very slow heating.

Hydrolysis of the diacetate with cold concentrated sulphuric acid (cf. Takahashi and Shibata, *loc. cit.*) afforded 7-acetyl-4 : 6-dihydroxy-3 : 5-dimethylcoumaran-2-one (VI; R = H), m. p. 233—234°, $\lambda_{max.}$ 238, 284, and 332 mμ (ε = 12,000, 18,000, and 3300 respectively). The mixed m. p. with the tetrahydroxy-dilactone (XIII; R = R′ = H) [m. p. 270—271° (decomp.)] ranged from 230° to 263° even on very slow heating.

Oxidation of 4 : 6-*Diacetoxy-7-acetyl-3* : 5-*dimethylcourmaran-2-one with Potassium Permanganate.*—The lactone (120 mg.) and finely powdered potassium permanganate (60 mg.) in "AnalaR" acetone (5 ml.) were shaken for 30 minutes. The excess of oxidant was destroyed by ethanol, and the manganese dioxide removed. The filtrate was concentrated, whereupon the tetra-acetoxy-dilactone crystallised. Recrystallised from chloroform–methanol, this (65 mg.) had m. p. and mixed m. p. 225—226°, $\lambda_{max.}$ 220 and 297 mμ (ε = 19,000 and 2800). The identity was further confirmed by conversion by methanolic hydrochloric acid (Takahashi and Shibata, *loc. cit.*) into the diacetoxy-dilactone (XIII; R = H, R′ = Ac), $\lambda_{max.}$ 220, 254, and 337 mμ (ε = 12,000, 11,000 and 2700), m. p. 194—195° alone or mixed with the material prepared as above.

Ozonolysis of 4 : 6-*Diacetoxy-7-acetyl-3* : 5-*dimethylcoumaran-2-one.*—The lactone (50 mg.) in carbon tetrachloride (5 ml.) was treated with ozonised oxygen for 1 hour at room temperature. Water was then added and the mixture refluxed on the steam-bath for 20 minutes. Working up in the usual way afforded the tetra-acetoxy-dilactone (XII; R = R′ = Ac), m. p. and mixed m. p. 226—227°, $\lambda_{max.}$ 220 and 297 mμ (ε = 18,000 and 2900).

Dihydrousnic Acid Diacetate.—(+)- and (−)-Usnic acid diacetate were hydrogenated according to the directions of Asahina, Yanagita, and Mayeda (*Ber.*, 1937, **70**, 2462). Recrystallised from methanol, (+)-dihydrousnic acid diacetate had m. p. 148—149°, $[\alpha]_D$ +4·5° (*c*, 4·68), $\lambda_{max.}$ 220, 276, and 316 mμ (ε = 29,000, 11,000, and 6100 respectively), $\lambda_{inflex.}$ 239 mμ (ε = 18,000). Hydrolysis with cold concentrated sulphuric acid gave (−)-dihydrousnic acid, m. p. 147—148°, $[\alpha]_D$ −88° (*c*, 2·86), $\lambda_{max.}$ 228, 283, and 336 mμ (ε = 19,000, 25,500, and 3600 respectively). Asahina, Yanagita, and Mayeda (*loc. cit.*) gave m. p. 150°, $[\alpha]_D$ −84°. (−)-Dihydrousnic acid diacetate likewise had m. p. 148—149°, $[\alpha]_D$ −6° (*c*, 4·88), −6° (*c*, 4·64), −6° (*c*, 1·00), and the derived (+)-dihydrousnic acid, m. p. 147—148°, $[\alpha]_D$ +83° (*c*, 2·38), $\lambda_{max.}$ 228, 283, and 336 mμ (ε = 22,000, 26,500, and 3900 respectively).

(+)-Dihydrousnic acid diacetate (100 mg.) in carbon tetrachloride (5 ml.) was treated with ozonised oxygen for 1 hour at room temperature. After addition of water and refluxing on the steam-bath for 15 minutes, the starting material was recovered (m. p. and mixed m. p. 147—148°).

(+)-Dihydrousnic acid diacetate (200 mg.) was unchanged when refluxed in xylene (20 ml.) for 6 hours {m. p. and mixed m. p. 147—148°, $[\alpha]_D$ +3·5° (*c*, 4·64)}.

Miscellaneous Derivatives.—Resacetophenone diacetate had m. p. 38—38·5°, $\lambda_{max.}$ 248 mμ (ε = 13,500). Resacetophenone phenylhydrazone had m. p. 161—162°, $\lambda_{max.}$ 246, 304, and 337 mμ (ε = 15,500, 13,000, and 25,500, respectively). Resacetophenone 4-acetate had m. p. 74—75°, $\lambda_{max.}$ 257 and 318 mμ (ε = 12,000 and 4600). Phloroacetophenone had λ_{max} 228 and 288 mμ (ε = 15,000 and 19,000 respectively). *Phloracetophenone triacetate*, prepared by treating the keto-phenol with pyridine and acetic anhydride overnight at room temperature and, crystallised from chloroform–light petroleum, formed needles, m. p. 58—59°, $\lambda_{max.}$ 239 mμ (ε = 6500) (Found: C, 57·3; H, 4·7. $C_{14}H_{14}O_7$ requires C, 57·15; H, 4·8%); it gave no colour with ferric chloride whereas the compound previously described under the same name (see Beilstein, Vol. VIII, 2nd Suppl. Vol., p. 394) was said to give a colour and have m. p. 90°. Phlor-

acetophenone triacetate was, in part, recovered unchanged when shaken for 30 minutes with its own weight of finely powdered potassium permanganate in " AnalaR " acetone (m. p. and mixed m. p. 58—59°).

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