451. *Usnic Acid. Part XII.* Pummerer's Ketone.*

By Vincent Arkley, F. M. Dean, Alexander Robertson, and Padet Sidisunthorn.

The structure (II) allocated by Pummerer *et al.*[1] to the ketone formed by the ferricyanide oxidation of *p*-cresol has been modified to (III), thus aligning it with the structure of usnic acid. The revision was necessitated both by the failure of attempts to convert 2 : 5′-dihydroxy-5 : 2′-dimethyldiphenyl into the ketone and by the non-identity of the dihydro-derivative of this ketone with authentic 1 : 2 : 3 : 4 : 10 : 11-hexahydro-6 : 10-dimethyl-3-oxodibenzofuran, a difference shown not to be stereochemical. The ketone has been converted into, and recovered from, derivatives of the isomeric dienone (VII; R = H) considered to be an intermediate in the formation of the ketone from *p*-cresol.

When proposing structure (I) for usnic acid, Curd and Robertson (*J.*, 1937, 894) remarked that this system could arise from the linking—indicated in (I) by the broken bond—of two molecules of *C*-methylphloracetophenone. Pummerer, Puttfarcken, and Schapflocher [1] had previously shown that one of the products of ferricyanide oxidation of *p*-cresol was a neutral ketone to which they ascribed formula (II), and it was suggested by one of us [2] that this reaction might be a prototype for the genesis of usnic acid though the different positions allocated to the angular methyl groups prevented a direct correlation at that time. A study of the *p*-cresol oxidation product (which it is now convenient to call Pummerer's ketone) has caused us to discard formula (II) and to establish formula (III) in its place. Barton, Deflorin, and Edwards [3] recently reached the same conclusion by a different route and showed that usnic acid can be formed in this type of reaction.

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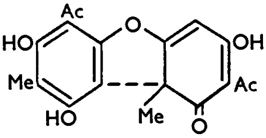
* Part XI, *J.*, 1955, 2166.

[1] Pummerer, Puttfarcken, and Schopflocher, *Ber.*, 1922, **55**, 3116; 1925, **58**, 1808.

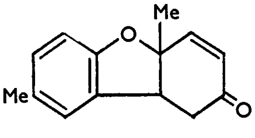
[2] Dean, *Sci. Progress*, 1952, **40**, 635.

[3] Barton, Deflorin, and Edwards *Chem. and Ind.*. 1955, **33**, 1039.

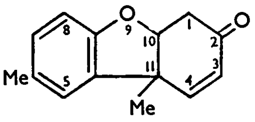
Because ferricyanide oxidations are of the one-electron type, the oxidation of *p*-cresol probably involves radical intermediates that can take the forms (IV*a*, *b*, *c*) and can therefore lead to intermediates (V) and (VII; R = H), of which we considered the latter to be the more attractive because it provides a convenient means for cyclisation to (III). However, the attack on phenols by lead tetra-acetate,[4] benzoyl peroxide,[5] nitrous acid and ferric chloride,[6] and certain more complex oxidising agents [7] does produce compounds akin to (V) so that this possibility cannot be excluded immediately; even the less obvious structure (VI) is reasonable mechanistically and structurally because of its close relation to 3 : 3′-di-*p*-cresol (2 : 2′-dihydroxy-5 : 5′-dimethyldiphenyl), a major component of the ferricyanide oxidation mixture.



(I)



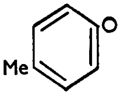
(II)



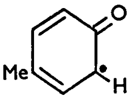
(III)

The isomerisation of the *p*-cresol oxidation product to a dihydric phenol, induced by mineral acids, was first noted by Pummerer and his collaborators [1] who interpreted it as the production of 2 : 3′-di-*p*-cresol (2 : 5′-dihydroxy-5 : 2′-dimethyldiphenyl) (VIII; R = H) from the ketone (II). The formulation (VIII; R = H) for the dicresol was adduced from comparisons with the known and different 2 : 2′- and 3 : 3′-di-*p*-cresols and was later partially supported by the work of Westerfeld and Lowe [8] who recorded the relevant ultra-violet spectra and converted the new dicresol into a dimethoxydiphenic acid, which, however, was not oriented.

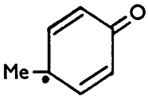
Because of its relation to a β-hydroxy-ketone, a compound of structure (III) would be relatively easily affected by acids and thus 2 : 3′-di-*p*-cresol would be formed by preferential Wagner migration of the aryl group [9] in the intermediate dienone (VII; R = H). Although isomerisation of the ketone (VI) would probably yield 3 : 3′-di-*p*-cresol, migration of the methyl group preceding ring fission could result in a derivative (IX) of *m*-cresol with properties indistinguishable from those mentioned above. From Pummerer's view of the isomerisation, which assumes that no change in the carbon skeleton occurs, it follows that the dicresol should regenerate the ketone when treated with ferricyanide; it is therefore significant that in preliminary experiments (personal communication from Mr. E. Evans of this Department) the dicresol was found to be unaffected by this reagent.[10]



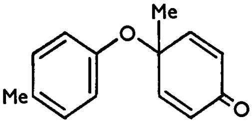
(IV*a*)



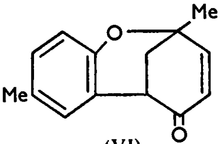
(IV*b*)



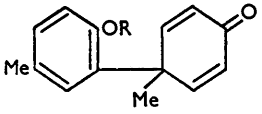
(IV*c*)



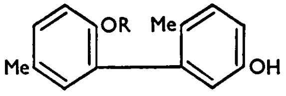
(V)



(VI)



(VII)



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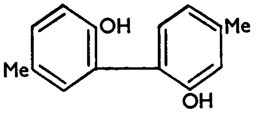

(IX)

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[4] Von Wessely and Sinwel, *Monatsh.*, 1950, **81**, 1055.

[5] Cosgrove and Waters, *J.*, 1951, 388.

[6] Pummerer and Cherbuliez, *Ber.*, 1914, **47**, 2957.

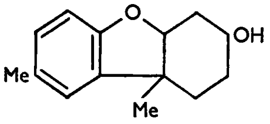
[7] Pummerer, Schmidutz, and Seifert, *Chem. Ber.*, 1952, **85**, 535.

[8] Westerfeld and Lowe, *J. Biol. Chem.*, 1942, **145**, 463.

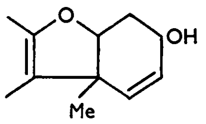
[9] Arnold and Buckley, *J. Amer. Chem. Soc.*, 1949, **71**, 1781.

[10] Cf. Bacon, Grime, and Munro, *J.*, 1954, 2275.

Hydrogenation of Pummerer's ketone gave an alcohol, now considered to be (X), which differed from the compound (XI) formed by reduction with aluminium *iso*propoxide. As expected, Oppenauer oxidation of the latter compound (XI) regenerated Pummerer's ketone, whereas the former (X) gave a compound (XII), which, had Pummerer's formulation (II) been correct, would have had structure (XIX). Ketone (XIX) was synthesised independently and shown to differ from our product (XII).



(X)



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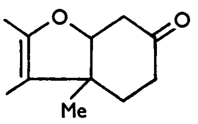
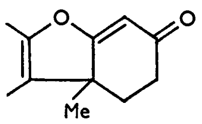
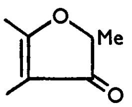


(XII)



(XIII)



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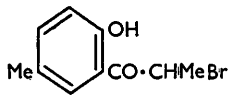

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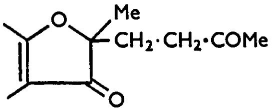
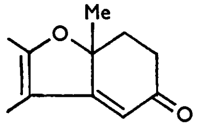
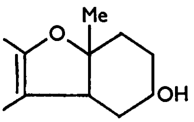


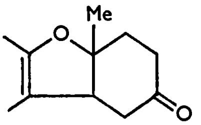
(XVI)



(XVII)



(XVIII)



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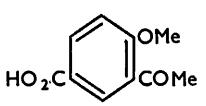

(XX)

For the synthesis of the ketone (XIX), 2 : 5-dimethylcoumaran-3-one (XIV) was required. Prepared according to von Auwers,[11] the bromo-ketone (XV) could not be cyclised to the coumaranone (XIV) with sodium acetate as described by this author until it was discovered that pyridine catalysed the reaction. Interaction of methyl vinyl ketone and the coumaranone (XIV) readily gave the adduct (XVI), which was cyclised to the unsaturated ketone (XVII), having the requisite characteristic absorption in the ultraviolet and the infrared region. Its stability to acids contrasted sharply with the behaviour of the isomeric Pummerer's ketone. When hydrogenated, the unsaturated ketone (XVII) furnished an alcohol (XVIII) easily converted into the desired compound (XIX) by the method of Oppenauer.

The non-identity of this product (XIX) and the corresponding substance from Pummerer's ketone could, of course, have resulted from a difference in ring fusion at the 10 : 11-positions. Hückel and Linstead [12] consider *cis-* to have greater thermodynamic stability than *trans*-fused systems when a five-membered is involved with a six-membered ring. On this basis Pummerer's ketone and its reduction products, and also compounds (XVIII) and (XIX), would all have the stable *cis*-configuration. In agreement with this it was not possible to induce isomerisation of either compound (XII) or (XIX) by means of palladium [13] at 350° or to obtain any product other than the saturated alcohol (XVIII) by varying the conditions in which unsaturated ketone (XVII) was hydrogenated. Stereochemical differences were finally excluded by the results of chromic acid oxidations.

With chromic acid, the alcohol (XVIII) reverted to the unsaturated ketone (XVII), whereas the corresponding alcohol (X) from Pummerer's ketone gave a new isomeric αβ-unsaturated ketone. The methyl group in the 10-position of (II) makes impossible an inversion at this point, and so saturation and regeneration of the double bond in (II) could not affect the type of ring fusion. Had Pummerer's ketone possessed structure (II), then,

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[11] Von Auwers, *Ber.*, 1914, **47**, 3307; 1926, **59**, 2630.

[12] Hückel and Linstead, *Ann. Reports*, 1935, **32**, 306.

[13] Bachmann, Ross, Dreiding, and Smith, *J. Org. Chem.*, 1954, **19**, 222.

this sequence of reactions must have resulted in either the regeneration of (II) or the production of its isomer (XVII) where there is no duplicity of ring fusion. Thus structure (II) cannot account for the formation of the new isomer. Further, structure (VI) is also inadequate, for here the only other possible αβ-unsaturated ketone contravenes Bredt's rule. On the other hand, because oxidation of the alcohol (X) would be expected to generate ketone (XIII) rather than Pummerer's ketone, the formulation (III) does provide a satisfactory expression for the *p*-cresol oxidation product and it follows that the dicresol is indeed 2 : 3′-di-*p*-cresol.

The expectation that acid-catalysed fission of the tetrahydrodibenzofuran (III) to the dicresol (VIII; R = H) would have a base-catalysed counterpart not involving Wagner rearrangement has been realised. Sodium ethoxide in ether converted Pummerer's ketone (III) into a sodium salt which by interaction with acetic anhydride, benzoyl chloride, or methyl iodide, furnished respectively an acetate (VII; R = Ac), a benzoate (VII; R = Bz) and a methyl ether (VII; R = Me), all of which possessed carbonyl activity and ultraviolet and infrared absorption characteristic of the *cyclo*hexa-2 : 5-dienone system together with those of the appropriate aromatic residues. The same compounds could be prepared more readily by treatment of Pummerer's ketone with, respectively, pyridine and acetic anhydride or benzoyl chloride, and with methyl sulphate and aqueous alkali. Although oxidation of the acetate (VII; R = Ac) with permanganate gave a mixture which included *p*-cresotic acid and 2-hydroxy-5-methylacetophenone (identified as the 2 : 4-dinitrophenylhydrazone), a more satisfactory result was obtained from oxidation of the methyl ether (VII; R = Me) which furnished 3-acetyl-4-methoxybenzoic acid (XX), thus confirming the position allocated to the angular methyl group in the benzofuran (III). The methyl ether (VII; R = Me) also suffered the dienone–phenol rearrangement when treated with acids and then formed the methoxyphenol (VIII; R = Me) correlated with Pummerer's dicresol (VIII; R = H) through the dimethyl ether.

It did not seem possible to isolate the ketone (VII; R = H) because the sodium derivative rapidly regenerated Pummerer's ketone when added to water. This ready cyclisation agrees well with the postulated mode of formation of the *p*-cresol oxidation product and confirms the stereochemical prediction made above since the geometry of this ketone (VII; R = H) makes it virtually impossible that the 10 : 11-ring fusion could be *trans*. Thus Pummerer's ketone is regarded as having structure (III) with *cis*-fusion.

EXPERIMENTAL

1 : 2 : 10 : 11-*Tetrahydro*-6 : 11-*dimethyl*-2-*oxodibenzofuran* (*Pummerer's Ketone*) (III).—This was prepared from *p*-cresol by the methods of Pummerer *et al.*[1] and Westerfield and Lowe.[8] Its infrared spectrum (in Nujol) showed strong bands at 1656 (conjugated carbonyl), weaker bands at 1616, 1460, and 1400 cm.$^{-1}$ (olefinic and aromatic absorption). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in prisms, m. p. 222°, $\lambda_{max.}$ (in $CHCl_3$) 388 mμ (Found : N, 14·0. $C_{20}H_{18}O_5N_4$ requires N, 14·2%).

2 : 5-*Dimethylcoumaran*-3-*one* (XIV).—Hydrated sodium acetate (20 g.) and β-bromo-2-hydroxy-5-methylpropiophenone (10 g.) were heated in boiling alcohol (100 ml.) containing pyridine (1 ml.). After ½ hr. the solution was poured on ice, and the solid was distilled, giving 2 : 5-dimethylcoumaran-3-one (6 g.), b. p. 135°/12 mm., m. p. 63°, which with alkaline sodium nitroprusside gave a blue-red colour and was oxidised by air to 2-acetoxy-5-methylbenzoic acid as described by von Auwers.[11]

2 : 5-*Dimethyl*-2-3′-*oxo*-n-*butylcoumaran*-3-*one* (XVI).—Methyl vinyl ketone (b. p. 35°/120 mm.), in methanol (14 ml.) and ether (30 ml.), was added to 2 : 5-dimethylcoumaran-3-one in methanol (40 ml.) and ether (105 ml.) containing sodium methoxide (0·05 g.) during 30 min. under nitrogen. The mixture was stirred for 4 hr., acidified at about 25°, and extracted with ether. The extracts were washed with aqueous sodium hydrogen carbonate, dried, and evaporated in a vacuum. Distillation of the residual oil supplied the *coumaranone* (10 g.), b. p. 210°/15 mm. (Found : C, 72·1; H, 7·0. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%). Crystallised from benzene, the *semicarbazone* formed needles, m. p. 213° (Found : C, 62·0; H, 6·5; N, 14·3. $C_{15}H_{19}O_3N_3$ requires C, 62·3; H, 6·6; N, 14·5%).

1 : 2 : 3 : 10-*Tetrahydro*-6 : 10-*dimethyl*-3-*oxodibenzofuran* (XVII).—A mixture of 2 : 5-dimethyl-2-3′-oxo-*n*-butylcoumaran-3-one (1 g.) in water (100 ml.), alcohol (20 ml.), and potassium

hydroxide (2·5 g.) was boiled under nitrogen for 2 hr., and the cooled solution neutralised and extracted with ether, giving the *compound* (XVII) which separated from light petroleum (b. p. 40—60°) in pale yellow needles (0·8 g.), m. p. 80—81°, $\lambda_{max.}$ (in EtOH) 228, 288, 375 mμ (log ε 4·063, 4·169, 4·135) (Found : C, 78·6; H, 6·9. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·6%). Infrared spectrum (in Nujol) : strong bands at 1631 (heavily conjugated carbonyl combined with olefinic frequencies), and at 1560, 1475, and 1410 cm.$^{-1}$ (aromatic system). When boiled with 48% hydrobromic acid for 1 hr. this ketone was recovered unchanged in high yield; an alkali-soluble product could not be detected. The 2 : 4-*dinitrophenylhydrazone* crystallised from benzene in dark red needles, m. p. 270° (Found : C, 60·8; H, 4·4; N, 14·1. $C_{20}H_{18}O_5N_4$ requires C, 60·9; H, 4·6; N, 14·2%).

1 : 2 : 3 : 4 : 10 : 11-*Hexahydro*-6 : 10-*dimethyl*-3-*oxodibenzofuran* (XIX).—When the foregoing ketone (0·5 g.) was shaken with Raney nickel (1 g.) and hydrogen at the ordinary temperature and pressure 2 mols. of hydrogen were absorbed in 1 hr. Evaporation of the filtrate yielded an oil (0·5 g.), devoid of carbonyl activity, which, in spite of erratic analytical results, appeared to be 1 : 2 : 3 : 4 : 10 : 11-hexahydro-3-hydroxy-6 : 10-dimethyldibenzofuran since it gave a well-defined *phenylurethane* crystallising from light petroleum (b. p. 60—80°) in needles, m. p. 130—131° (Found : C, 74·8; H, 6·8; N, 4·2. $C_{21}H_{23}O_3N$ requires C, 74·8; H, 6·9; N, 4·2%). This alcohol (0·5 g.) was oxidised in acetic acid (5 ml.) at 60° with chromium trioxide (0·5 g.) in acetic acid (2·5 ml.) and water (1 ml.) added during 30 min. An hour later the product was isolated and purified from benzene with aluminium oxide, giving 1 : 2 : 3 : 10-tetrahydro-6 : 10-dimethyl-3-oxodibenzofuran which was characterised as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 269—270°. Oxidation of the alcohol (2 g.) with aluminium *tert.*-butoxide (5 g.) in a boiling mixture of benzene (50 ml.) and acetone (25 ml.) for one day gave an oil which was isolated with ether and distilled, yielding the *hexahydro*-3-*oxodibenzofuran* (XIX) as a viscous oil (1·3 g.), b. p. 190°/2 mm. (Found : C, 77·6; H, 7·8. $C_{14}H_{16}O_2$ requires C, 77·8; H, 7·4%). The orange 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate and alcohol in needles, m. p. 181° (Found : C, 60·8; H, 5·1; N, 13·9. $C_{20}H_{20}O_5N_4$ requires C, 60·6; H, 5·1; N, 14·1%), and had $\lambda_{max.}$ 368 mμ (ε 23,560) typical of the 2 : 4-dinitrophenylhydrazones of saturated ketones. The *semicarbazone* separated from alcohol in needles, m. p. 250° (Found : C, 65·8; H, 7·0; N, 15·1. $C_{15}H_{19}O_2N_3$ requires C, 65·9; H, 7·0; N, 15·4%).

Attempts to obtain a Stereoisomer of Ketone (XIX).—(*a*) Hydrogenation of the ketone (XVII) with Adams catalyst either in neutral alcohol at 55 lb./sq. in. at room temperature for 10 hr. or in acetic acid at the ordinary temperature and pressure for 2 hr. gave 1 : 2 : 3 : 4 : 10 : 11-hexahydro-3-hydroxy-6 : 10-dimethyldibenzofuran, which was converted into the identified phenylurethane, m. p. and mixed m. p. 130°, and by oxidation (Oppenauer) into the ketone (XIX) characterised as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 179—180°.

(*b*) The ketone (XVII) (0·2 g.) was heated with 5% palladised charcoal (0·3 g.) to 250° for 8 min. and an ethereal solution of the product freed from phenolic material with 2N-aqueous sodium hydroxide. On isolation, the compound (XIX) was converted into the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 179°.

1 : 2 : 3 : 4 : 10 : 11-*Hexahydro*-6 : 11-*dimethyl*-2-*oxodibenzofuran* (XII).—Pummerer's ketone (5 g.) was agitated with Raney nickel (5 g.) in hydrogen at room temperature and pressure for 6 hr. After isolation the product (0·5 g.) was distilled, giving 1 : 2 : 3 : 4 : 10 : 11-hexahydro-2-hydroxy-6 : 11-dimethyldibenzofuran (X), b. p. 140°/0·5 mm., which slowly solidified and then crystallised from light petroleum (b. p. 40—60°) in needles, m. p. 70°, insoluble in alkali and devoid of carbonyl activity (Pummerer *et al.*[1] give m. p. 71°) (Found : C, 77·0; H, 8·1. Calc. for $C_{14}H_{18}O_2$: C, 77·0; H, 8·3%). The *phenylurethane* separated from light petroleum in needles, m. p. 134°, depressed to about 100° on admixture with the phenylurethane of the alcohol (XVII) (Found : C, 75·1; H, 6·7; N, 4·5. $C_{21}H_{23}O_3N$ requires C, 74·8; H, 6·9; N, 4·2%). When oxidised in boiling benzene (50 ml.) with aluminium *tert.*-butoxide (5 g.) and acetone (30 ml.) for 48 hr., this alcohol (2·3 g.) furnished 1 : 2 : 3 : 4 : 10 : 11-hexahydro-6 : 11-dimethyl-2-oxodibenzofuran which was isolated from the acidified mixture with ether and purified by distillation; it formed an oil (1·5 g.), b. p. 146—154°/0·5 mm., that solidified and then had m. p. 82° (Barton *et al.*[3] give m. p. 82°) (Found : C, 78·1; H, 7·7. Calc. for $C_{14}H_{16}O_2$: C, 77·8; H, 7·4%). The 2 : 4-*dinitrophenylhydrazone* separated from ethyl acetate–alcohol in orange-yellow plates, m. p. 208°, having $\lambda_{max.}$ (in EtOH) 368 mμ (ε 22,570) as expected for this derivative of a saturated ketone (Found : C, 60·6; H, 5·2; N, 13·9. $C_{20}H_{20}O_5N_4$ requires C, 60·6; H, 5·1; N, 14·1%). The *semicarbazone* formed needles, m. p. 231°, from ethyl acetate–alcohol (Found : C, 66·1; H, 7·2; N, 15·4. $C_{15}H_{19}O_2N_3$ requires C, 65·9; H, 7·0; N, 15·4%). Both derivatives depressed the m. p.s of the corresponding derivatives of the 6 : 10-dimethyl isomer.

When heated to 250° with palladised charcoal as described for the 6 : 10-dimethyl isomer this ketone (XII) was unaffected (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 208°).

Chromic Acid Oxidation of the Alcohol (X).—The preceding alcohol (0·4 g.), in acetic acid (5 ml.), was oxidised by chromium trioxide (0·5 g.) in the same solvent (2·5 ml.) containing water (1 ml.). After 1 hr. the mixture was diluted with water, and the product was collected with ether and freed from acidic material by aqueous sodium hydrogen carbonate. The resulting non-phenolic oil was at once converted into the 2 : 4-dinitrophenylhydrazone which was chromatographed from benzene on aluminium oxide. The one band obtained yielded 2 : 3 : 4 : 11-*tetrahydro*-2-*oxo*-6 : 11-*dimethyldibenzofuran* 2 : 4-*dinitrophenylhydrazone* which separated from ethyl acetate–alcohol in orange-red prisms, m. p. 180—181° (depressed markedly by the 2 : 4-dinitrophenylhydrazone of Pummerer's ketone) (Found: N, 14·5. $C_{20}H_{18}O_5N_4$ requires N, 14·2%), having $\lambda_{max.}$ 382 mμ (ε 25,220) as befits an αβ-unsaturated ketone derivative.

1:2:10: 11-*Tetrahydro*-2-*hydroxy*-6: 11-*dimethyldibenzofuran* (XI).—Pummerer's ketone (2 g.) and aluminium *iso*propoxide (2 g.) in *iso*propyl alcohol (10 ml.) was heated under reflux so that acetone could escape. After 3 hr., removal of the solvent under reduced pressure and decomposition of the residue with 2N-hydrochloric acid (40 ml.) liberated a product that was purified by distillation giving an oily *alcohol*, b. p. 130—135°/1 mm., which crystallised from light petroleum in needles, m. p. 80°, having no carbonyl activity (Found : C, 78·1; H, 7·5. $C_{14}H_{16}O_2$ requires C, 77·8; H, 7·4%). This furnished a *phenylurethane* separating from alcohol in needles, m. p. 126—127°, clearly different from the material obtained by hydrogenation (Found: C, 75·2; H, 6·3; N, 4·4. $C_{21}H_{21}O_3N$ requires C, 75·2; H, 6·3; N, 4·2%). Oxidised by aluminium *tert.*-butoxide (2 g.) and acetone (25 ml.) in boiling benzene (8 ml.) for 26 hr., this alcohol (0·6 g.) regenerated Pummerer's ketone, b. p. 120—130°/1 mm., which was distilled and crystallised from light petroleum, then having m. p. and mixed m. p. 124°.

4-(2-*Acetoxy*-5-*methylphenyl*)-4-*methyl*cyclo*hexa*-2 : 5-*dienone* (VII; R = Ac).—When Pummerer's ketone (2 g.) in ether (20 ml.) was added to sodium ethoxide from sodium (0·24 g.) and alcohol (0·6 ml.) in boiling ether (40 ml.), a yellow salt (1·14 g.) was formed rapidly which was collected after 30 min., washed with ether, and kept in a dry atmosphere. With acetic anhydride (0·15 ml.) in boiling ether (30 ml.) for 1 hr., this salt formed a gum which was purified from benzene on aluminium oxide and then crystallised from light petroleum (b. p. 60—80°), to yield the *dienone acetate* in needles (0·05 g.), m. p. 99°, $\lambda_{max.}$ (in MeOH) 235 mμ (log ε 4·18), strong infrared absorption bands (in Nujol) at 1758 (aryl acetate), 1661 (dienone carbonyl), and at 1621, 1495, and 1406 cm.$^{-1}$ (conjugated olefinic and aromatic absorption) (Found : C, 75·3; H, 6·2; OAc, 17·3. $C_{14}H_{13}O{\cdot}OAc$ requires C, 75·0; H, 6·3; OAc, 16·8%). The 2 : 4-*dinitrophenylhydrazone* formed red needles, m. p. 209—210°, $\lambda_{max.}$ (in $CHCl_3$) 400 mμ (log ε 4·56), from ethyl acetate (Found : C, 60·7; H, 4·6; N, 12·1. $C_{22}H_{20}O_6N_4$ requires C, 60·6; H, 4·6; N, 12·8%).

When heated for 1 hr. with acetic anhydride (10 ml.) and (i) pyridine (10 ml.) or (ii) sodium acetate (0·7 g.), Pummerer's ketone (1 g.) was smoothly converted into the same acetoxydienone (0·9 g.).

The sodium salt was regenerated by treatment of the acetoxydienone with sodium ethoxide in ether by the method used for Pummerer's ketone, and when added to water it first dissolved and then rapidly gave a quantitative precipitate of Pummerer's ketone, m. p. and mixed m. p. 124°. Alternatively, Pummerer's ketone was regenerated by hydrolysis of the acetate (0·3 g.) with potassium hydroxide (0·1 g.) in methanol (4 ml.) and water (1 ml.) at 80° for 10 min. and was precipitated when the mixture was diluted.

4-(2-*Benzoyloxy*-5-*methylphenyl*)-4-*methyl*cyclo*hexa*-2 : 5-*dienone* (VII; R = Bz).—The sodium salt (0·24 g.) of Pummerer's ketone was warmed for 1 hr. with benzoyl chloride (0·14 ml.) in ether (25 ml.). Evaporation of the filtrate from the precipitated sodium chloride left a semi-solid mass which was purified on aluminium oxide from benzene and then crystallised from light petroleum (b. p. 60—80°), giving the *benzoyloxydienone* in needles (0·1 g.), m. p. 156—157°, $\lambda_{max.}$ (in MeOH) 232 mμ (log ε 4·52), strong infrared absorption bands (in Nujol) at 1729 (aryl benzoate), 1661 (dienone carbonyl), and at 1621, 1596, 1495, and 1404 cm.$^{-1}$ (aromatic and conjugated ethylenic absorption) (Found : C, 79·1; H, 5·5. $C_{21}H_{18}O_3$ requires C, 79·2; H, 5·7%). The 2 : 4-*dinitrophenylhydrazone* separated from chloroform in orange needles, m. p. 281—282°, $\lambda_{max.}$ (in $CHCl_3$) 400 mμ (log ε 3·82) (Found : C, 64·7; H, 4·3. $C_{27}H_{22}O_6N_4$ requires C, 65·1; H, 4·4%).

The same benzoate, m. p. and mixed m. p. 156—157°, was produced by the interaction of Pummerer's ketone (0·5 g.) with benzoyl chloride (0·3 ml.) in boiling pyridine (5 ml.) for 4 hr.

4-(2-*Methoxy*-5-*methylphenyl*)-4-*methyl*cyclo*hexa*-2 : 5-*dienone* (VII; R = Me).—(i) A mixture of Pummerer's ketone, methyl iodide (1 ml.), the sodium salt, and acetone (20 ml.) was heated under reflux for 2 hr. and on evaporation the filtered solution left a viscous oil, b. p. 125°/1 mm. which on crystallisation from light petroleum (b. p. 40—60) gave the *methoxydienone* in prisms, m. p. 70—71°, $\lambda_{max.}$ (in MeOH) 228 mμ (log ε 4·39), strong infrared absorption bands (in Nujol) at 1645 (dienone carbonyl), and at 1601, 1491, and 1400 cm.$^{-1}$ (aromatic and conjugated ethylenic absorption) (Found: C, 79·1; H, 7·2; OMe, 13·6. $C_{14}H_{13}O{\cdot}OMe$ requires C, 78·9; H, 7·1; OMe, 13·6%). The 2 : 4-*dinitrophenylhydrazone* separated from ethyl acetate as red needles, m. p. 202—203°, $\lambda_{max.}$ (in $CHCl_3$) 395 mμ (log ε 4·57) (Found: C, 61·8, 61·9; H, 5·2, 5·1; N, 14·0, 14·2. $C_{21}H_{20}O_5N_4$ requires C, 61·8; H, 4·9; N, 13·7%).

(ii) The reddish solution of Pummerer's ketone (3 g.) in warm methanol (30 ml.) containing 40% sodium hydroxide solution (3 ml.) was treated dropwise with methyl sulphate (3 ml.) with stirring; more methyl sulphate (9 ml.) and alkali were added, the mixture was then heated with 10% aqueous sodium hydroxide (80 ml.) on the steam-bath for 15 min., and the methanol removed by distillation. Isolated with ether the product solidified in contact with light petroleum (b. p. 40—60°) and on crystallisation from the same solvent gave the methoxydienone in needles (1·8 g.), m. p. and mixed m. p. 70—71°.

5-Hydroxy-2′-methoxy-2 : 5′-dimethyldiphenyl (VIII; R = Me).—A solution of the methoxydienone (VII; R = Me) (1 g.) in acetic anhydride (10 ml.) was treated with sulphuric acid (0·1 ml.) in the same solvent (4 ml.), kept for 5 hr., and slowly added to ice. The oily product gradually solidified and on crystallisation from dilute methanol gave *5-acetoxy-2′-methoxy-2 : 5-dimethyldiphenyl* in needles (0·6 g.), m. p. 61° [Found: C, 75·4; H, 6·8; OAc, 14·9; OMe, 11·6. $C_{14}H_{12}(OAc)(OMe)$ requires C, 75·5; H, 6·7; OAc, 15·9; OMe, 11·5%]. On hydrolysis with potassium hydroxide (0·5 g.) in boiling methanol (7 ml.) and water (3 ml.) for 1 hr. and acidification this acetate (0·3 g.) gave the *phenol* (VIII; R = Me) which separated from benzene–light petroleum (b. p. 60—80°) in rhombs, m. p. 72° (Found: C, 79·0; H, 7·0; OMe, 13·2. $C_{15}H_{16}O_2$ requires C, 78·9; H, 7·1; OMe, 13·6%). Methylation of this phenol by the methyl sulphate and alkali method gave 2′ : 5-dimethoxy-2 : 5′-dimethyldiphenyl, m. p. 66°, undepressed by authentic material, m. p. 66°, prepared from 2 : 3′-di-*p*-cresol (Pummerer *et al.*[1] give m. p. 86°) [Found: C, 79·5; H, 7·9; OMe, 27·3. Calc. for $C_{14}H_{12}(OMe)_2$: C, 79·3; H, 7·5; OMe, 25·6%].

*Oxidative Degradation of 4-(2-Acetoxy-5-methylphenyl)-4-methyl*cyclo*hexa-2 : 5-dienone.*—Potassium permanganate (8 g.) was added during 1 hr. to a stirred solution of the acetoxydienone (2 g.) in acetone and after 14 hr. the precipitate was collected, washed with acetone followed by hot water, and extracted with 1% sodium hydroxide solution. The combined extracts were freed from neutral material with ether and saturated with carbon dioxide. Isolated with ether the resulting product was a low-melting solid, with a violet ferric reaction, which gave an excellent yield of *2-hydroxy-5-methylacetophenone 2 : 4-dinitrophenylhydrazone*, forming red prisms, m. p. 263—265°, from benzene (Found: C, 54·7; H, 4·2; N, 16·9. $C_{15}H_{14}O_5N_4$ requires C, 54·5; H, 4·3; N, 17·0%). This derivative was identified with an authentic specimen by mixed m. p. determinations and by their identical behaviour on an aluminium oxide column. After separation of 2-hydroxy-5-methylacetophenone the liquor was strongly acidified, volatile material was removed with steam, and the solution extracted with ether. From the extracts 5-methylsalicylic acid was isolated with aqueous sodium hydrogen carbonate and crystallised from hot water, forming needles, m. p. and mixed m. p. 149—150°, having a deep blue ferric reaction (Found: C, 63·5; H, 5·3. Calc. for $C_8H_8O_3$: C, 63·2; H, 5·2%).

The acetone washings of the crude oxidation product gave unchanged acetoxy-dienone.

*Oxidative Degradation of 4-(2-Methoxy-5-methylphenyl)-4-methyl*cyclo*hexa-2 : 5-dienone.*—Addition of zinc permanganate (9 g.) to a stirred solution of the methoxydienone (2 g.) in acetone (80 ml.) at 15° gave during ¾ hr. a precipitate which was washed with acetone and extracted with 1% aqueous sodium hydroxide. Liberated by acidification of the extract and isolated with a large volume of ether, *3-acetyl-4-methoxybenzoic acid* formed plates (0·4 g.), m. p. 225—226°, from alcohol (Found: C, 61·4; H, 5·6; OMe, 16·0. $C_9H_7O_3{\cdot}OMe$ requires C, 61·9; H, 5·2; OMe, 16·0%). The same acid, m. p. and mixed m. p. 225—226°, resulted when 3-acetyl-4-hydroxybenzoic acid [14] was methylated by methyl sulphate and an excess of aqueous sodium hydroxide (Found: OMe, 16·3%).

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[14] Rohmann and Wilms, *Arch. Pharm.*, 1942, **28**, 76; *Chem. Zentr.*, 1942, II, 1228.