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REINVESTIGATION OF THE REACTIONS OF MALEIC ANHYDRIDE WITH ACETYLACETONE, ETHYL ACETOACETATE AND RESORCINOL

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Abstract New structures are proposed for the condensation products of maleic anhydride with acetylacetone, ethyl acetoacetate and resorcinol.

STRUCTURES 1a and 1b were originally assigned to the 2:1 condensation products of maleic anhydride with acetylacetone and ethyl acetoacetate.[1] The unusual mode of reaction of maleic anhydride postulated has led us to reinvestigate these compounds.

Most of the evidence for these structures was derived from the degradation sequence outlined in Scheme I for the acetylacetone (A) and the ethyl acetoacetate (B) adducts. The degradation sequence leading from adduct (A) to *p*-xylenol was repeated in this laboratory and confirmed, the intermediates having the anticipated spectral properties. The conversion of **2** to **3** with diazomethane was confirmed spectroscopically as the possibility of converting benzofuranones to 2-methoxybenzofurans does not appear to have been generally recognized.[2] Not only is the characteristic furanone carbonyl band, ca. 1820 cm^{-1}, absent from the IR spectrum of **3** but the NMR spectrum shows bands at 5·84 τ and 3·90 τ attributable to the 2-methoxyl and 3-hydrogen of the benzofuran. Comparison of the m.p. of the acid **12** and its trimethyl ester with those since reported[3] for the isomeric acids confirms the original identification.

Previous work[1] indicated the presence of an anhydride and a carboxyl group in both adducts. This was confirmed by their IR spectra, which showed bands characteristic of a 5-membered anhydride (1875, 1790 cm^{-1}), additional carbonyl groups (1700-1730 cm^{-1} unresolved) and carboxyl O—H (2400-3300 cm^{-1}). The low solubility and stability of these adducts in suitable solvents made it difficult to obtain good NMR spectra, however a freshly prepared hexadeuteroacetone solution of the acetylacetone adduct showed signals at 8·28 τ $(CH_3-\overset{|}{\underset{|}{C}}-)$, 7·61 τ $(CH_3\ CO-)$, an AB system (J = 18 c/s) at 6·81 τ ($-CH_2-$) and a series of signals equivalent to three protons between 5·6 and 6·4 τ. The less satisfactory spectrum obtained for the ethyl acetoacetate adduct supported the above assignments. This data is incompatible with structure **1**, or **14** which we proposed[4] in a preliminary communication before

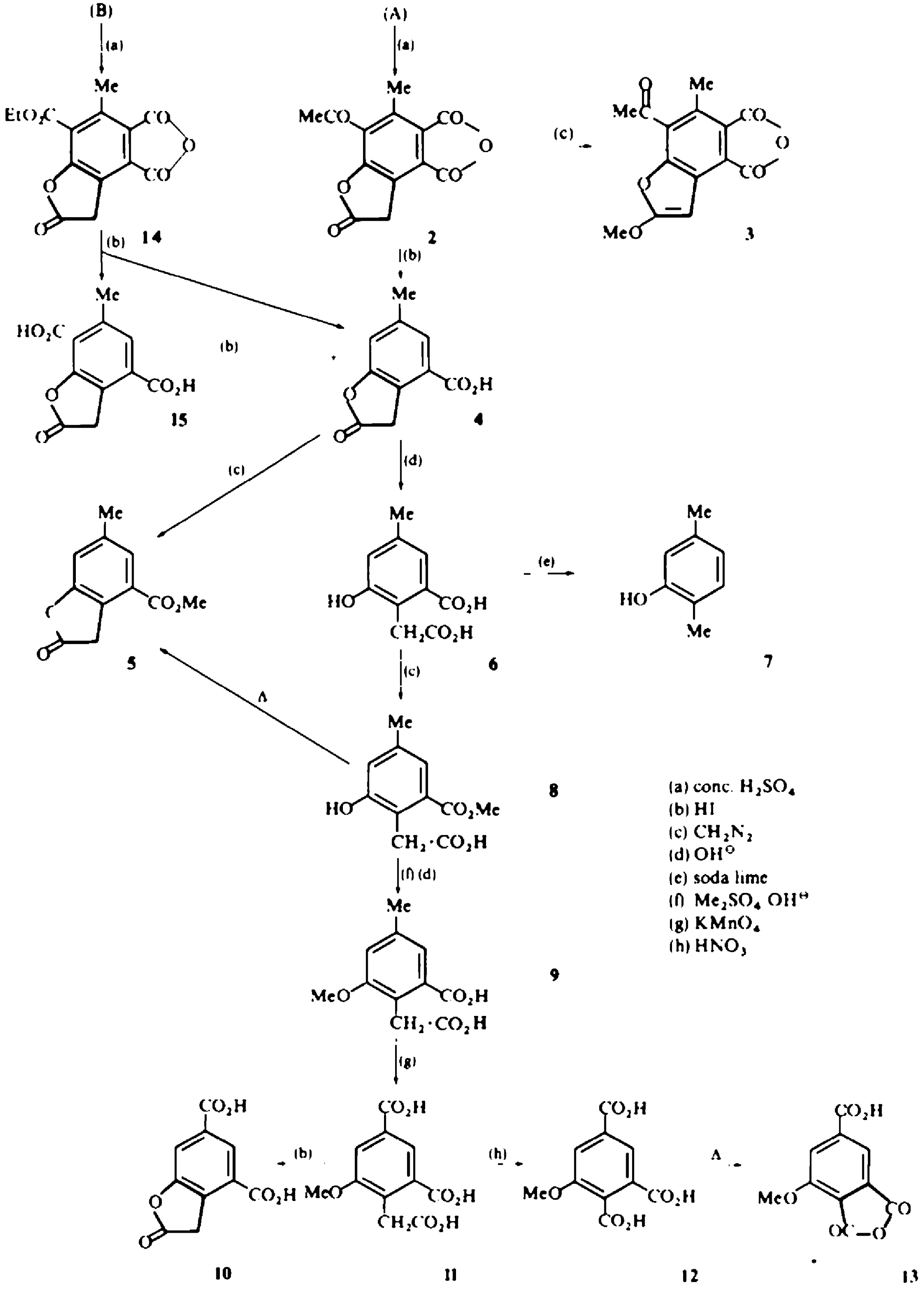
[1] E. Berner, *J. Chem. Soc.*, 1052 (1946).

[2] R. C. Elderfield and V. B. Meyer, *Heterocyclic Compounds* Vol 2, p. 1. Wiley, New York (1951).

[3] D. Gardner, J. F. Grove and D. Ismay, *J. Chem. Soc.* 1817 (1954).

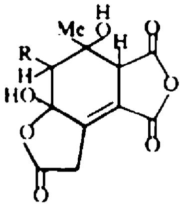
[4] C. W. Bird and P. Molton, *Tetrahedron Letters* 1891 (1966).

Scheme 1



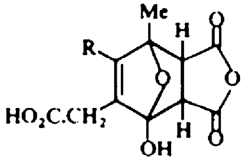
(a) conc. H_2SO_4
(b) HI
(c) CH_2N_2
(d) $OH^{\ominus}$
(e) soda lime
(f) Me_2SO_4 $OH^{\ominus}$
(g) $KMnO_4$
(h) HNO_3

the NMR spectra of the adducts were available. In this light the most satisfactory structure for these adducts is **15**.[5] An unexpected feature is the lack of appreciable enolic character even in the acetylacetone adduct as indicated both by the NMR, and the IR spectrum which shows no bands between 1700 and 1500 cm^{-1}. Ostensibly analogous bicycloheptanone compounds are extensively enolized,[6a] the enolic double bond being exocyclic. Possibly the extra strain, resulting from the fused anhydride ring, may be responsible for the lack of enolic character in these adducts.

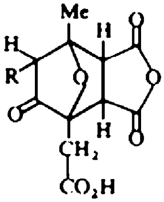


1 a R = Ac

b R = CO_2Et



14



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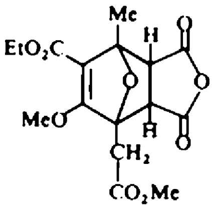

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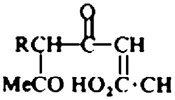
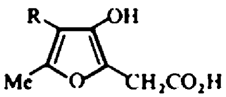


$RCH(COMe)-C(=O)-CH=CH-CO_2H$



17 **18**

Additional support for structure **15** is provided by the spectral properties of the dimethyl derivative **16** obtained by reaction of the ethyl acetoacetate adduct with diazomethane. Apart from characteristic adsorptions for the ester methyl and ethyl

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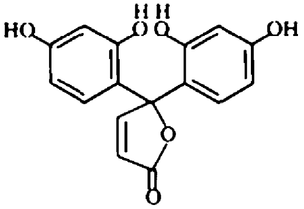
[5] Structure **15** has been independently deduced for this adduct by Dr. G. M. Strunz (private communication); R. D. Bailey and G. M. Strunz, *Canad. J. Chem.* **44**, 2584 (1966).

[6] [a] E. W. Garbisch, *J. Am. Chem. Soc.* **85**, 1696 (1963); [b] P. Laszlo and P. von R. Schleyer, *Ibid.* **86**, 1171 (1964).

groups at 6·27 τ and 8·68 τ (J = 7·0), 5·74 τ (J = 7·3 c/s), singlets were observed at 8·22 τ ($CH_3{-}C{-}O$), 6·94 τ ($-CH_2-$) and 5·97 τ ($CH_3{-}O{-}\overset{|}{C}{=}$). A quadruplet centred at 6·37 τ (2H, J = 6·5 c/s) is assigned to the two protons at the anhydride ring junction but the stereochemistry cannot be deduced in the absence of the isomeric[6b] compound.

The formation of these products can be envisaged as involving initial acylation of acetylacetone or ethyl acetoacetate by maleic anhydride giving **17**, followed by addition of the enolic O--H to the maleyl double bond with formation of the furan **18**. Diels Alder addition of a second molecule of maleic anhydride to the furan **18** would then yield **15**. Although recent work[7] indicates that 3-hydroxyfurans exist predominantly



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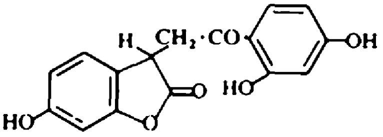

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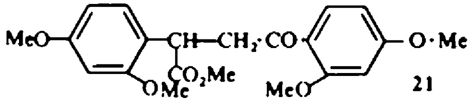

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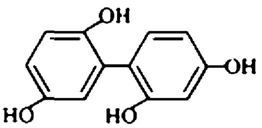

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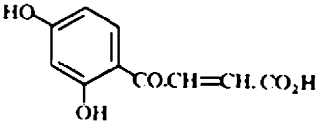
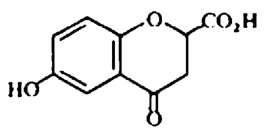


23



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[7] R. E. Rosenkranz, K. Allner, R. Good, W. v. Philipsborn and C. H. Eugster, *Helv. Chim. Acta* **46**, 1259 (1963).

as their keto tautomers it seems likely that **18** would exist extensively in the enolic form. An earlier report[8] that 3-hydroxyfuran forms a maleic anhydride adduct must be regarded with suspicion as the authenticity of the 3-hydroxyfuran used is in doubt.[9]

Resorcinol, which can be regarded as a fully enolized β-diketone, is reported[10] to form a 2:1 condensate with maleic anhydride. Structure **19** has been ascribed to this compound by analogy with formation of fluoresceins. In our hands the reaction proceeded more cleanly at 90° in the presence of a trace of sulphuric acid. The IR spectrum agreed with that previously reported showing the presence of phenolic hydroxyl, 3350 cm^{-1} and two carbonyl groups, 1785 and 1640 cm^{-1}; the former in a strained environment and the latter strongly hydrogen bonded. The UV spectrum in ethanol showed absorption bands at 235 mμ (ε 8220), 286 mμ (ε 12,780) and 326·5 mμ (ε 6140) and is practically identical with that of resacetophenone, λ_{max} 232 mμ (ε 8250), 278 mμ (ε 13,750) and 317 mμ (ε 6560). The NMR spectrum of the triacetyl derivative showed the absence of exchangeable protons, and the expected signal at 7·87 τ (9H) of the acetyl methyl groups. The remaining three protons constituted an ABX system with the A and B proton quadruplets centred at 6·61 and 6·32 τ (J = 18 c/s). The X proton quadruplet centred at 5·88 τ showed further signs of splitting and a decoupling experiment indicated that this was due to coupling with one of the 6 aromatic protons. Taken together this spectral data indicates structure **20** for the resorcinol-maleic anhydride adduct.

Chemical proof for this structure was obtained as follows. Treatment of **20** with dimethyl sulphate and aqueous sodium hydroxide produced a tetramethoxy acid converted by methanolic hydrogen chloride into the methyl ester **21**, although the original workers[10] only obtained a trimethoxy methyl ester using methyl iodide and potassium hydroxide. The ester **21** had been obtained previously[11] from the Friedel Crafts reaction of maleic anhydride with resorcinol dimethyl ether. In our hands the ester **21** proved identical with the major product from the Friedel Crafts reaction of 2,4-dimethoxyphenylsuccinic anhydride with resorcinol dimethyl ether.

Comparison of the structure **20** deduced for the resorcinol-maleic anhydride adduct with the products (e.g. **22**) obtained from resorcinol and benzoquinone[12] indicate that the first stage in these reactions is acid catalysed addition of resorcinol to the double bond. This is in contrast to the aluminium chloride catalysed reaction between resorcinol and maleic anhydride,[13] where the products **23** and **24** appear to arise by initial acylation.

EXPERIMENTAL

IR spectra were recorded for Nujol mulls on a Perkin Elmer model 237 spectrophotometer and UV spectra were measured on EtOH solns with a Unicam SP.700 spectrophotometer. NMR spectra were variously recorded on Varian A 60 and HA 100 instruments for $CDCl_3$ or acetone-d_6 solns.

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[8] H. H. Hodgson and R. R. Davies, *J. Chem. Soc.* 806 (1939).

[9] A. P. Dunlop and F. N. Peters, *The Furans* pp. 170–175. Reinhold (1953).

[10] Y. Graff, J. Calando and M. Gardin, *Bull. Soc. Chim. Fr.* 1106 (1961).

[11] G. P. Rice, *J. Am. Chem. Soc.* **53**, 3153 (1931).

[12] N. E. Stjernstrom, *Arkiv Kemi* **21**, 57 (1963).

[13] K. P. Barr, F. M. Dean and H. D. Locksley, *J. Chem. Soc.* 2425 (1959).

Reaction of the ethyl acetoacetate maleic anhydride adduct with diazomethane. The adduct[1] (1·0 g) was treated with excess ethereal diazomethane. Slow evaporation of the soln deposited the *dimethyl derivative* (**16**; 0·54 g) m.p. 115·5–117°. (Found: C, 53·8; H, 4·8. $C_{16}H_{18}O_9$ requires: C, 54·2; H, 5·1%.)

Reaction of resorcinol with maleic anhydride. Maleic anhydride (9·8 g) was finely powdered and mixed with resorcinol (22·0 g). The mixture was melted and heated at 90° for 20 hr in the presence of 3 drops conc H_2SO_4. The semisolid product was heated with water (200 ml) and 3-(2,4-dihydroxyphenacyl)-6-hydroxybenzofuran-2-one (6·8 g) m.p. 258° (lit.[10] 265°), crystallized on standing. This was converted by refluxing in Ac_2O (15 min) into its *triacetyl derivative*, m.p. 163° from EtOH. (Found: C, 61·5; H, 4·5. $C_{22}H_{18}O_9$ requires: C, 61·9; H, 4·3%.)

Methylation of **20**. Compound **20** (7·3 g) was dissolved in NaOH aq (9 g in 250 ml) and flushed with N_2. Me_2SO_4 (20 g) was added and the mixture shaken vigorously until the reaction subsided. After refluxing for 2 hr the cooled soln was acidified with HCl. The reddish-brown product was filtered off and dried. The crude acid proved difficult to purify and was esterified with methanolic HCl. The crude ester was purified by chromatography on silica gel in CCl_4. Elution with pet. ether–ether (1:1) yielded **21** (3·7 g) m.p. 142–143° from ether–pet. ether. (Found: C, 64·6; H, 6·0. $C_{21}H_{24}O_7$ requires: C, 64·9; H, 6·2%.)

Friedel–Crafts reaction of resorcinol dimethyl ether with dimethoxyphenylsuccinic anhydride. The reaction was carried out as previously described[11] using resorcinol dimethyl ether (10 g), dimethoxyphenylsuccinic anhydride (3·3 g) and $AlCl_3$ (7·0 g). Crystallization of the crude product from aqueous AcOH yielded 2,4-bis(2,4-dimethoxyphenyl)-4-ketobutyric acid (1·35 g), m.p. 180–182° (lit.[11] 160°), methyl ester m.p. 144–145° (lit.[11] 140°) identical with the above sample. The mother liquors were evaporated to dryness and the residue esterified with methanolic HCl. The mixture of isomeric esters were chromatographed on silica gel. Elution with pet. ether–ether (2:1) gave firstly a mixture of isomers (1·0 g) and subsequently with pet. ether–ether (1:1) methyl 3,4-bis-(2,4-dimethoxyphenyl)-4-ketobutyrate (0·49 g) m.p. 134·5° (lit.[11] 104°). (Found: C, 64·9; H, 6·2. $C_{21}H_{24}O_7$ requires: C, 64·9; H, 6·2%.)

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