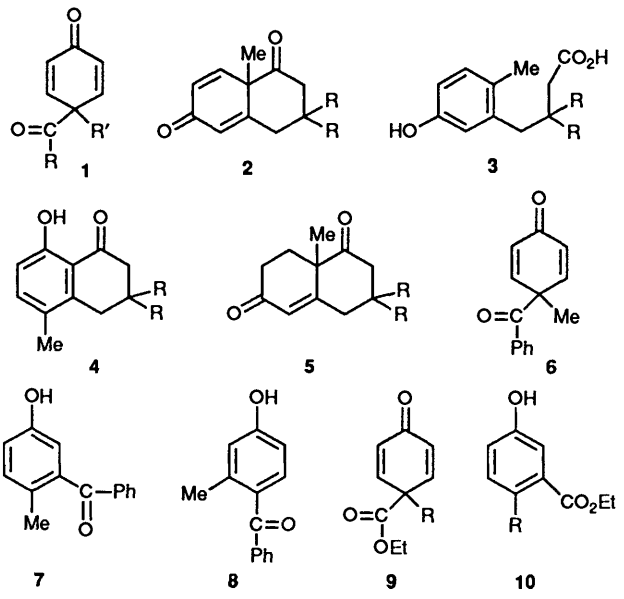
Reactions of 4-Benzoyl-4-methylcyclohexa-2,5-dienone in Acids: Retro-Fries Rearrangements†

Lorraine B. Jackson and Anthony J. Waring*
School of Chemistry, The University of Birmingham, Edgbaston, Birmingham B15 2TT, UK

4-Benzoyl-4-methylcyclohexa-2,5-dienone is known as one of the few relatively stable 4-acylcyclohexa-2,5-dienones. In attempts to achieve dienone-phenol rearrangements with acyl migration it has been treated with Lewis acids and with non-nucleophilic acids in non-polar solvents. In each case rapid acyl migration occurs to give 4-methylphenyl benzoate by a retro-Fries rearrangement, along with some cleavage to the phenol. The benzoyl group can be trapped by another phenol, and the mechanism is formulated as a dissociation-recombination process with significant leakage of the 4-methylphenol and benzoyl cation. The reaction is compared with the Fries/retro-Fries equilibrium which has been induced between phenyl esters and 2- and 4-acyl phenols. Observations are made on the photochemical Fries rearrangement of 4-methylphenyl acetate, which has been suggested to proceed *via* 4-acetyl-4-methylcyclohexa-2,5-dienone, and of 4-methylphenyl benzoate.

It is known that 4-acylcyclohexa-2,5-dienones are compounds of low stability. They have been implicated as unstable intermediates in the photo-Fries rearrangement of carboxylate esters of phenols. For example, UV irradiation of phenyl acetate causes rearrangement to 4-acetylphenol, with the 4-acetyl-4-protiocyclohexa-2,5-dienone **1** (R = Me, R′ = H) as the possible intermediate.[1–3] The 4-benzoyl dienone **1**



(R = Ph, R′ = H) would similarly be involved in the formation of 4-hydroxybenzophenone from phenyl benzoate.[4] The 4-acylcyclohexadienones are similarly implicated as reactive intermediates in the thermal, acid-induced Fries rearrangement equilibria between aryl carboxylates and 2- and 4-acylphenols.[5,6] In our early attempts to prepare 4-acylcyclohexa-2,5-dienones we aimed for the simplest representative, 4-acetyl-4-methylcyclohexa-2,5-dienone. However, all our routes led to cleavage products (4-methylphenol and acetic acid), and the product of an apparent retro-Fries rearrangement, 4-methylphenyl acetate.[7] To avoid the latter rearrangement, and to hinder nucleophilic attack at the acyl group we then prepared 3,4-dihydro-3,3,8*a*-trimethylnaphthalene-1,6(2*H*,8*aH*)-dione **2** (R = Me). Although in aqueous acid this suffered cleavage at the acyl group to give **3** (R = Me), we found that it was possible to effect rearrangement under suitable non-aqueous conditions to give **4** (R = Me), the product of acyl migration. The simpler bicyclic dienone **2** (R = H) appears to undergo similar rearrangement to **4** (R = H) upon its formation, by dehydrogenation of the related cyclohexenone **5** (R = H).[7]

More recently we reported the preparation of the relatively stable 4-benzoyl-4-methylcyclohexa-2,5-dienone **6** and its 4-chlorobenzoyl- and 4-methoxybenzoyl-analogues.[8] One reason for our interest in these compounds was the possibility of effecting acyl migrations from C-4 to C-3, to form the phenols **7** and possibly **8** in the manner typical of dienone-phenol rearrangements. Kinetic and product-ratio measurements should then allow us to determine unambiguous values for migratory aptitudes (migration tendencies) of benzoyl groups in these carbocation rearrangements, as we have done previously for alkyl groups.[9,10] We believed at the outset of this work that the acyl groups would migrate more readily than the alkyl group of the dienone. This is certainly found for migration of the ethoxycarbonyl group in **9** (R = Me or Et) and **10** (R = Me or Et),[11] and seems to be apparent in the formation of **4** (R = H) from the incipient dienone **2** (R = H). Much evidence is accumulating that acyl groups generally undergo 1,2-migration in cations with considerable ease.[12–19]

Acid-induced Rearrangements of the Dienone **6**.—Reaction of the parent dienone **6** in aqueous mineral acids gave only 4-methylphenol and benzoic acid. Our mechanistic studies of this and the related alkaline cleavage have been reported elsewhere.[20] In order to reduce nucleophilic attack we treated the benzoyl dienone **6** with a dilute solution of trifluoroacetic acid in deuteriodichloromethane at −10 °C, monitoring the reaction by ^{1}H NMR spectroscopy. Similar conditions had allowed the reaction of **2** (R = Me) to be followed.[7] However, **6** had completely reacted by the time the first spectrum was recorded (within 100 s): *ca.* 50% of the dienone had cleaved

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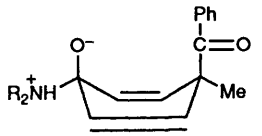
to 4-methylphenol and benzoic acid, and 50% had rearranged to 4-methylphenyl benzoate. The latter product was shown not to arise from esterification of the phenol by benzoic acid under the conditions used, but is assumed to arise by migration of the benzoyl group from C-4 to the dienone carbonyl group. This process represents the reverse of the normal Fries rearrangement, in which phenol esters rearrange under acidic conditions, sometimes reversibly, [5,6] to 4- and 2-acylphenols.[21–23] Other acidic conditions gave comparable results. Treatment of the dienone **6** with 0.5 mol equiv. of trifluoromethanesulphonic acid in deuteriochloroform in the NMR tube showed 'immediate' reaction to give 74% of 4-methylphenyl benzoate and 26% of cleavage products. Qualitatively similar results were obtained using 1.0% w/w fluorosulphuric acid in sulphuryl fluoride chloride at −70 to −10 °C. In the hope that Lewis acids rather than proton acids might complex more effectively with the dienone and benzoyl groups, and reduce the tendency towards retro-Fries rearrangement, we treated the dienone **6** with a slight deficiency of boron trifluoride etherate in benzene, and separately with anhydrous zinc chloride in benzene. The former conditions gave rapid rearrangement to 4-methylphenyl benzoate; the latter conditions gave slow conversion into 64% of 4-methylphenyl benzoate and 36% of cleavage product. In order to obtain evidence regarding the inter- or intramolecular nature of the retro-Fries rearrangement, the dienone **6** was treated in the presence of an equivalent amount of 3,5-dimethylphenol with boron trifluoride etherate in benzene. Analysis of the product mixture by GLC and NMR spectroscopy showed the presence of 4-methylphenyl benzoate and 3,5-dimethylphenyl benzoate in a molar ratio 76:24, together with the two phenols. Further 3,5-dimethylphenol was added to samples of this mixture, with more boron trifluoride etherate, but the ratio of the two aryl benzoates was effectively unchanged at 72:28. A similar experiment using a 2:1 molar ratio of 3,5-dimethylphenol to dienone gave 4-methylphenyl benzoate and 3,5-dimethylphenyl benzoate in a ratio of 66:34. Critical analysis of the ^{13}C NMR spectrum of these reaction mixtures, and comparison with the peaks due to 4-methylphenol, 3,5-dimethylphenol and their benzoates, showed no additional peaks. In particular, there was no signal which could be ascribed to a carbonyl group in ring-benzoylated phenols (*i.e.* hydroxybenzophenones) near 200 ppm.

Mechanism of the Acid-induced Rearrangements.—We now consider the mechanism of the retro-Fries rearrangement found for **6**. The most important feature is the very high rate and ease of this reaction. In a dilute solution of trifluoroacetic acid in deuteriochloroform (2.5% w/v; 0.22 mol dm^{-3}) at −10 °C the reaction is completed in less than 100 s. Our rearrangement of **2** (R = Me) to **4** (R = Me) in 2% w/w trifluoroacetic acid in CD_2Cl_2 at −10 °C has a half-life of 310 s.[7] In contrast, the relatively rapid 1,2-migrations of the ethoxycarbonyl group in **9** (R = Me) and **9** (R = Et) have half-lives of 120 and 277 min, respectively, in neat trifluoroacetic acid at 38.5 °C.[11] Initially we might consider the reaction in the context of our other findings,[20] *i.e.* reaction of the dienone **6** with secondary amines such as diethylamine or pyrrolidine gives rapid rearrangement to 4-methylphenyl benzoate, which is then more slowly attacked by further amine. For this process we postulated an intramolecular reaction in which the dienone carbonyl group reacts with the amine to form an intermediate



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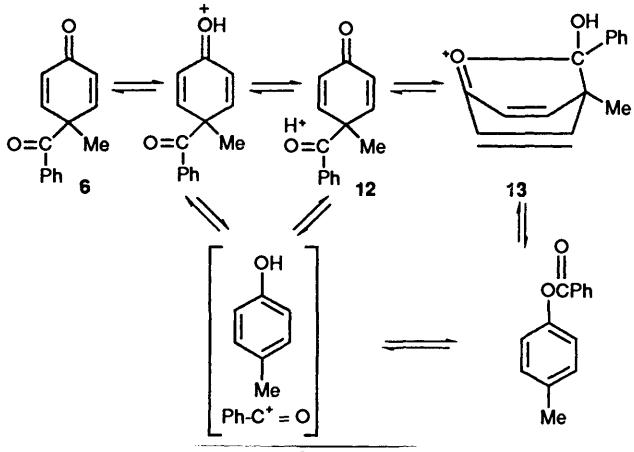
11, which then suffers an intramolecular *trans*-acylation with elimination of the amine molecule. Analogies were given for such [1,5]-shifts involving groups attached at the 1- and 4-positions of 6-membered rings.[20] In the present case, an intramolecular migration would presumably have to be formulated as shown in Scheme 1. All the indications are that



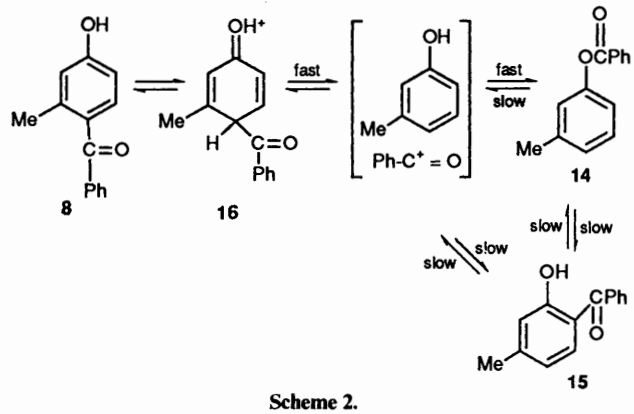
Scheme 1.

the dienone would be protonated predominantly at the dienone carbonyl group. The benzoyl-protonated cation **12** would be present also, in smaller concentration, but would possibly be able to rearrange as shown in **13**. This would not be as attractive geometrically as in the rearrangement in the presence of secondary amines, because C-1 is sp^2 rather than sp^3 hybridised in the intermediates and in the final aryl benzoate. The geometry of the intermediate **13** is almost identical to that postulated by Anderson and Reese for the *para* photo-Fries rearrangement, which they believed to be concerted.[1,*] One might, however, also postulate that solvent or an anion could temporarily attack the dienone carbonyl carbon atom, to change its hybridisation towards sp^3 and then be eliminated during the rearrangement step, much as in the reaction with amines.[20] Our later arguments, we think, exclude this idea. The cross-over experiments using 3,5-dimethylphenol suggest strongly that the rearrangement is at least partly intermolecular. This is supported by the finding that the relative amounts of rearrangement and of cross-over (benzoylation of 3,5-dimethylphenol) are not greatly changed when the amount of dimethylphenol is increased. The relatively close agreement of the (rearrangement:cleavage) ratio in the proton acids with the (rearrangement:cross-over) ratio in the Lewis acids suggests that both types of acid act as such, and that specific effects due to their counterions or the solvents are not particularly important. The possibility that the cross-over product is formed by nucleophilic attack of the 3,5-dimethylphenol on the benzoyl group of the benzoyl dienone (as is found for attack by water, methanol and ethanol)[20] seems to be excluded by the very modest increase in cross-over product when the concentration of 3,5-dimethylphenol was doubled. We believe the most probable mechanism involves dissociation of the protonated or coordinated dienone to give two species, a benzoyl cation and 4-methylphenol or 4-methylphenoxy-Lewis acid complex, which are held together rather tightly, but can partially escape to give the cleavage or cross-over product (depending on the nucleophiles present). We did not detect any significant amount

* Extensive measurements of kinetic isotope effects in the *ortho* photo-Fries reaction of methyl 4-methoxybenzoate gave no evidence of a concerted, intramolecular process. However, the *para* rearrangement was not accessible.[24]

of 2-benzoyl-4-methylphenol, which would arise by capture of the benzoyl cation at C-2 of the 4-methylphenol, or of 3-benzoyl-4-methylphenol or 4-benzoyl-3-methylphenol which would have arisen from a 4-3 migration of the dienone-phenol type. Thus our hopes of using the 4-benzoyl-4-methylcyclohexa-2,5-dienone to measure migratory aptitudes in their dienone-phenol rearrangements were thwarted.

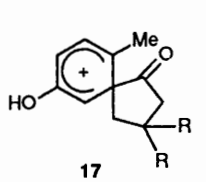
The studies of the retro-Fries rearrangements reported by Effenberger and co-workers[5,6] offer useful comparisons with the present work. Their reactions were carried out, as shown in Scheme 2, using 0.10 mol equiv. of *ca.* 9×10^{-3} mol



Scheme 2.

dm^{-3} trifluoromethanesulphonic acid in 1,2-dichloroethane at 170 °C. Treatment of 4-benzoyl-3-methylphenol (4-hydroxy-2-methylbenzophenone) **8** gave 98.7% reaction in 20 min, setting up an equilibrium with 3-methylphenyl benzoate **14** (71.3%) and 2-benzoyl-5-methylphenol **15** (6.9%), and forming 3-methylphenol (5.2%). In this case, and the much slower reaction of 4-benzoylphenol (4-hydroxybenzophenone), the retro-Fries rearrangement [to form **14**] is at least 20 times faster than benzoylation at C-2 (to form **15**) or at C-4. No benzoylation at C-6 could be detected due, it was believed, to twisting of the benzoyl group from planarity with the ring, and consequent instability of this isomer. Our inability to detect significant amounts of 2-benzoyl-4-methylphenol from the rearrangement of **6** is in accord with this result. Very similar results were found for the compounds containing a chloro- group instead of the ring-methyl group, and it was concluded that all the results spoke in favour of a dissociative, and against a synchronous mechanism when proton acids were employed, particularly for the steps **8**→**14**→**15**.[5] The reaction of **8** is assumed to occur by initial protonation of C-4, to produce a protonated cyclohexadienone **16** which then reacts in the manner suggested for the dienone **6**. We must assume that the difficulty in producing the cation **16** must be responsible for the slowness of the reaction **8**→**16**→**14**, in contrast to the ease and speed of our reaction of **6** to 4-methylphenyl benzoate. The protonation of **8** must be very slow and endothermic. If this were not so, any cation **16** would presumably react rapidly to 3-methylphenyl benzoate in the manner found for **6**.

It was of interest to gain further information on the rearrangement of **2** (R = Me) to **4** (R = Me) in trifluoroacetic acid. We believed this to involve two concerted intramolecular 1,2-acyl migrations, *via* the spiran intermediate **17**. However,



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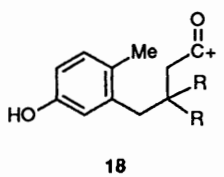

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analogy with the behaviour of dienone **6** could suggest a dissociation-recombination process in which the phenol and acyl cation are held together by the chain (see **18**), and recombination has to occur *ortho* to the phenolic function rather than at it, due to steric constraints. A mixed rearrangement was performed on an equimolar mixture of **2** (R = Me) and **6** using a dilute solution of trifluoroacetic acid in CD_2Cl_2 at −10 °C in the NMR spectrometer. When the first spectrum was taken (within 200 s) all of **6** and 85% of **2** (R = Me) had reacted. After a further 10 min all of **2** (R = Me) had reacted. Analysis by ^1H NMR spectroscopy showed the products to be 4-methylphenyl benzoate (75%), 4-methylphenol (25%) and 'benzoic acid' (25%) from **6**, and the phenol **4** (R = Me) from **2** (R = Me). A careful search by GLC/MS showed no trace of cross-products [*e.g.* a combination of **18** (R = Me) with 4-methylphenol]. The only unexpected products were small amounts of benzoic anhydride, probably 3-trifluoroacetoxy-4-benzoyl-4-methylcyclohexanone (assumed to arise from Michael addition of the acid to 4-benzoyl-4-methylcyclohexenone, an impurity in the dienone), and a trace of material having *m/z* 212 which could be 2-benzoyl- or 3-benzoyl-4-methylphenol, corresponding to <1% of the starting dienone. These results are not quite as clear as we hoped. Although the two dienones were chosen to have rearrangement rates which were as closely similar as we could achieve, **6** reacts significantly faster than **2** (R = Me), but by an unknown factor. If most of **6** has rearranged before there is much phenol **4** (R = Me) available for attack by the benzoyl cation, we would obtain the result found. However, if **2** (R = Me) were to react by a dissociation-recombination process, it could not suffer rapid internal acylation at its phenolic oxygen atom, due to steric constraints, but only the attack at one *ortho* site, which is normally not preferred. This reaction would happen in the presence of 4-methylphenol from **6**, and should give a significant cross-product. The absence of such a product provides evidence in favour of the intramolecular path for **2** (R = Me)→**17** (R = Me)→**4** (R = Me), which is only seen as a default when the retro-Fries formation of an ester is impossible.

We now enquire why the 4-acetyl and 4-benzoyl dienones **1** (R = R′ = Me) and **6** rearrange rapidly, under very mild acidic conditions, to the acetate and benzoate of 4-methylphenol (with the former being apparently much the faster). In contrast, the 4-methoxycarbonyl analogues **9** (R = Me, and R = Et) do not appear to give this retro-Fries reaction. Under much more stringent conditions they give the slower dienone-phenol rearrangement, with a 1,2-ester migration, by default. We assume that the slow step of the retro-Fries reaction is the cleavage which produces the phenol and acylium ion. The simplest analogy is the S_N1 hydrolysis of acyl halides. Although the mechanisms are not unambiguously defined as S_N1, the relative rates for hydrolysis of MeCOCl, PhCOCl and MeOCOCl are 9000:35:1 (aq. acetone at 25 °C), and for ethanolysis of MeCOCl, PhCOCl and EtOCOCl, 7000:37:1.[25–27] We would therefore expect that the rate of (*para*) retro-Fries reactions which proceed *via* the dissociation-recombination mechanism would show migration rates in the order acetyl > benzoyl > alkoxycarbonyl, as we observe. Any part of the rearrangement which is by an intramolecular, synchronous process is a [1,5] sigmatropic shift. A number of [1,5] shifts of acyl groups are known,[28–33] particularly 6–2 shifts in cyclohexa-2,4-dienones.[30–33] None, however, has been reported to be quite as fast as in our present work. Ester groups do not migrate as readily.[32] Some relative rates, determined at 300 °C for thermal [1,5] shifts of PhCO, MeCO and MeOCO were 380:138:1,[28] and in four different compounds, in Ph_2O as solvent, MeCO migrated as fast at 140 °C as MeOCO at 255 °C.[29] Accordingly, acyl groups should also migrate more rapidly than alkoxycarbonyl in any part of our retro-Fries reaction which occurs by a [1,5] sigmatropic pathway.

Photochemical Studies.—*4-Methylphenyl benzoate.* It occurred to us that UV irradiation of 4-methylphenyl benzoate might lead to photo-Fries rearrangement, with the formation of the 4-benzoyl-4-methylcyclohexa-2,5-dienone **6**. This was based on the report by Pathak and Khanna[34] (see later) regarding similar irradiation of 4-methylphenyl acetate, about which we had some scepticism. If **6** were formed in a slightly acidic solution, possibly a small part would undergo the dienone-phenol rearrangement which we sought, although most would suffer the retro-Fries reaction, and be recycled. In effect, the irradiation would then replenish the dienone. However, irradiation in acidified ethanol gave only 2-hydroxy-5-methylbenzophenone (2-benzoyl-4-methylphenol, the known product of the photo-Fries reaction),[35] 4-methylphenol, ethyl benzoate, unchanged 4-methylphenyl benzoate, and a number of unidentified minor products. No trace was found by GLC/MS of material which could be 3-benzoyl-4-methylphenol, or of 4-benzoyl-3-methylphenol.

4-Methylphenyl acetate. It has been reported that UV irradiation of 4-methylphenyl acetate in methanol gives 4-acetyl-3-methylphenol as product.[34] This was suggested to arise by photo-Fries rearrangement to produce 4-acetyl-4-methylcyclohexa-2,5-dienone which then undergoes a 4–3 methyl migration of the dienone-phenol type. This seemed very surprising because we would expect to obtain 3-acetyl-4-methylphenol from this process, but also because the reaction seemed to have been well studied before, and had given 2-acetyl-4-methylphenol, the normal product of *ortho* migration.[35] We also had available spectra and other data for the purported product for direct comparison.[9] We therefore reinvestigated the reaction, trying (with no success) to reproduce the reported results.[34,*] It was possible that minor impurities in the 4-methylphenyl acetate could modify the course of the reaction, so this was prepared by two different routes, in which there might be acidic or basic impurities, and in the presence of small amounts of the phenol. The photolysis was performed in methanol and in ethanol (with the same results), and the photolysis mixture was worked up in a variety of ways, including those used in refs. 1 and 34. In all cases the products matched those reported by Sandner and coworkers; in particular, the rearranged product was 2-acetyl-4-methylphenol.[35] No component had an NMR spectrum which matched those reported for 4-acetyl-3-methylphenol.[9,34]

Conclusion

The 4-benzoyl-4-methylcyclohexa-2,5-dienone **6** upon treatment with low concentrations of non-nucleophilic proton and Lewis-acids in non-polar solvents gives a retro-Fries rearrangement to 4-methylphenyl benzoate. This reaction is surprisingly rapid, and completely obscures observation of any dienone-phenol rearrangement, particularly that involving benzoyl migration, which would itself be expected to be relatively fast. The reaction proceeds largely or exclusively by a dissociation-recombination process involving 4-methylphenol and a benzoyl cation, or closely related species, which partially separate and can be intercepted. A reported photo-Fries rearrangement of 4-methylphenyl acetate, which was believed to proceed *via* the 4-acetyl-4-methyl dienone **1** (R = R′ = Me) followed by a dienone-phenol rearrangement, could not be reproduced. Samples of 4-methylphenyl benzoate were irradiated in acidic solution with the hope of using the preceding idea to continually 'pump-up' the amount of the dienone **6** by a *para* photo-Fries reaction, so that any products of its irreversible dienone-phenol rearrangement might be found. However, only the known product of its (*ortho*) photo-Fries rearrangement was observed.

* The experiments have also been carried out by a number of final year undergraduates, to maximise the possibility of variation in the starting materials and other conditions.

Experimental

GLC analyses employed a Pye 104 instrument with flame-ionisation detector and glass columns (7 ft × $\frac{1}{4}$ inch), packed with silicone gum (E30, 2%), cyanoethyl silicone fluid (XF1150, 25%), neopentyl glycol succinate (NGS, 20%) or fluorosilicone gum (QFI, 10%), on silanized Supasorb (60–80 mesh, BDH). Silica for column chromatography was Merck Kieselgel 60, mesh 70–230, or for medium-pressure use, mesh 230–400. ^{1}H NMR spectra were recorded on Varian XL 100 or Perkin-Elmer R14 instruments at 100 MHz, and ^{13}C NMR spectra on a JEOL FX60 instrument at 15.03 MHz (Me_4Si internal standard). IR spectra were recorded on Pye-Unicam SP1050 or SP3-100 instruments, calibrated using polystyrene film. UV spectra were measured with a Pye-Unicam SP8-100 spectrometer. Mass spectra, and GLC/MS measurements were made using a Kratos MS80RF instrument. M.p.s were measured on a microscope hot-stage, using Anschütz thermometers, and are uncorrected.

Materials.—*4-Benzoyl-4-methylcyclohexa-2,5-dienone* **6** was made in our earlier work.[8]

3,4-Dihydro-3,3,8a-trimethylnaphthalene-1,6(2H,8aH)-dione **2** (R = Me).—As an alternative to the route employed previously,[7] the method based on the preparation of **6**[8] was used. Triethylamine (87 mg, 8.6 × 10^{-4} mol) and chlorotrimethylsilane (94 mg, 8.6 × 10^{-4} mol) were added to 3,4,7,8-tetrahydro-3,3,8*a*-trimethylnaphthalene-1,6(2*H*,8*aH*)-dione (169 m
iodide (0.13 g, 8.6 × 10^{-4} mol) in dry acetonitrile (1.0 cm^3) was added, and stirring was continued for 45 min. The mixture was extracted with warm pentane (30 cm^3), the extract dried ($CaSO_4$), and the solvent evaporated to give the crude silyl enol ether, 3,4,8,8*a*-tetrahydro-3,3,8*a*-trimethyl-6-trimethylsilyloxynaphthalene-1(2*H*,8*aH*)-one (114 mg), $\delta_H(CCl_4)$: 0.20 (9 H, s, $-OSiMe_3$), 0.86 (3 H, s, 8*a*-Me), 1.11 and 1.13 (6 H, 2 × s, 3-Me), 1.95–2.60 (6 H, m, 2-, 4- and 8-H), 4.63–4.84 (1 H, m, 7-H) and 5.42 (1 H, br s, 5-H); ν_{max}(film)/cm^{-1} 2960, 2920, 2870, 1670, 1660, 1620, 1250 and 845. The silyl ether in dry acetonitrile (1.0 cm^3) was stirred with palladium(II) acetate (92 mg, 4.1 × 10^{-4} mol) for 45 min, then extracted with pentane (80 cm^3), and the solution filtered through Celite, and the solvent evaporated to give the dienone as a solid which was washed with small amounts of cold pentane, and had m.p. 70–73 °C (from hexane) (lit.,[7] 71–73 °C), with a ^{1}H NMR spectrum identical to previous samples.

Reaction of 4-Benzoyl-4-methylcyclohexa-2,5-dienone with Trifluoroacetic Acid.—The dienone **6** (28.1 mg, 1.3 × 10^{-4} mol) was dissolved in CD_2Cl_2 (0.50 cm^3) and the ^{1}H NMR spectrum recorded at −10 °C. At a known time, 0.05 cm^3 of a solution of trifluoroacetic acid (74.0 mg) in CD_2Cl_2 (0.30 cm^3) at −10 °C was added, mixed well, and the sample returned to the spectrometer. The acid (1.1 × 10^{-4} mol dm^{-3}) is 2.5% w/v. The spectrum was run immediately, but all peaks due to dienone had been lost after 100 s. The aryl proton region of the spectrum was very complex, and spin-decoupling was used to distinguish the peaks. The total integration over this region was too large for the products 4-methylphenyl benzoate, 4-methylphenol and 4-benzoyl-4-methylcyclohexenone present as an impurity in the starting dienone. These were measured using their other signals. The additional peaks and excess integral were consistent with the presence of benzoic acid (in a quantity equivalent to the 4-methylphenol), or a very similar material such as benzoic

anhydride. Benzoic anhydride was detected in a later experiment. When work-up was performed using aqueous base this component was removed, and the NMR analysis became clearer. In subsequent experiments using ^1H NMR analysis, any 'benzoic acid' mentioned is inferred, but was not isolated. The molar ratio of 4-methylphenyl benzoate to 4-methylphenol and benzoic acid was *ca.* 50:50. A spectrum run 12 min later was identical. Spectra run after warming to 20 °C, at 3.25 and 6 h had slightly different ratios. Work-up of the sample after 6 h, by extraction with dichloromethane and water, then drying and evaporation of solvent, gave a pale yellow oil (26.6 mg, 95% recovery), whose ^1H NMR spectrum was clearer, and allowed more precise determination of the molar ratio of products, 4-methylphenyl benzoate:4-methylphenol, as 65:35. A GLC analysis (XF1150 column at 200 °C) confirmed the identity of the sole components of the mixture. In a check experiment to find whether any esterification could occur before work-up or NMR analysis, benzoic acid and 4-methylphenol (8.2×10^{-3} mol of each) were mixed and treated with trifluoroacetic acid (0.75 g) in dichloromethane (30.0 cm^3), at −10 °C for 1.45 h, then at 25 °C for 4 h. Work-up as before, and analysis of the solid residue by ^1H NMR spectroscopy showed the phenol and benzoic acid to be present in a 33:25 molar ratio, with no evidence of the presence of 4-methylphenyl benzoate.

Reaction of the Dienone **6** *with Acetic Anhydride and Sulphuric Acid.*—The dienone (25.0 mg, 1.18×10^{-4} mol) was stirred in redistilled acetic anhydride (2.0 cm^3) at 20 °C. Samples removed and analysed by UV (in ethanol) showed no change within 2.5 h. A small sample of conc. H_2SO_4 (1.17×10^{-6} mol), freshly dissolved in acetic anhydride, was added and samples were removed for UV analysis during 1.5 h. The dienone peak at 260 nm decreased rapidly (to 25% in 450 s). Work-up was effected by stirring with ice, warming to 20 °C over 65 h, extracting with ether, washing of the extract with aqueous sodium hydrogen carbonate then brine, drying, and evaporation of the solvent, to give a yellow residue (31.0 mg). NMR analysis of this showed peaks due to 4-methylphenyl acetate, 4-methylphenyl benzoate and 'benzoic acid' in a molar ratio 40:20:40%, showing that 33% of the dienone had reacted 'intramolecularly' and 67% by reaction involving acetic anhydride. Analysis by IR and GLC (XF 1150 column at 210 °C, and E30 column at 150 °C) confirmed the identity of the products, and also showed a trace of 4-methylphenol.

Reaction of Dienone **6** *with Trifluoromethanesulphonic Acid.*—The dienone **6** (20.0 mg) was dissolved in $CDCl_3$ (0.5 cm^3) in an NMR tube, and the spectrum recorded. Trifluoromethanesulphonic acid [0.05 cm^3 of a 1.03 mol dm^{-3} solution in $CDCl_3$ (5.15×10^{-5} mol)] was added to give a final concentration of 94×10^{-3} mol dm^{-3}. The first spectrum was completed after 195 s, and showed 4-methylphenyl benzoate, 4-methylphenol and 'benzoic acid' to be present in a ratio of 85:15:15. Subsequent spectra at 12, 125 and 250 min gave ratios of the benzoate:phenol as 80:20, 82:18 and 81:19, respectively, and a little 4-benzoyl-4-methylcyclohex-2-enone present as impurity in the dienone sample. Work-up as before, and NMR analysis showed 85% of the dienone to have rearranged, and 15% to have cleaved.

Reactions of Dienone **6** *with Boron Trifluoride Etherate.*—The dienone **6** (22.8 mg, 1.1×10^{-4} mol) was dissolved in sodium-dried benzene (0.18 cm^3) and redistilled boron trifluoride etherate (0.015 cm^3, 1.1×10^{-4} mol) was added. After being stirred at 25 °C for 30 min the solution was diluted with water (0.10 cm^3) and 20% sodium hydroxide solution (0.08 cm^3), and extracted with chloroform. The combined organic extracts were dried, and the solvent evaporated, to give a yellow oil (16.0 mg, 70% recovery), whose NMR spectrum showed the presence of 4-methylphenyl benzoate and 4-methylphenol in a ratio 57:43.

Because the dienone **6** is known to suffer cleavage upon treatment with aqueous hydroxide,[20] an alternative work-up was used in subsequent studies, exemplified by the following experiments.

Reactions of Dienone **6** *and* 3,5-*Dimethylphenol with Boron Trifluoride Etherate.*—(*a*) The dienone **6** (44.0 mg, 2.07×10^{-4} mol) and 3,5-dimethylphenol (25.0 mg, 2.07×10^{-4} mol) in benzene were stirred with boron trifluoride etherate (0.016 cm^3, 1.3×10^{-4} mol) at 20 °C during 45 min. Chloroform (30 cm^3) was added, and the solution was washed quickly with water (0.5 cm^3) containing triethylamine (1.3×10^{-4} mol). Solvent was removed from the dried solution, and the residue (75.0 mg, 100% recovery) was shown by quantitative GLC analysis to contain 4-methylphenyl benzoate and 3,5-dimethylphenyl benzoate in the molar ratio 75:25, and the two phenols. The proportions of the latter could not be determined accurately from the ^1H NMR spectrum. The sample was examined by ^{13}C NMR spectroscopy, and comparison with authentic samples of the four components. No trace was present of benzophenones (absence of peaks near 200 ppm).

(*b*) The dienone **6** (20.0 mg, 9.43×10^{-5} mol) and 3,5-dimethylphenol (11.5 mg, 9.43×10^{-5} mol) in benzene (0.5 cm^3) were treated as above with boron trifluoride etherate (0.01 cm^3, 8.1×10^{-5} mol) and stirred at 20 °C during 45 min. Work-up using aqueous trimethylamine and chloroform gave an oil which contained 4-methylphenyl benzoate, 3,5-dimethylphenyl benzoate, 4-methylphenol and 3,5-dimethylphenol. Calibrated GLC analysis gave the molar ratio of 4-methylphenyl benzoate to 3,5-dimethylphenyl benzoate as 76:24, and confirmed the presence of only these four products. The ratio of the two esters was unchanged over 14 days. To the oily product was added further 3,5-dimethylphenol (2.4 mg, to equal the amount of 4-methylphenol remaining in it) in benzene (0.25 cm^3), and a drop of boron trifluoride etherate. The mixture was worked up as before, and analysed by quantitative GLC after 45 min and then after a few days at 20 °C. The ratio of 4-methylphenyl benzoate to 3,5-dimethylphenyl benzoate was essentially unchanged at 72:28.

(*c*) A similar experiment in which the dienone was treated with a two-fold excess of 3,5-dimethylphenol gave a product mixture containing the two phenols, 4-methylphenyl benzoate and 3,5-dimethylphenyl benzoate in the ratio 66:34.

Reaction of Dienone **6** *with Zinc Chloride.*—The dienone **6** (20.0 mg, 9.4×10^{-5} mol) in dry benzene (1.0 cm^3) was added to zinc chloride (1.3 mg, 9.5×10^{-6} mol), which had been freshly fused under vacuum and cooled under nitrogen. The mixture was stirred at 20 °C and samples were analysed by GLC (XF1150 column at 200 °C). No detectable change occurred within 100 h. Further zinc chloride (17.0 mg, 1.25×10^{-4} mol) was added and the reaction continued for 46 h at 34 °C. Direct NMR analysis was unsatisfactory, so the mixture was worked up with water and chloroform, and the dried and evaporated product was shown by GLC, as above, to contain 4-methylphenyl benzoate and 4-methylphenol, in a ratio of 64:36 (as determined by NMR spectroscopy).

UV Irradiation of 4-*Benzoyl*-4-*methylcyclohexa*-2,5-*dienone.*—The dienone (20 mg, 9.4×10^{-5} mol) in hexane (100 or 490 cm^3) was irradiated through Pyrex or quartz using a Hanovia 450 W high pressure lamp, with monitoring by TLC until virtually all the dienone was consumed (20 h in quartz, no reaction using Pyrex). The residue after evaporation of solvent was examined by NMR spectroscopy and GLC, and showed the presence of 4-methylphenol and benzoic acid,

with six other minor, rapidly eluted compounds, but no 4-methylphenyl benzoate or hydroxybenzophenones which would have resulted from photo-retro-Fries reactions or dienone-phenol rearrangements.

UV Irradiation of 4-Methylphenyl Benzoate.—The ester (4.0 g, 1.89 × 10^{-2} mol) and sulphuric acid (2.15 g, 2.2 × 10^{-2} mol) were dissolved in spectroscopic ethanol (490 cm^3) and irradiated for 70 h, through quartz in an immersion-type apparatus using a Hanovia 125 W lamp. The reaction was monitored by GLC (XF1150 column at 200 °C). After 70 h the solvent was removed by evaporation and the residue in ether was washed with sodium hydrogen carbonate solution then water, and dried. The resulting oil (3.90 g) included (NMR analysis) unchanged ester, 4-methylphenol and ethyl benzoate. The mixture was then steam-distilled, and the distillate dissolved in ether was dried and the solvent was removed. This fraction contained the compounds already identified, plus an additional compound which was identified as 2-hydroxy-5-methylbenzophenone (dinitrophenylhydrazone m.p. 243–245 °C) (from ethanol–ethyl acetate) (lit.,[35] 244–245 °C). The distillation residue was studied by GLC/MS (OV-101 column), and showed ten minor components none of which had a mass or breakdown pattern which could correspond to 3-benzoyl-4-methylphenol (2-methyl-5-hydroxybenzophenone) or its positional isomers.

UV Irradiation of 4-Methylphenyl Acetate.—The ester was prepared by the methods of Sandner and his coworkers (using acetyl chloride, with pyridine as base, and the quantities given for '[$^2H_3$]-*p*-tolyl acetate', but using toluene instead of benzene as solvent),[35] and of Chattaway (from the phenol, aqueous sodium hydroxide and acetic anhydride).[36] Samples were distilled once, or twice (to achieve apparent absence of all impurities, GLC, NMR and IR spectroscopy). Solutions in methanol,[34] and in ethanol,[35] were used, with a range of concentrations and of work-up methods which included those used in refs. 1 and 34. In all cases the results of irradiation were the same. The rearrangement product had ^1H NMR peaks at δ (ranges given for five samples, in $CDCl_3$ or CCl_4), 11.9–12.0 (1 H, s, OH), 7.5–7.4 (3 H, d, *J* 2.5 Hz, 3-H), 7.20–7.23 (1 H, d, *J* 8–9 Hz, of d, *J* 2.0–2.5 Hz, 5-H), 6.75–6.80 (1 H, d, *J* 8–9 Hz, 6-H), 2.25–2.29 (3 H, s, ring Me) and 2.51–2.55 (3 H, s, acetyl), in full agreement with that of 2-acetyl-4-methylphenol (2-hydroxy-5-methylacetophenone), as prepared by thermal Fries rearrangement of 4-methylphenyl acetate (refs. 35 and 37, and this work). The spectra are different from those reported for 4-acetyl-3-methylphenol (4-hydroxy-2-methylacetophenone).[9,34,37]

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References

1 J. C. Anderson and C. B. Reese, *J. Chem. Soc.*, 1963, 1781.
2 C. E. Kalmus and D. M. Hercules, *Tetrahedron Lett.*, 1972, 1575.
3 S. M. Beck and L. E. Brus, *J. Am. Chem. Soc.*, 1982, **104**, 1805.
4 For reviews, see D. Bellus and P. Hrdlovic, *Chem. Rev.*, 1967, **67**, 599; D. Bellus, *Adv. Photochem.*, 1971, **8**, 109.
5 F. Effenberger and R. Guttmann, *Chem. Ber.*, 1982, **115**, 1089.
6 F. Effenberger, H. Klenk and P. L. Reiter, *Angew. Chem., Int. Ed. Engl.*, 1973, **72**, 775.
7 J. H. Zaidi and A. J. Waring, *J. Chem. Soc., Chem. Commun.*, 1980, 618; A. J. Waring and J. H. Zaidi, *J. Chem. Soc., Perkin Trans. 1*, 1985, 631.
8 L. B. Jackson and A. J. Waring, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1791.
9 J. W. Pilkington and A. J. Waring, *J. Chem. Soc., Perkin Trans. 2*, 1976, 1349.
10 J. D. Palmer and A. J. Waring, *J. Chem. Soc., Perkin Trans. 2*, 1979, 1089.
11 J. N. Marx, J. C. Argyle and L. R. Norman, *J. Am. Chem. Soc.*, 1974, **96**, 2121.
12 H. O. House and R. L. Wasson, *J. Am. Chem. Soc.*, 1957, **79**, 1488.
13 H. O. House and G. D. Ryerson, *J. Am. Chem. Soc.*, 1961, **83**, 979, and previous papers in the series.
14 V. Tortorella, L. Toscano, C. Vetuschi and A. Romeo, *J. Chem. Soc., C*, 1971, 2422.
15 P. Bakuzis, G. C. Magalhaes, H. Martins and M. L. F. Bakuzis, *J. Org. Chem.*, 1974, **39**, 2427.
16 E. Lee-Ruff and P. Khazanie, *Can. J. Chem.*, 1975, **53**, 1708.
17 Y. Sawaki and Y. Ogata, *J. Am. Chem. Soc.*, 1978, **100**, 856.
18 R. D. Bach and J. M. Domagala, *J. Org. Chem.*, 1984, **49**, 4181.
19 R. C. Klix and R. D. Bach, *J. Org. Chem.*, 1987, **52**, 580.
20 L. B. Jackson and A. J. Waring, *J. Chem. Soc., Perkin Trans. 2*, 1990, 907.
21 M. J. S. Dewar and L. S. Hart, *Tetrahedron*, 1970, **26**, 973.
22 R. Martin, *Bull. Soc. Chim. Fr.*, 1974, 983.
23 Briefly reviewed by J. March in *Advanced Organic Chemistry*, Wiley, New York, 1985, 3rd edn., p. 499. For recent examples, see B. P. Munday and M. G. Ellerd in *Name Reactions and Reagents in Organic Synthesis*, Wiley, New York, 1988, p. 88.
24 H. J. Shine and W. Subotkowski, *J. Org. Chem.*, 1987, **52**, 3815.
25 A. Kivinen, in *The Chemistry of Acyl Halides*, ed. S. Patai, Interscience, New York, 1972, p. 177.
26 E. K. Euranto, in *The Chemistry of Carboxylic acids and Esters*, ed. S. Patai, Wiley, New York, 1969, p. 575.
27 R. J. E. Talbot, in *Comprehensive Chemical Kinetics*, eds. C. H. Bamford and C. F. H. Tipper, Elsevier, New York, 1972, vol. 10, ch. 3.
28 P. Schiess, R. Dinkel and P. Fünfschilling, *Helv. Chim. Acta*, 1981, **64**, 787.
29 D. J. Field, D. W. Jones and G. Kneen, *J. Chem. Soc., Perkin Trans. 1*, 1978, 1050.
30 C. P. Falshaw, S. A. Lane and W. D. Ollis, *J. Chem. Soc., Chem. Commun.*, 1973, 491.
31 S. C. Cooper and P. G. Sammes, *J. Chem. Soc., Perkin Trans. 1*, 1984, 2407.
32 F. B. H. Ahmad, J. M. Bruce, J. Khalafy, V. Pejanovic, K. Sabetian and I. Watt, *J. Chem. Soc., Chem. Commun.*, 1981, 166.
33 F. B. H. Ahmad, J. M. Bruce, J. Khalafy and K. Sabetian, *J. Chem. Soc., Chem. Commun.*, 1981, 169.
34 V. P. Pathak and R. N. Khanna, *Synthesis*, 1981, 882.
35 M. R. Sandner, E. Hedaya and D. J. Trecker, *J. Am. Chem. Soc.*, 1968, **90**, 7249.
36 F. D. Chattaway, *J. Chem. Soc.*, 1931, 2495.
37 *Aldrich Library of NMR Spectra*, ed. C. J. Pouchert, Aldrich, Milwaukee, 1983, 2nd edn., spectra 37D and 38D.

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