Synthesis of (*E*)- and (*Z*)-Pulvinones

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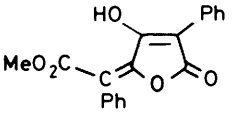
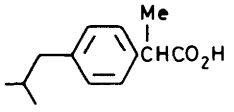
Two new routes to pulvinones have been developed, one of which involves a novel Wittig reaction. For the first time, members of the *E*-series, including the parent (*E*)-pulvinone, are reported and the structural elucidation of the geometric isomers is described. A method for quantitatively converting (*E*)-pulvinones into (*Z*)-pulvinones is presented, together with a technique for differentiating between the isomers.

In recent years, Imperial Chemical Industries[1] and Smith Klyne and French[2] have filed numerous patents on derivatives of vulpinic acid (**1**) claiming anti-inflammatory (a.i.), anti-pyretic and analgesic activities. Many a.i. agents, *e.g.* ibuprofen (**2**), indomethacin (**3**) and naproxen (**4**) contain an arylacetic acid moiety but a study of the structure of vulpinic acid (**1**) led us to consider that perhaps the phenylacetic acid residue was not necessary for the observed activity and that the enolic hydroxy group, being part of a vinylogous carboxylic acid group, was the required acidic function. (The analogous phenylbutazone (**5**) is an anti-inflammatory agent). Consequently, we tested the compound lacking the methoxycarbonyl group, *viz.* the pulvinone (**9a**), and found that it also exhibits good a.i. activity and is considerably less toxic than vulpinic acid. More recently, we have shown that pulvinones stabilise cellular membranes and inhibit complement activation by blocking the action of C1 esterase and reducing C4 utilisation.[3]



(**1**)



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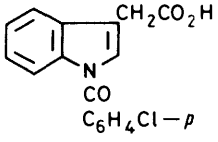

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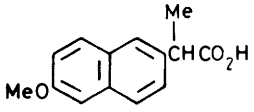

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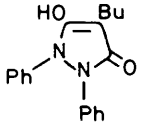
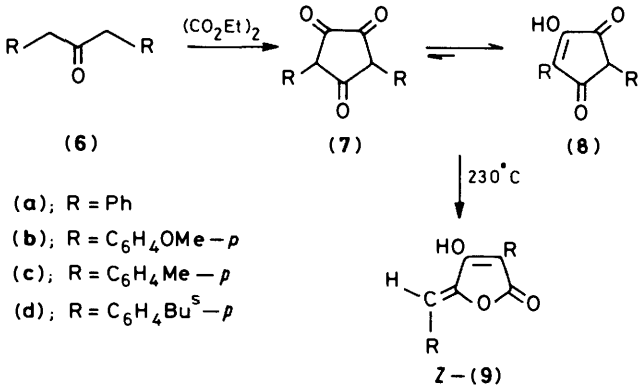


(**5**)

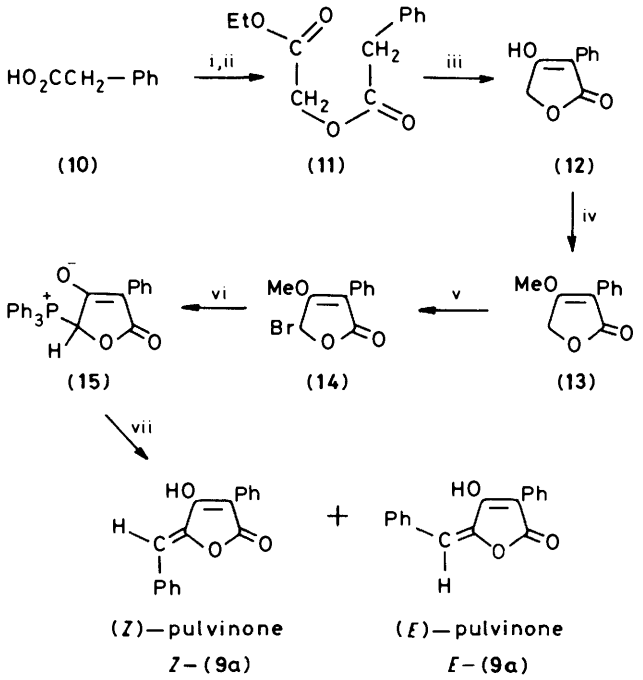
Pulvinone is the generic name used to describe the parent of a new family of substituted benzylidene-4-hydroxy-3-phenyl-5-furan-2(5*H*)-one pigments recently isolated from the common larch mushroom *Suillus grevillei* and from cultures of *Aspergillus terreus*[4–7] and recent papers by Pattenden and co-workers[8] describe the total syntheses of the methyl enol ethers of these naturally occurring pulvinones. This report includes new syntheses and structural elucidations of (*Z*)- and (*E*)-pulvinone and some derivatives and analogues which were considered interesting candidates for biological evaluation.

The parent compound (**9a**) was first prepared by us from dibenzyl ketone (**6a**) in 49% overall yield by the method described by Claisen and Ewan (Scheme 1).[9] The intermediate trione (**7a**) exists almost entirely in the enolic form (**8a**)[10] as does the pulvinone (**9a**). The *p,p'*-disubstituted pulvinones (**9b,c,d**) were obtained by the same method but because of the generally poor yields of substituted hydroxydiarylcyclopentenediones (**8**) obtained by this method and the need for



Scheme 1.

the separation of the isomeric pulvinones from asymmetrical dibenzylketones, a more versatile regiospecific route was developed. The preparation of the pulvinone (**9a**) is typical for the series (Scheme 2). Treatment of the sodium salt of phenylacetic acid (**10**) with ethyl bromoacetate in ethanolic



Scheme 2. *Reagents:* i, NaOEt,EtOH; ii, $BrCH_2COOEt$; iii, Bu^{t}OK, Bu^{t}OH; iv, K_2CO_3,Me_2SO_4, Me_2CO; v, NBS, azoisobutyronitrile, $(CH_2)_2Cl_2$; vi, Ph_3P, C_6H_6; vii, NaOEt, EtOH, ArCHO.

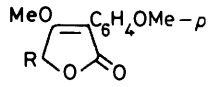
solution afforded, in nearly quantitative yield, the ester (**11**) which on reaction with potassium t-butoxide in t-butyl alcohol furnished 4-hydroxy-3-phenylfuran-2(5*H*)-one (**12**) in 68% yield. Previous strategies[11,12] to this compound are less convenient and give lower yields. Bromination of the methyl enol ether (**13**) with *N*-bromosuccinimide in 1,2-dichloroethane using azoisobutyronitrile as initiator afforded, in 86% yield, the 5-bromo derivative (**14**) which was treated with triphenylphosphine (1.1 mol equiv.) in boiling benzene to give the inner salt (**15**).

The structure assigned to the inner salt (**15**) is based on the following evidence: in the ^{13}C n.m.r. spectrum, a double doublet at δ 71.8 (J_{CP} 55 Hz, J_{CH} 162 Hz) indicates the presence of the carbon atom at position 5 directly coupled to phosphorus and hydrogen. The C-2, C-3 and C-4 atoms resonate within the ranges expected[13] and the signals for the aromatic carbons are also entirely in accord with the structure: absorptions at 1 726 cm^{-1} and 268 nm (ε 19 200) indicate the presence of the α,β-unsaturated γ-lactone. In the ^{31}P n.m.r. spectrum of (**15**), the phosphorus atom resonates at δ +22.1 (o-H_3PO_4 as reference), confirming that the compound exists as the inner salt and not as the alternative oxaphosphetane form in which the ^{31}P resonance would occur upfield of the reference.[14] The release of methyl bromide during the preparation of the inner salt (**15**) from the 5-bromo compound (**14**) was verified by trapping the evolved gas as a condensate. The ready formation of methyl bromide presumably occurs by attack of bromide ion on the methyl group, the H_3C–O bond having been weakened by the attraction of the phosphonium centre. The production of methyltriphenylphosphonium bromide (*ca.* 25%), obtained as a by-product by the action of triphenylphosphine on the released methyl bromide, was reduced to *ca.* 8% by adding the triphenylphosphine (1.3 mol equiv.) in benzene dropwise to a solution of the bromo compound (**14**) in benzene. The phosphonium bromide was removed entirely from the crude reaction product by leaching with a mixture of methylene chloride and hexane (2:1) in which the salt (**15**) is essentially insoluble.

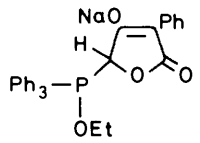
By methods similar to those described above, the following phenyl substituted derivatives of (**12**), (**13**), (**14**), and (**15**) were prepared in yields similar to those obtained for the parent compound: *o*-F, *o*-Cl, *m*-F, *m*-Cl, *p*-F, *p*-Br, *p*-Cl, *o*-OMe, *m*-OMe, *p*-OMe; *m,p* – diCl, *p*-Ph, *o,m*-benzo. No effort has been made to optimise the yields.

Base catalysed condensation of the inner salt (**15**) with benzaldehyde gave a mixture (60:40 by ^1H n.m.r.) of the *Z*- and *E*-isomers of pulvinone (**9a**) in 93% yield. The condensation was best effected by adding the aldehyde (no α-H) to freshly prepared sodium ethoxide (1.1 mol equiv.) and then immediately adding the inner salt. If the base is in contact with the salt before the addition of the aldehyde (normal procedure), the yield is poor (*ca.* 30%) and a large amount of 4-hydroxy-3-phenylfuran-2(5*H*)-one (**12**) is formed. Using this 'reverse procedure' very little of the furan-2(5*H*)-one (**12**) was produced and, in general, the pulvinones were obtained in good yields (>90%) as a mixture of *Z*- and *E*-isomers. It was shown subsequently that treatment of the inner salt (**15**) with sodium ethoxide (1.1 mol equiv.) in ethanol for 10 min afforded 4-hydroxy-3-phenylfuran-2(5*H*)-one (**12**) in 38% yield. A likely intermediate in the reaction is the pentavalent phosphorus compound (**17**). Collapse of this in the presence of ethanol would explain the formation of the observed by-products, triphenylphosphine oxide and diethyl ether.

The foregoing preparation of the inner salt (**15**) and (*Z*)-pulvinone *Z*-(**9a**) contrasts with the report by Pattenden and Knight[8b] that treatment of 4-methoxy-3-(4-methoxyphenyl)furan-2(5*H*)-one (**16a**) with *N*-bromosuccinimide and then triphenylphosphine gave the triphenylphosphonium salt (**16c**) in which

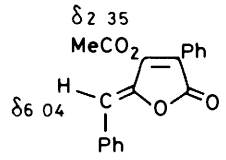


(**16a**) R = H
(**16b**) R = Br
(**16c**) R = $P^+(Ph_3)Br^-$

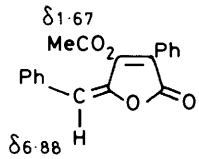


(**17**)

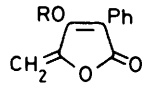
the methyl enolate function is retained, which then condensed with aryl aldehydes to furnish pulvinones in low yields only. No experimental details of their procedures were given, however, but we observed none of the methyl ether in our product from the reaction of the bromo compound (**16b**) with triphenylphosphine (benzene/reflux).



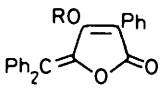
(**18**)



(**19**)



(**20**) R = H
(**21**) R = Ac

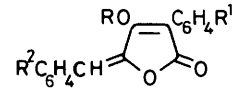


(**22**) R = H
(**23**) R = Ac

The geometry of the isomers of pulvinone was deduced in the following way. The signals for the acetyl groups in the ^1H n.m.r. spectra of (Z)- and (E)-*O*-acetylpulvinones (**18**) and (**19**) appear at δ 2.35 and 1.67 respectively and this difference is attributable to the anisotropic shielding effect of the aromatic ring on the methyl group. Confirmation of this effect was obtained by a comparison of the ^1H n.m.r. spectra of the *O*-acetyl-5-methylenefuran-2(5*H*)-one (**21**) and the 5-diphenylmethylene analogue (**23**), prepared by base-catalysed condensation of the inner salt (**15**) with formaldehyde and thiobenzophenone respectively and then treatment of the free enols (**20**) and (**22**) with acetic anhydride and pyridine. For the unsubstituted methylene compound (**21**), the hydrogen atoms of the acetyl group resonate at δ 2.34 whereas in the diphenylmethylene compound (**23**), the signal for the acetyl group appears at δ 1.48. We have observed chemical shifts in the range δ 1.60—1.80 and δ 2.20—2.40 for a number of *E*- and *Z*-isomers of *O*-acetylpulvinones and this property, together with the difference in the chemical shifts between their vinylic protons, has been used to assign the structures of many *Z*- and *E*-isomers in the pulvinone series, (see Tables 1 and 2). It is noteworthy that for the 6-furyl analogues of *O*-acetylpulvinone the signals for the acetyl groups are coincident (Table 2) and care should be exercised when applying this identification method to C-6 heterocyclic analogues of pulvinones. Presumably, the anisotropic effect of the furyl group or its orientation with respect to the rest of the molecule is different from that of phenyl.

Recently Pelter and Ayoub[13] have suggested that ^{13}C n.m.r. might be used to differentiate between (Z)- and (E)-5-methylenefuran-2(5*H*)-ones. They observed that for the 5*Z*- and 5*E*-isomers of the 4-methoxy compounds (**24**)—(**26**) and for the 4-methyl compound (**27**), the differences in the chemical shifts of the C-6 carbon atom were similar and that the direction of the

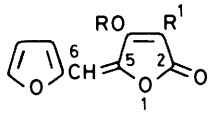
Table 1



Compd.	R^1	R^2	R=H M.p. (°C)	R=H δArCH=[a]	R=Ac δArCH=[b]	R=Ac δMeCO–[b]
Z-(**9a**)	H	H	250—254	6.78	6.04	2.35
E-(**9a**)	H	H	185—187	6.80	6.88	1.67
Z-(**50**)	H	*m*-Cl	258—260	6.67	5.94	2.36
E-(**50**)	H	*m*-Cl	152—154	6.75	6.75	1.80
Z-(**51**)	H	*o*-Cl	220—224	7.06	6.55	2.40
E-(**51**)	H	*o*-Cl	165—169	6.75	6.86	1.64
Z-(**52**)	H	*p*-OMe	239—242	6.71	5.99	2.33
E-(**52**)	H	*p*-OMe	191—193	6.78	6.79	1.79
Z-(**53**)	*m*-Cl	*o*-Cl	238—241	7.04	6.56	2.40
E-(**53**)	*m*-Cl	*o*-Cl	187—189	6.70	6.85	1.64
Z-(**54**)	*p*-Cl	*m*-Cl	262—265	6.70	6.00	2.40
E-(**54**)	*p*-Cl	*m*-Cl	185—187			
Z-(**55**)	*m*-OMe	H	225—229	6.71	6.10	2.37
E-(**55**)	*m*-OMe	H	162—164	6.80	6.82	1.67
Z-(**56**)	*m*-OMe	*m*-Cl	224—228	6.70		
E-(**56**)	*m*-OMe	*m*-Cl	132—135	6.76		

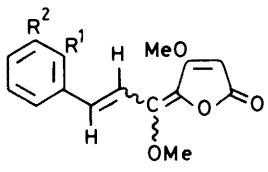
[a] For solutions in [$^2H_6$]dimethyl sulphoxide unless otherwise stated. [b] For solutions in [^2H]chloroform unless otherwise stated.

Table 2



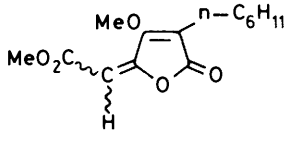
Compd.	R^1	R=H M.p. (°C)	R=H δ(6-H)[a]	R=Ac δ(6-H)[b]	R=Ac δ(CH_3CO)[b]
Z-(**57**)	Ph	220—230 (decomp.)	6.70	6.04	2.30
E-(**57**)	Ph	204—207	6.64	6.50	2.30
Z-(**58**)	*p*-ClC_6H_4	251—256 (decomp.)	6.73		
E-(**58**)	*p*-ClC_6H_4	241—243	6.60	6.50	2.30

[a] For solutions in [$^2H_6$]dimethyl sulphoxide. [b] For solutions in [^2H]chloroform.

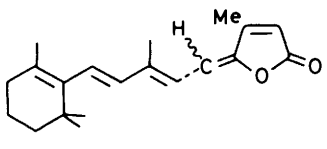


(**24**) $R^1 = R^2 = H$

(**25**) $R^1, R^2 = OCH_2O$



(**26**)



(**27**)

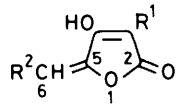
change was the same [$\Delta\delta(Z \longrightarrow E)$ was in the range 4.0 and 6.1].

We have examined the ^{13}C n.m.r. spectra of a series of *Z*- and *E*-isomers for analogous pulvinones (see Table 3) and found that $\Delta\delta$ values for the C-6 carbon atoms are of the same sign and similar magnitudes as those reported by Pelter. Moreover, $\Delta\delta$ ($Z \longrightarrow E$) for C-3 in the series is in the range +3.2 to +4.9. Although the corresponding $\Delta\delta$ for C-4 and C-5 is not as large as for C-3 or C-6, the sign is consistently negative for C-4 and positive for C-5; C-2 is little affected by the geometry at C-5. The foregoing differences in chemical shifts have been used to confirm the geometry of the 2-furylmethylene compounds *Z*-(**57**) and *E*-(**57**), and *Z*-(**58**) and *E*-(**58**) (Table 3).

Interestingly, conversion of (*E*)-pulvinone to its acetate (**19**) and then hydrolysis with cold dilute alkali gave (*Z*)-pulvinone and this reaction was found to be a general one within the series. Usually, two such treatments effected a nearly quantitative conversion of the *E*-isomer into the *Z*-form. Using this serendipitous transition, high yields of (*Z*)-pulvinones were obtained from these reaction sequences.

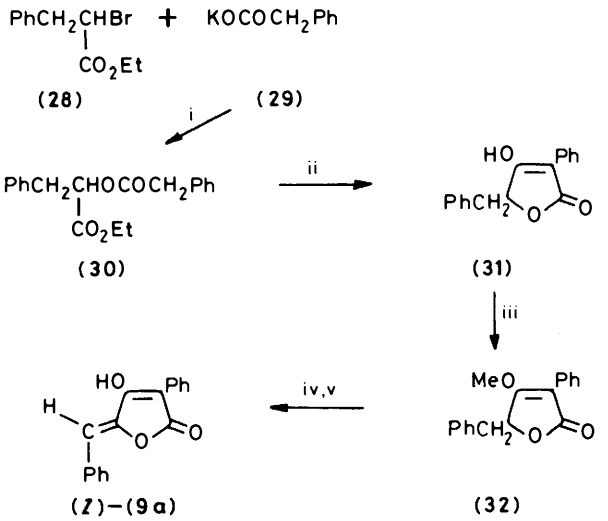
The *Z*-isomers of the pulvinone series have the higher melting points, are more polar on t.l.c. systems, are the less soluble and crystallise preferentially from the mixture of isomers. The one exception to this has been observed for some *o*-substituted 5-benzylidene compounds. Although the *Z*-isomer of these *o*-substituted derivatives have the higher melting points, on t.l.c. systems the polarities are sometimes the same and crystallisation of the mixture can lead to isolation of the *Z*- or the *E*-isomer preferentially. (Of over 100 pulvinones prepared, no *cis* isomer was more polar than the *trans* isomer on t.l.c. systems). Indeed, sometimes a duplication reaction using apparently identical conditions and the same solvent for crystallisation afforded the isomers in different order.

Table 3. ^{13}C Chemical shifts[a] for some 5-methylenefuran-2(5*H*)-ones



Compd.	R^1	R^2	δ C-2	δ C-3	δ C-4	δ C-5	δ C-6	Δδ(Z → E) C-3	Δδ(Z → E) C-6
Z-(**9a**)	Ph	C_6H_5	167.8	100.2	163.8	142.4	107.5	+3.7	+7.0
E-(**9a**)	Ph	Ph	167.7	104.9	161.9	143.8	114.5		
Z-(**50**)	Ph	*m*-ClC_6H_4	167.7	100.4	163.8	143.6	105.6	+4.3	+6.9
E-(**50**)	Ph	*m*-ClC_6H_4	167.7	104.7	162.2	144.9	112.5		
Z-(**52**)	Ph	*p*-$MeOC_6H_4$	167.9	99.7	163.8	140.6	107.7	+4.9	+7.2
E-(**52**)	Ph	*p*-$MeOC_6H_4$	167.6	104.6	161.8	142.3	114.9		
Z-(**56**)	*m*-$MeOC_6H_4$	*m*-ClC_6H_4	167.6	100.3	163.3	143.5	105.8	+3.6	+6.7
E-(**56**)	*m*-$MeOC_6H_4$	*m*-ClC_6H_4	167.7	103.9	162.9	145.1	112.3		
Z-(**57**)	Ph	2-Furyl	167.4	100.4	163.1	140.3	97.0	+3.9	+5.1
E-(**57**)	Ph	2-Furyl	167.3	104.3	161.5	141.9	102.1		
Z-(**58**)	*p*-ClC_6H_4	2-Furyl	167.2	99.0	163.7	140.1	97.4	+3.2	+4.6
E-(**58**)	*p*-ClC_6H_4	2-Furyl	167.4	102.2	162.8	142.2	102.0		

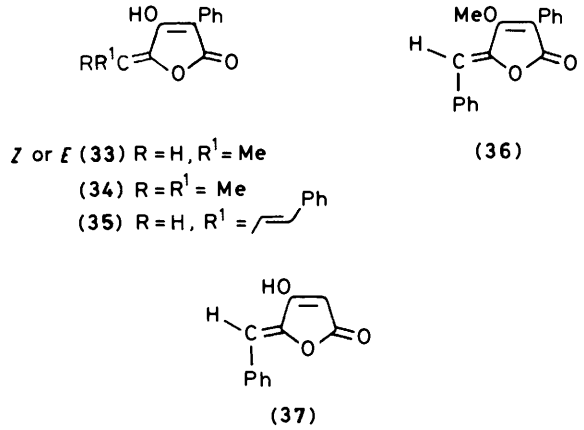
[a] For solutions in [$^2H_6$]dimethyl sulphoxide using a Varian XL 100 spectrometer.



Scheme 3. *Reagents:* i, t-pentyl alcohol; ii, Bu^{t}OK, Bu^{t}OH; iii, K_2CO_3, Me_2SO_4; iv, NBS, $(CH_2)_2Cl_2$; v, LiBr, $CaCO_3$, DMF.

Scheme 3 outlines an alternative synthesis of *Z*-pulvinone (*Z*)-(**9a**). Treatment of ethyl 2-bromo-3-phenylpropionate (**28**)[15] with potassium phenylacetate gave the condensation product (**30**) which was converted into the known[12,16] 5-benzyl-4-hydroxy-3-phenylfuran-2(5*H*)-one (**31**) using potassium t-butoxide in t-butyl alcohol, in 53% yield from the bromopropionate (**28**). The dihydropulvinone (**31**) was treated with dimethyl sulphate and potassium carbonate to give the enol ether (**32**) (78% yield) which was elaborated by treatment with *N*-bromosuccinimide and then lithium bromide and calcium carbonate in dimethylformamide to (*Z*)-pulvinone (*Z*)-(**9a**) (64% yield) identical with the samples prepared previously.

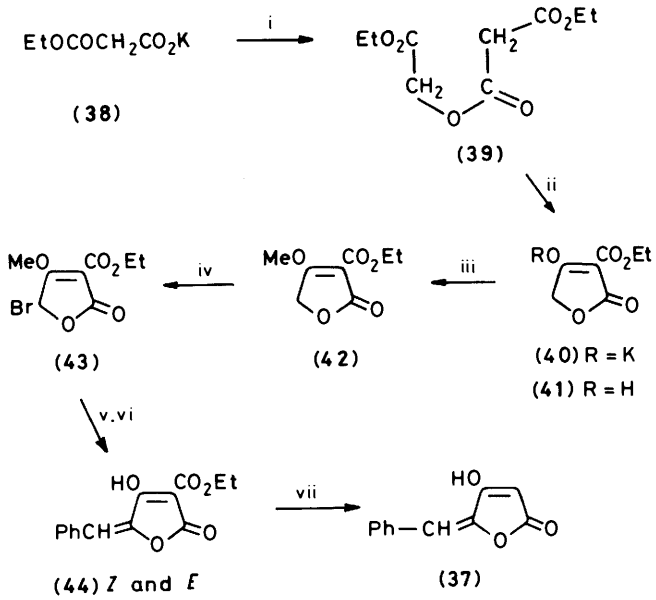
In an attempt to ascertain which functions in pulvinone are required for anti-inflammatory activity, a number of analogues were prepared for biological evaluation. These included the ylidenes (**33**)—(**37**). Compounds (**33**) and (**35**) were prepared from the inner salt (**15**) essentially by the procedure described above using the appropriate aldehyde or ketone. Sodium hydride was employed as base for the preparation of the methylethylidene analogue (**34**). When a significant amount of the furan-2(5*H*)-one (**12**) was formed, *e.g.* in reactions involving ketones in which reaction times were longer, it was usually removed from the crude product by extraction with sodium hydrogen carbonate solution at 0 °C or by chromatography.



The methyl enol ether (**36**)[17] was prepared from the (*Z*)-pulvinone *Z*-(**9a**) by treatment with potassium carbonate and dimethyl sulphate. It is noteworthy that although attempts to hydrolyse the methyl enol ethers of pulvinones with acid and base under normal conditions were unsuccessful, the cleavage was effected readily and cleanly with lithium bromide in boiling dimethylformamide for 2 min.

(*Z*)-5-Benzylidene-4-hydroxyfuran-2(5*H*)-one (**37**) was synthesised by the sequence shown in Scheme 4. Treatment of ethyl potassium malonate (**38**)[18] with ethyl bromoacetate in boiling ethanol afforded ethoxycarbonylmethyl ethyl malonate (**39**) (89%), which reacted with potassium t-butoxide in t-butyl alcohol to give, in 89% yield, the ethoxycarbonyl-4-hydroxyfuran-2(5*H*)-one potassium salt (**40**). A sample of this was converted by treatment with ethanolic hydrogen chloride into the free enol (**41**), m.p. 113—117 °C (lit.,[19] m.p. 75—77 °C hydrated; 124—125 °C anhydrous). Spectroscopic data was in accord with the designated structure.

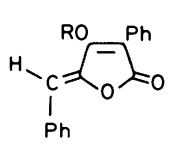
Treatment of the potassium salt (**40**) with dimethyl sulphate in dry acetone gave in 45% yield the enol ether (**42**) which was brominated with *N*-bromosuccinimide to afford the 5-bromofuran-2(5*H*)-one (**43**) in 41% yield. This was converted into the



Scheme 4. *Reagents:* i, $BrCH_2CO_2Et$, EtOH; ii, Bu^{t}OK, Bu^{t}OH; iii, Me_2SO_4; iv, NBS, $(CH_2)_2Cl_2$; v, Ph_3P, C_6H_6; vi, PhCHO, EtONa, EtOH; vii, NaOH, H_2O.

Wittig intermediate which was immediately treated with benzaldehyde and sodium ethoxide to give a mixture (1:1) of the *Z*- and *E*-isomers of the 3-ethyloxycarbonylfuran-2(5*H*)-one (**44**) (45% overall yield). Decarboxylation of the higher melting isomer with aqueous sodium hydroxide by the method described by Fleming and Harley-Mason [20] gave (*Z*)-5-benzylidene-4-hydroxyfuran-2(5*H*)-one (**37**) (64%).

In addition to (*Z*)-*O*-acetylpulvinone (**18**) and pulvinone methyl ether (**36**) already described, the esters (**45**)—(**47**) and ethers (**48**) and (**49**) were prepared in order to study the effects of increase in lipophilicity of the molecule and protection of the enol function. The isobutyrylpulvinone (**45**) was prepared by treatment with isobutyric anhydride and pyridine while the pivaloyl and benzoyl esters (**46**) and (**47**) were best prepared using the appropriate acid chloride and pyridine. The allyl ether (**48**) and ethyloxycarbonylmethyl ether (**49**) were obtained by alkylation of (*Z*)-pulvinone in acetone containing potassium carbonate with allyl bromide and ethyl bromoacetate respectively.



(45) R = $Me_2CH.CO$
(46) R = $Me_3C.CO$
(47) R = PhCO
(48) R = $CH_2:CH-CH_2$
(49) R = $EtO.CO.CH_2$

Experimental

Melting points were determined on a Kofler hot-stage apparatus. Unless otherwise stated, u.v. spectra were measured for solutions in ethanol with a Pye-Unicam S.P. 1 700 spectrophotometer, i.r. spectra for solids at a concentration of 1% (w/w) in potassium chloride discs with a Perkin-Elmer 457 spectrophotometer and ^1H n.m.r. spectra for solutions in [^2H]chloroform with a Perkin-Elmer R12B spectrometer. ^{13}C and ^{31}P N.m.r. spectra were measured using a Bruker WM-250 spectrometer. Ether refers to diethyl ether. The results for compounds said to have satisfactory analyses are available as a Supplementary publication [Sup. no. 56312 (15pp.)].*

4-Hydroxy-2,5-diphenylcyclopent-4-ene-1,3-dione (**8a**).—Treatment of dibenzyl ketone (**6a**) (42 g) with diethyl oxalate (30 g) by the method described by Claisen and Ewan [9] afforded, after crystallisation from acetone, the cyclopentenedione (**8a**) (33.2 g) as yellow needles, m.p. 194—195 °C (lit.,[9] m.p. 192—193 °C), $\lambda_{max.}$(237) (ε 17 000) and 320 nm (ε 14 550); $\nu_{max.}$ 3 260, 1 735, 1 670, and 1 630 cm^{-1}; δ[$(CD_3)_2SO$] 4.39 [1 H, s, PhCH (enol form only)] (Found: C, 76.95; H, 4.4. $C_{17}H_{12}O_3$ requires C, 77.25; H, 4.6%).

Similarly prepared were *4-hydroxy-2,5-bis(4-methoxyphenyl)-cyclopent-4-ene-1,3-dione* (**8b**)[6b] (12% yield), m.p. 220 °C (decomp.), $\lambda_{max.}$ 226 (ε 16 600), 269 (ε 20 000), and 360 nm (ε 11 700); $\nu_{max.}$ 3 250, 1 736, and 1 665 cm^{-1}; δ[$(CD_3)_2SO$] 3.71 and 3.77 (3 H each, s, OMe), 4.31 (1 H, s, ArCH), 6.90, and 6.98 (4 H, A_2B_2 [appears as AB] J_{ab} 9.5 Hz, ArH) and 7.02 and 8.10 (4 H, A_2B_2 [appears as AB] J_{ab} 9.5 Hz, ArH) (Found: C, 70.2; H, 4.8. $C_{19}H_{16}O_5$ requires C, 70.4; H, 5.0%): *4-hydroxy-2,5-bis(4-p-tolylcyclopent-4-ene-1,3-dione* (**8c**), recrystallised from ether and then methanol (20% yield), m.p. 199—200 °C; $\lambda_{max.}$ 242 (ε 17 900) and 334 nm (ε 13 800); $\nu_{max.}$ 1 734, 1 664, 1 622, and 1 611 cm^{-1}; $\nu_{max.}$ (CH_2Cl_2) 3 420, 1 740, 1 690, 1 640, and 1 611 cm^{-1}; δ [$(CD_3)_2CO$] 2.27 and 2.35 (3 H each, s, 2 × ArMe), 4.2 (1 H, s, ArCH), 7.10 (4 H, s, ArH), and 7.27 and 8.13 [4 H, A_2B_2 (appears as AB) J_{ab} 7.5 Hz, ArH] (Found: C, 77.7; H, 5.5. $C_{19}H_{16}O_3$ requires C, 78.1; H, 5.5%): *4-hydroxy-2,5-bis[p-(2-methylpropyl)phenyl]cyclopent-4-ene-1,3-dione* (**8d**) recrystallised from methylene chloride–ether (30% yield), m.p. 223—233 °C, $\lambda_{max.}$ 248 (ε 16 400), 280 (ε 12 600), and 348 nm (ε 11 600); $\nu_{max.}$ 3 270, 1 738, 1 670, and 1 630 cm^{-1}; δ[$(CD_3)_2SO$] 0.85 (12 H, d, *J* 6 Hz, 4 × Me), 1.85 (2 H, br m, 2 × Me_2CH), 2.41 (4 H, m, 2 × CH_2), 4.36 (1 H, s, ArCH), 7.10 (4 H, s, ArH), and 7.26 and 8.04 [4 H, A_2B_2 (appears as AB), J_{ab} 7.5 Hz, ArH]. (Found: C, 80.0; H, 7.8. $C_{25}H_{28}O_3$ requires C, 79.75; H, 7.5%).

(Z)-5-Benzylidene-4-hydroxy-3-phenylfuran-2(5H)-one[(Z)-Pulvinone]Z-(**9a**).—The trione (**8a**) (19 g) was heated at 230 °C for 30 min and the solid recrystallised from acetone to furnish (*Z*)-pulvinone *Z*-(**9a**) (14.7 g) as yellow plates, m.p. 250—251 °C (lit.,[9] 248—249 °C), $\lambda_{max.}$ 230 (ε 14 100) and 343 nm (ε 24 300); $\nu_{max.}$ 1 690 and 1 625 cm^{-1}; δ[$(CD_3)_2SO$] 6.75 (1 H, s, PhCH–C), 7.15—8.2 (10 H, ArH) (Found: C, 77.3; H, 4.3. $C_{17}H_{12}O_3$ requires C, 77.25; H, 4.6%).

In a similar way were prepared the following derivatives of (*Z*)-pulvinone: *p,p'-dimethoxy* (**9b**), m.p. 250—253 °C (lit.,[6a] m.p. 214—215 °C; lit.[6b] m.p. 230—250 °C, (decomp.), 83% yield; *p,p'-dimethyl* (**9c**), m.p. 265—266 °C, 78% yield; *p,p'-di-isobutyl* (**9d**), m.p. 255—258 °C, 59% yield.

Ethoxycarbonylmethyl Phenylacetate (**11**).—Phenylacetic acid (500 g) was added to a solution of sodium ethoxide (246 g) in ethanol (2.75 l) and the mixture was stirred at 20 °C in an atmosphere of nitrogen for 10 min. Ethyl bromoacetate (409 ml) was added and the stirred mixture was heated under reflux temperature for 4 h. The precipitated salt was filtered off and the filtrate concentrated under reduced pressure; addition of ether gave a further precipitate of salt. Filtration and evaporation of the filtrate to dryness gave ethoxycarbonylmethyl phenylacetate (**11**) as an oil (774 g); δ 1.21 (3 H, t, *J* 7 Hz, OCH_2CH_3), 3.69 (2 H, s, $PhCH_2CO$), 4.16 (2 H, q, *J* 7 Hz, OCH_2CH_3), 4.58 (2 H, s, OCH_2CO) and 7.29 (5 H, s, ArH).

* For details of the Supplementary publications scheme, see Instructions for Authors (1985), *J. Chem. Soc., Perkin Trans 1*, 1985, Issue 1.

4-*Hydroxy*-3-*phenylfuran*-2(5H)-*one* (**12**).—*Method A*. The foregoing oil (**11**) 773 g) was added to a solution of potassium t-butoxide (394 g) in t-butyl alcohol (3.5 l) and the mixture was stirred at reflux temperature for 1 h. Water (7 l) was added and the solution was extracted with ether (2 × 1.5 l). The aqueous phase was acidified with hydrochloric acid (2M) to give a solid precipitate (446 g), m.p. 253—260 °C. Recrystallisation from ethanol furnished an analytical sample of the *furan*-2(5H)-*one* (**12**) as needles, m.p. 259—263 °C (lit.,[11] m.p. 254 °C), $\lambda_{max.}$ 262 (ε 18 500) and 274 nm (ε 17 850); $\nu_{max.}$ 3 300—2 000, 1 695, and 1 595 cm^{-1}; δ[$(CD_3)_2SO$] 4.73 (2 H, s, CH_2) and 7.10—8.15 (5 H, ArH) (Found: C, 68.0; H, 4.4. $C_{10}H_8O_3$ requires C, 68.2; H, 4.6%).

In a similar manner were prepared the following substituted 4-*hydroxy*-3-*phenylfuran*-2(5H)-*ones* (yields are overall from the phenylacetic acid): *o*-Cl, m.p. 195—197 °C, 35%; *m*-Cl, m.p. 168—178 °C, 76%; *p*-Cl, m.p. 279—283 °C, 52%; *o*-F, m.p. 198—>200 °C, 64%; *m*-F, m.p. 265—267 °C (decomp.), 52%; *p*-F, m.p. 200 °C (decomp.), 55%; *o*-OMe, m.p. 158—159 °C, 47%; *m*-OMe, m.p. 179—181 °C, 52%; *p*-OMe, m.p. 228—229 °C, 67%; *p*-Br, m.p. >200 °C (decomp.), 53%; *m*, *p*-Cl_2, m.p. 247—250 °C, 74%; *p*-Ph, m.p. >240 °C, 68%; *o*, *m*-benzo, m.p. 160—200 °C (decomp.), 54%; *p*-Me, m.p. 241—248 °C, 57%. All compounds gave satisfactory elemental analysis.

Method B. Sodium (0.11 g) was added to ethanol (20 ml) and the inner salt (**15**) (2 g) was added to the stirred solution. After 10 min, the suspension was acidified (2 M-HCl; 5 ml) and the mixture partitioned between water and ethyl acetate. The unchanged starting material (0.48 g) was filtered off, the organic phase was washed thrice with sodium hydroxide solution (1M) and the combined extracts were acidified with hydrochloric acid (2M). The precipitated pale yellow solid (0.31 g) was identical (^{1}H n.m.r.) with the sample of 4-hydroxy-3-phenylfuran-2(5*H*)-one (**12**) prepared previously.

The ethyl acetate fraction was evaporated to dryness to give a solid (0.39 g) which was shown to be mainly triphenylphosphine oxide by comparison (i.r.) with an authentic sample.

When the above reaction time was extended to 20 h in a sealed system, the diethyl ether content of the resulting solution was 0.2 (v/v) [theoretical value *ca.* 2% v/v; g.l.c.]. This reaction yielded the furan-2(5*H*)-one (**12**) in 57% yield.

4-*Methoxy*-3-*phenylfuran*-2(5H)-*one* (**13**).—4-Hydroxy-3-phenylfuran-2(5*H*)-one (**12**) (446 g) was added to a mixture of dimethyl sulphate (450 ml) and potassium carbonate (223 g) in acetone (2.8 l) and the mixture was heated under reflux with stirring in an atmosphere of nitrogen for 1 h. The mixture was cooled, filtered, and the filtrate evaporated to dryness under reduced pressure. The residue was dissolved in methylene chloride and the solution passed through a short column of silica. Elution with methylene chloride and recrystallisation of the major fraction from methylene chloride—ether afforded the methyl ether (**13**) (424 g) as needles, m.p. 122—124 °C (lit.,[8a] m.p. 124—124.5 °C), $\nu_{max.}$ 1 735 and 1 636 cm^{-1}; $\nu_{max.}$ (CH_2Cl_2) 1 756 and 1 660 cm^{-1}; δ 3.84 (3 H, s, OMe), 4.73 (2 H, s, CH_2) and 7.20—8.10 (5 H, ArH) (Found: C, 69.2; H, 5.4. $C_{11}H_{10}O_3$ requires C, 69.45; H, 5.3%).

In a similar manner were prepared the following substituted 4-*methoxy*-3-*phenylfuran*-2(5H)-*ones*: *o*-Cl, m.p. 97.5—98.5 °C, 84%; *m*-Cl, m.p. 123—125 °C, 78%; *p*-Cl, 86—88 °C, 78%; *o*-F, 58—59 °C, 84%; *m*-F, 133—135 °C, 85%; *p*-F, 128—130 °C, 88%; *o*-OMe, 107—108 °C, 98%; *m*-OMe, 117—120 °C, 64%; *p*-OMe, 110—115 °C, 78%; *p*-Br, 113—114 °C, 73%; *m*,*p*-Cl_2, 141—143 °C, 75%; *p*-Ph, 146—148 °C, 82%; *o*,*m*-benzo, 158—162 °C, 77%; *p*-Me, 121—122 °C, 90%. All compounds gave satisfactory elemental analysis.

5-*Bromo*-4-*methoxy*-3-*phenylfuran*-2(5H)-*one* (**14**).—To a solution of 4-methoxy-3-phenylfuran-2(5*H*)-one (**13**) (422 g) in boiling 1,2-dichloroethane (3.5 l) was added azoisobutyronitrile (12 g) and *N*-bromosuccinimide (422 g) in portions over 2 h. The solvent was removed under reduced pressure and the residue was shaken with water. After decantation, the residual solid was dissolved in methylene chloride and the solution was washed with water and dried over sodium sulphate. Passage through a column of silica and recrystallisation from ether–light petroleum (b.p. 40—60 °C) gave the 5-*bromo*-O-*methyl ether* (**14**) (513 g) as rhombic needles, m.p. 63—65 °C, $\nu_{max.}$ 1 765 and 1 639 cm^{-1}; $\nu_{max.}$ (CH_2Cl_2) 1 778, 1 660, and 1 645 cm^{-1}; δ 4.0 (3 H, s, OMe) 6.81 (1 H, s, CHBr), and 7.20—8.00 (5 H, ArH) (Found: C, 49.2; H, 3.4. $C_{11}H_9BrO_3$ requires C, 49.1; 3.4%).

In a similar manner were prepared the following substituted 5-*bromo*-4-*methoxy*-3-*phenylfuran*-2(5H)-*ones*: *o*-Cl, gum, 98%; *m*-Cl, 89—90 °C, 90%; *p*-Cl, 99—100 °C, 90%; *o*-F, oil, 98%; *m*-F, 75—76 °C, 86%; *p*-F, 87—88 °C, 83%; *o*-OMe, 98—99 °C, 81%; *m*-OMe, gum, 94%; *p*-OMe, 139—140 °C, 76%; *p*-Br, 125—128 °C, 90%; *m*,*p*-Cl_2, 123—125 °C, 78%; *p*-Ph, 103—105 °C, 91%; *o*,*m*-benzo, gum, 95%.

2,5-*Dihydro*-2-*oxo*-3-*phenyl*-5-*triphenylphosphoniofuran*-4-*olate* (**15**).—To a stirred, boiling solution of 5-bromo-4-methoxy-3-phenylfuran-2(5*H*)-one (**14**) (50 g) in benzene (150 ml) under nitrogen was added dropwise a solution of triphenylphosphine (60 g) in benzene (200 ml) and the mixture was maintained under reflux for 2 h. The condensate in a cold trap (−40 °C) was identified as methyl bromide [b.p. 4 °C, δ (CCl_4) 2.59(s)]. The reaction mixture was cooled and the colourless precipitated solid (74 g) was shown to contain *ca.* 8% of methyltriphenylphosphonium bromide (^{1}H n.m.r.). A suspension of this solid in a mixture of methylene chloride (150 ml) and n-hexane (75 ml) was stirred for 1 h at ambient temperature. After filtration, the residue was dried under reduced pressure to give the *Wittig salt* (**15**) (65.3 g), m.p. >280 °C (decomp.), $\lambda_{max.}$ (CH_2Cl_2) 268 nm (ε 19 200); $\nu_{max.}$ 1 726 and 1 600 cm^{-1}; ν (CH_2Cl_2) 1 726 and 1 602 cm^{-1}; δ[$(CD_3)_2SO$] (Varian XL-100) 6.72—7.20 and 7.60—8.05 (5-H and ArH); δ_C [$(CD_3)_2SO$] 181.6 (C-2 or C-4, J_{CP} 2 Hz), 173.8 (C-2 or C-4, J_{CP} 4 Hz), 88.2 (C-3, J_{CP} 1 Hz) and 71.8 (C-5, J_{CP} 55 Hz, J_{CH} 162 Hz). δ_p [$CDCl_3$] + 22.1 (*o*-H_3PO_4 as reference) (Found: C, 77.2; H, 5.0; P, 6.95. $C_{28}H_{21}O_3P$ requires C, 77.05; H, 4.85; P, 7.1%).

Preparation of (Z)- *and* (E)-*Pulvinones* Z-(**9a**) *and* E-(**9a**) *from the Wittig Salt* (**15**).—To a solution of benzaldehyde (7.2 ml) and sodium ethoxide (4.24 g) in ethanol (240 ml) was added the foregoing Wittig salt (**15**) (24.8 g) and the mixture was stirred in an atmosphere of nitrogen at ambient temperature for 1.5 h. Water (400 ml) was added and the mixture was extracted with toluene (800 ml). The organic phase was extracted with water (200 ml) and the combined aqueous fractions were acidified with hydrochloric acid (5M). The precipitate was washed with water to neutrality and dried under reduced pressure to afford a yellow solid (**A**) (13.96 g) [mixture *ca.* 3:2 by n.m.r.)]. A suspension of this mixture (**A**) (5 g) in benzene (50 ml) was stirred for 1 h at ambient temperature and the phases separated by filtration. The solid phase was recrystallised from methanol to give (*Z*)-pulvinone *Z*-(**9a**) (2.8 g) as yellow plates, m.p. 249—250 °C, identical with the sample prepared previously. The filtrate was extracted with sodium hydroxide (0.5 M; 3 × 50 ml) and the aqueous extracts were combined and acidified with hydrochloric acid (5M) to give a yellow precipitate (1.7 g) [a mixture of (*Z*)- and (*E*)-pulvinones (20:80) by n.m.r.]. This was recrystallised from acetone to give a further amount (160 mg) of the *Z*-isomer, m.p. 250—251 °C. The mother liquor was evaporated to dryness, and the residue dissolved in methylene chloride–methanol (95:5; 10 ml) and chromatographed on

silica using methylene chloride as eluant to give the E-*isomer* *E*-(**9a**) (1.16 g), m.p. 183—187 °C. The analytical sample was prepared by crystallisation from methylene chloride as yellow plates, m.p. 185—187 °C, $\lambda_{max.}$ 230 (ε 14 700) and 304 nm (ε 22 100); $\nu_{max.}$ 1 707, 1 612, and 1 592 cm^{-1}; δ [$(CD_3)_2SO$] (Varian XL-100) 6.80 (1 H, s, PhCH=C) and 7.20—7.90 (10 H, ArH) (Found: C, 77.3; H, 4.7. $C_{17}H_{12}O_3$ requires C, 77.3; H, 4.6%).

Conversion of a Mixture of (Z)- *and* (E)-*pulvinones solely into the Z-Isomer.*—The remainder (8.25 g) of the solid (**A**) was treated with acetic anhydride and pyridine (1:1) (8 ml) at ambient temperature for 24 h. The mixture was poured into methanol (20 ml) containing aqueous sodium hydroxide solution (4M; 8 ml). After 30 min at 5 °C, the solution was neutralised with hydrochloric acid (0.5M) to give a yellow precipitate (6.46 g) which was recrystallised from methanol to give the (*Z*)-pulvinone *Z*-(**9a**) (6.01 g), m.p. 250—251 °C, identical with the sample prepared previously.

(Z)-4-*Acetoxy*-5-*benzylidene*-3-*phenylfuran*-2[(5H)-*one* (**18**).—To a solution of (*Z*)-pulvinone (1.5 g) in pyridine (10 ml) was added acetic anhydride (5 ml) and the mixture was set aside for 16 h. The solution was poured into water (75 ml) at 0 °C and the precipitated solid was filtered off, dried under reduced pressure and recrystallised from ethyl acetate to furnish the (Z)-*acetate* (**18**) (1.5 g) as yellow needles, m.p. 138—140 °C, $\lambda_{max.}$ 225 (ε 11 400) and 347 nm (ε 28 700); $\nu_{max.}$ 1 785 and 1 765 cm^{-1}; δ 2.35 (3 H, s, MeCO), 6.04 (1 H, s, ArCH=C) and 7.20—7.90 (10 H, ArH) (Found: C, 74.5; H, 4.5. $C_{19}H_{14}O_4$ requires C, 74.45; H, 4.5%).

(E)-4-*Acetoxy*-5-*benzylidene*-3-*phenylfuran*-2(5H)-*one* (**19**).—The crude acetate (**19**) was obtained from (*E*)-pulvinone *E*-(**9a**) in the same way as the foregoing (*Z*)-pulvinone acetate. For n.m.r. data, see Table 1. Similarly prepared were the acetates described in Tables 1 and 2.

4-*Hydroxy*-5-*methylene*-3-*phenylfuran*-2(5H)-*one* (**20**).—To a solution of sodium ethoxide [from Na (0.22 g) and ethanol (50 ml)] was added paraformaldehyde (0.56 g). The Wittig salt (**15**) (5 g) was added and the mixture was stirred at ambient temperature for 0.5 h. The mixture was diluted with water (50 ml) and then filtered through Dicalite. The filtrate was extracted with ether (2 × 50 ml) and the aqueous phase was acidified with hydrochloric acid (2M). Recrystallisation of the precipitated solid from ether gave the *furan*-2(5H)-*one* (**20**) (1.18 g), m.p. 150 °C (decomp.), $\lambda_{max.}$ 256 (ε 15 500) and 322 nm (ε 8 140); $\nu_{max.}$ 1 710, 1 662, 1 630, 1 596, and 1 500 cm^{-1}; δ ($CDCl_3$–CD_3OD) 5.10 and 5.26 (2 H, AB, *J* 3.5 Hz, CH_2=), and 7.00—8.05 (5H, ArH) (Found: C, 70.25; H, 4.35. $C_{11}H_8O_3$ requires C, 70.2; H, 4.3%).

4-*Acetoxy*-5-*methylene*-2-*phenylfuran*-2(5H)-*one* (**21**).—The enol (**20**) (50 mg) was dissolved in pyridine–acetic anhydride (1:1; 0.2 ml) and the mixture set aside for 1.5 h at 0 °C. Isolation through ether in the usual manner gave the crude acetate (**21**) as an oil; δ 2.34 (3 H, s, MeCO), 4.93 and 5.23 (2 H, AB, *J* 4 Hz, CH_2=) and 7.20—7.90 (5 H, ArH).

5-*Diphenylmethylene*-4-*hydroxy*-3-*phenylfuran*-2(5H)-*one* (**22**).—Sodium hydride (1.12 g) was added to a mixture of t-pentyl alcohol (2.5 ml) in ether (100 ml). After 10 min, thiobenzophenone (10 g) and the inner salt (**15**) (10 g) were added and the mixture was heated under reflux with stirring in an atmosphere of nitrogen for 4 h. Ether was removed by distillation under reduced pressure and hydrochloric acid (2M, 50 ml) was added. The mixture was extracted with ethyl acetate (3 × 50 ml) and the organic phase was extracted with aqueous sodium hydroxide (1M, 3 × 25 ml). The combined aqueous extracts were extracted with toluene (2 × 50 ml). With time, the sodium salt of the diphenylmethylene derivative crystallised from the aqueous phase. This was filtered off, stirred with hydrochloric acid (2M) and the precipitated solid filtered off and dried. Recrystallisation from methanol followed by trituration with ether furnished the *furan*-2(5H)-*one* (**22**) (1.55 g) as plates, m.p. 166—168 °C, $\lambda_{max.}$ 304 nm (ε 20 100); $\nu_{max.}$ 1 705 cm^{-1} (Found: C, 81.1; H, 4.75. $C_{23}H_{16}O_3$ requires C, 81.15; H, 4.75%).

4-*Acetoxy*-5-*diphenylmethylene*-3-*phenylfuran*-2(5H)-*one* (**23**).—The dihydrofuranone (**22**) (60 mg) was treated with pyridine (0.2 ml) and acetic anhydride (0.2 ml). Isolation in the usual way gave the *enol acetate* (**23**) as yellow needles, m.p. 184—186 °C, $\lambda_{max.}$ 230 (ε 14 400), 242 (ε 13 900), and 360 nm (ε 32 600); $\nu_{max.}$ 1 785, 1 760, and 1 609 cm^{-1}; δ (Varian XL-100) 1.48 (3 H, s, MeCO) and 7.20—7.80 (15 H, ArH) (Found: C, 78.6; H, 4.7. $C_{25}H_{18}O_4$ requires C, 78.5; H, 4.7%).

(±)-5-*Benzyl*-4-*hydroxy*-3-*phenylfuran*-2(5H)-*one* (**31**).—A mixture of phenylacetic acid (68 g) and potassium t-pentoxide (62.9 g) in t-pentyl alcohol (1 l) was stirred at 20 °C for 20 min. Ethyl 2-bromo-3-phenyl-propionate (**28**)[15] (122 g) was added and the reaction mixture stirred under reflux for 8 days. t-Pentyl alcohol (500 ml) was removed under reduced pressure and the precipitated potassium bromide was filtered off. Ether (500 ml) was added and a further quantity of precipitated salt removed. The solvent was removed under reduced pressure to furnish the crude diester (**30**) (150 g) as an oil. This was added to a solution of potassium t-butoxide (55.9 g) in t-butyl alcohol (1 l) and the reaction mixture boiled for 2 h. The mixture was cooled and water (2 l) was added. The mixture was adjusted to pH 10 with aqueous sodium carbonate (5%) and then extracted with ether. The ether phase was back extracted with aqueous sodium carbonate (1%) and the combined aqueous fractions were acidified with hydrochloric acid (5M) to afford a pale yellow solid (79 g). Trituration with ether and recrystallisation from acetone afforded the furan-2(5*H*)-one (**31**) (67 g) as colourless prisms, m.p. 222—224 °C (lit.,[16] m.p. 220—221 °C), $\lambda_{max.}$ 262 (ε 17 750) and 274 nm (ε 16 500); $\nu_{max.}$ 1 690 cm^{-1}; δ [$(CD_3)_2SO$] 2.96, 3.39, and 5.14 (3 H, ABX, J_{ab} 15, J_{ax} 7, J_{bx} 3 Hz, Ph, CH_2CH) and 7.20—7.90 (10 H, ArH) (Found: C, 76.85; H, 5.2. $C_{17}H_{14}O_3$ requires C, 76.7; H, 5.3%).

(±)-5-*Benzyl*-4-*methoxy*-3-*phenylfuran*-2(5H)-*one* (**32**).—A mixture of 4-hydroxyfuran-2(5*H*)-one (**31**) (5 g), potassium carbonate (2.5 g) and dimethylsulphate (5 ml) in acetone (50 ml) was stirred under reflux in an atmosphere of nitrogen for 1 h. The mixture was cooled and filtered, the filtrate was evaporated to dryness under reduced pressure and the residue was chromatographed on silica. Elution with toluene–ethyl acetate (9:1) afforded an oil. Crystallisation from ether gave the *furan*-2(5H)-*one* (**32**) (4.1 g) as colourless needles, m.p. 83—84 °C, $\nu_{max.}$ 1 760 and 1 655 cm^{-1}; δ 2.98, 3.28, and 4.99 (3 H, ABX, J_{ab} 13, J_{ax} 5, and J_{bx} 4 Hz, $PhCH_2CH$), 3.64 (3 H, s, OMe) and 7.00—7.40 (10 H, ArH) (Found: C, 77.3; H, 5.7. $C_{18}H_{16}O_3$ requires C, 77.1; H, 5.75%).

Conversion of (±)-5-*Benzyl*-4-*methoxy*-3-*phenylfuran*-2(5H)-*one* (**32**) *into* (Z)-*Pulvinone* Z-(**9a**).—To a boiling solution of the foregoing 4-methoxyfuran-2(5*H*)-one (**32**) (5 g) in 1,2-dichloroethane (50 ml) was added azoisobutyronitrile (300 mg) and *N*-bromosuccinimide (3.17 g) in portions and concurrently over 2 h. The solvent was removed under reduced pressure and the residue extracted with water. The water was decanted and the residue dissolved in methylene chloride. The organic phase was

dried (Na_2SO_4) and evaporated under reduced pressure to give a colourless gum (6.2 g). This was dissolved in dimethylformamide (10 ml) and added to a stirred suspension of calcium carbonate (5 g) and lithium bromide (2.5 g) in boiling dimethylformamide (50 ml). The reaction mixture was boiled for 30 min then poured into hydrochloric acid (2M, 200 ml). The precipitated solid was filtered off, dried and recrystallised from acetone to give (*Z*)-pulvinone *Z*-(**9a**) (3.1 g) as yellow plates, m.p. 251—252 °C, identical with the sample prepared previously.

(Z)- *or* (E)-5-*Ethylidene*-4-*hydroxy*-3-*phenylfuran*-2(5H)-*one* (**33**).—To a solution of freshly prepared sodium ethoxide [Na (0.44 g); ethanol (100 ml)] was added the Wittig salt (**15**) (10 g) and acetaldehyde (4.25 ml). After 1 h, the mixture was concentrated under reduced pressure, diluted with water and extracted with toluene. The aqueous phase was acidified with hydrochloric acid (2M) and the mixture was extracted with ethyl acetate. The organic phase was washed with aqueous sodium hydrogen carbonate (5%) and then with aqueous sodium hydroxide solution (1M). The latter extract was acidified with hydrochloric acid (2M) and the precipitated solid (2.8 g) was filtered off, recrystallised from aqueous methanol and then chromatographed on silica. Recrystallisation of the major fraction from ether afforded (Z)- or (E)-5-*ethylidene*-4-*hydroxy*-3-*phenylfuran*-2(5H)-*one* (**33**) (760 mg) as plates, m.p. 183—185 °C, $\lambda_{max.}$ 261 (ε 19 300) and 320 nm (ε 11 000); $\nu_{max.}$ 1 700, 1 672, and 1 625 cm^{-1}; δ [(CD_3OD (1 drop) + $CDCl_3$] 1.86 (3 H, d, *J* 7 Hz, CH_3CH=), 5.66 (1 H, q, *J* 7 Hz, CH_3CH=) and 7.20—7.90 (5 H, ArH) (Found: C, 71.4; H, 5.0. $C_{12}H_{10}O_3$ requires C, 71.3; H, 5.0%).

4-*Hydroxy*-5-(1-*isopropylidene*)-3-*phenylfuran*-2(5H)-*one* (**34**).—Ethanol (1.1 ml) was added to a stirred suspension of sodium hydride (0.56 g) in ether (100 ml) under nitrogen. When the evolution of hydrogen had ceased, acetone (4 ml) and the Wittig salt (**15**) (10 g) were added and the reaction set aside for 6 days. Water was added and the aqueous phase was extracted with ether, filtered, acidified with hydrochloric acid (2M) and then extracted with ethyl acetate. The organic phase was dried (Na_2SO_4) and the solvent removed under reduced pressure to afford a solid which was dissolved in methylene chloride–methanol (99:1). The mixture was chromatographed on silica and the major product recrystallised from acetone to afford the *furan*-2(5H)-*one* (**34**) (735 mg) as needles, m.p. 180—182 °C, $\lambda_{max.}$ 268 (ε 26 500) and 306 nm (ε 17 200); $\nu_{max.}$ 1 695 cm^{-1}; δ [$CDCl_3$ + CD_3OD (2 drops)] 1.95 and 2.14 [3 H each, s, Me_2C=] and 7.10—7.60 (5 H, ArH) (Found: 72.15; H, 5.5. $C_{13}H_{12}O_3$ requires C, 72.2; H, 5.6%).

(Z)-5-*Benzylidene*-4-*methoxy*-3-*phenylfuran*-2(5H)-*one* (**36**).—A mixture of the (*Z*)-pulvinone *Z*-(**9a**) (500 mg), potassium carbonate (500 mg) and dimethyl sulphate (0.5 ml) in acetone (10 ml) was stirred under reflux in an atmosphere of nitrogen for 1 h. The reaction mixture was cooled and filtered and the residue was evaporated to dryness under reduced pressure. The residue was dissolved in methylene chloride and passed through a short column of silica. Recrystallisation from acetone–hexane gave the methyl ether (**36**) as yellow needles, m.p. 104—105 °C (lit.[17] m.p. 104—105 °C), $\lambda_{max.}$ 328 nm (ε 31 600); $\nu_{max.}$ 1 760, 1 628, and 1 598 cm^{-1}; $\nu_{max.}$ (CH_2Cl_2), 1 765, 1 630, and 1 598 cm^{-1}; δ 3.77 (3 H, s, OMe), 6.26 (1 H, s, PhCH=), and 7.10—8.00 (10 H, ArH) (Found: C, 77.7; H, 5.15. $C_{18}H_{14}O_3$ requires C, 77.7; H, 5.05%).

Cleavage of (Z)-*Pulvinone Methyl Ether* (**36**).—The foregoing ether (**36**) (20 mg) and lithium bromide (6 mg) in dimethylformamide (0.4 ml) were heated at 150 °C for 2 min. The yellow solution was cooled and hydrochloric acid (2M; 1 ml) was added. The precipitated solid (14 mg) was filtered off and shown to be identical in all respects with (*Z*)-pulvinone.

(Z)- *or* (E)-4-*Hydroxy*-3-*phenyl*-5-(3-*phenylprop*-2-*enylidene*)*furan*-2(5H)-*one* (**35**).—To a stirred solution of freshly prepared sodium ethoxide [Na (0.56 g); ethanol (100 ml)] was added the Wittig salt (**15**) (10 g) and cinnamaldehyde (3.03 ml); the mixture was then then stirred for 1 h under an atmosphere of nitrogen. Hydrochloric acid (2M) was added and the precipitated solid (4.5 g) filtered off and then stirred as a suspension in benzene (10 ml). The residual solid (3.6 g) was recrystallised from methylene chloride–methanol to afford the *furan*-2(5H)-*one* (**35**) (2.2 g) as yellow plates, m.p. 245—247 °C, $\lambda_{max.}$ 337 (ε 39 600) and 353 nm (ε 35 900); $\nu_{max.}$ 1 693, 1 622, 1 605, and 1 595 cm^{-1} (Found: C, 78.8; H, 4.7. $C_{19}H_{14}O_3$ requires C, 78.6; H, 4.85%).

Ethoxycarbonylmethyl Ethyl Malonate (**39**).—Ethyl bromoacetate (140 ml) was added to a suspension of ethyl potassium malonate (**38**)[18] (140 g) in ethanol (1.4 l) and the mixture was stirred under reflux in an atmosphere of nitrogen for 3 h. After cooling, the precipitated solid was filtered off and the filtrate concentrated to one tenth of the volume. Ether (100 ml) was added and the precipitate removed by filtration. Removal of the solvent under reduced pressure afforded the *malonate* (**39**) (160 g) as a colourless oil. Distillation of an aliquot afforded an analytical sample, b.p. 140 °C at 0.5 mmHg; $\nu_{max.}$(film) 1 759 and 1 739 cm^{-1}; δ 1.30 (6 H, t, *J* 7 Hz, OCH_2CH_3), 3.49 (2 H, s, $EtO_2C{\cdot}CH_2CO$), 4.26 (4 H, q, *J* 7 Hz, OCH_2CH_3), and 4.69 (2 H, s, $EtO_2C{\cdot}CH_2O$) (Found: C, 49.35; H, 6.3. $C_9H_{14}O_6$ requires C, 49.55; H, 6.45%).

3-*Ethoxycarbonyl*-4-*hydroxyfuran*-2(5H)-*one* (**41**).—The foregoing malonate (**39**) (128 g) was added to a solution of potassium t-butoxide (66 g) in t-butyl alcohol (1.2 l) at 40 °C and the reaction mixture was stirred at reflux temperature for 1.5 h. The mixture was cooled and the precipitated solid was filtered off and dried to afford the furan-2(5*H*)-one potassium salt (**40**) (109 g) as a colourless solid; δ (D_2O) 1.28 (3 H, t, *J* 7 Hz, OCH_2CH_3), 4.21 (2 H, q, *J* 7 Hz, OCH_2CH_3), and 4.38 (2 H, s, 5-H_2).

A sample (400 mg) of the above salt (**40**) was treated with hydrogen chloride in ethanol for *ca.* 30 s. The solid was filtered off and the filtrate evaporated to dryness under reduced pressure. Benzene (20 ml) was added and the mixture was filtered. Removal of the solvent under reduced pressure and recrystallisation of the residue from water afforded the free furanone (**41**) (260 mg) as needles, m.p. 113—117 °C [lit.,[19] m.p. 75—77 °C (hydrated), 124—125 °C (anhydrous)], $\lambda_{max.}$ 247 nm (ε 14 150); $\nu_{max.}$ (CH_2Cl_2) 3 400—2 600, 1 778, 1 665, and 1 636 cm^{-1}; δ 1.32 (3 H, t, *J* 7 Hz, OCH_2CH_3), 4.36 (2 H, q, *J* 7 Hz, OCH_2Me), and 4.71 (2 H, s, 5-H_2) (Found: C, 48.55; H, 4.75. $C_7H_8O_5$ requires C, 48.85; H, 4.7%.

3-*Ethoxycarbonyl*-4-*methoxyfuran*-2(5H)-*one* (**42**).—To a suspension of the foregoing potassium salt (**40**) (105 g) in acetone (1 l) was added dimethyl sulphate (100 ml) and the reaction mixture stirred under reflux in an atmosphere of nitrogen for 16 h. The cooled reaction mixture was filtered and the filtrate evaporated to dryness under reduced pressure. The residual oil in methylene chloride was passed through a short column of silica. Recrystallisation from methylene chloride–methanol gave the *methyl ether* (**42**) (42 g) as needles, m.p. 96—99 °C, $\lambda_{max.}$ 237 nm (ε 13 250); $\nu_{max.}$ 1 770, 1 699, and 1 610 cm^{-1}. δ 1.31 (3 H, t, *J* 7 Hz, OCH_2CH_3), 4.11 (3 H, s, OMe), 4.27 (2 H, q, *J* 7 Hz, OCH_2Me), and 4.77 (2 H, s, 5-H_2) (Found: C, 51.75; H, 5.7. $C_8H_{10}O_5$ requires C, 51.6; H, 5.4%).

5-*Bromo*-3-*ethoxycarbonyl*-4-*methoxyfuran*-2(5H)-*one* (**43**).—To a solution of the foregoing 3-ethoxycarbonyl-4-methoxyfuran-2(5*H*)-one (**42**) (42 g) in boiling 1,2-dichloroethane (400 ml) was added azoisobutyronitrile (1.5 g) and *N*-bromosuccinimide (44.5 g) in portions over 0.5 h. The solvent was removed under reduced pressure and the residue shaken with water. The residual solid was then dissolved in methylene chloride and the solution was washed with water and dried (Na_2SO_4). Chromatography on silica afforded a solid which was recrystallised from ether to give the *furanone* (**43**) (24.7 g) as prisms, m.p. 63—65 °C, $\nu_{max.}$ 1 793, 1 698, and 1 620 cm^{-1}; $\nu_{max.}$ (CH_2Cl_2) 1 810, 1 793, 1 720, and 1 638 cm^{-1}; δ 1.34 (3 H, t, *J* 7.5 Hz, OCH_2CH_3), 4.23 (3 H, s, OMe), 4.29 (2 H, q, *J* 7.5 Hz, OCH_2Me), and 6.67 (1 H, s, 5-H) (Found: C, 36.25; H, 3.4; Br, 30.15. $C_8H_9BrO_5$ requires C, 36.5; H, 3.45; Br, 29.9%).

(Z)-5-*Benzylidene*-3-*ethoxycarbonyl*-4-*hydroxyfuran*-2(5H)-*one* Z-(**44**) *and the corresponding* E-*isomer* E-(**44**).—A stirred mixture of 5-bromo-3-ethoxycarbonyl-4-methoxyfuran-2(5*H*)-one (**43**) (23 g) and triphenylphosphine (23 g) in benzene (200 ml) was heated under reflux in an atmosphere of nitrogen for 2 h. The mixture was cooled and filtered to give the Wittig salt (30 g) as a dark grey solid. This was added to a solution of sodium ethoxide (3.85 g) and benzaldehyde (6.1 g) in ethanol (250 ml) and the mixture stirred at 20 °C for 1 h in an atmosphere of nitrogen. Hydrochloric acid (2M; 250 ml) was added and the precipitated two-component mixture (1:1 by n.m.r.) (10 g) was filtered off. Fractional recrystallisation from methylene chloride–ethanol afforded firstly the (*Z*)-furanone *Z*-(**44**) (1.2 g) as plates, m.p. 195—198 °C (decomp.) (lit.,[16] m.p. 196 °C), $\lambda_{max.}$ 306 nm (ε 28 600); $\nu_{max.}$ 3 200, 1 780, 1 669, 1 650, and 1 603 cm^{-1}; δ [$(CD_3)_2SO$] 1.26 (3 H, t, *J* 7 Hz, OCH_2CH_3), 4.20 (2 H, q, *J* 7 Hz, OCH_2Me), 6.58 (1 H, s, PhCH=), and 7.25—8.00 (5 H, ArH) (Found: C, 64.6; H, 4.6. $C_{14}H_{12}O_5$ requires C, 64.6; H, 4.65%), and then the E-*isomer* *E*-(**44**) (550 mg), m.p. 180—186 °C (decomp.), $\lambda_{max.}$ 308 nm (ε 26 000); $\nu_{max.}$ 3 170, 1 775, 1 664, 1 639, and 1 600 cm^{-1}; δ[$(CD_3)_2SO$] 1.20 (3 H, t, *J* 7 Hz, OCH_2CH_3), 4.14 (2 H, q *J* 7 Hz, O CH_2Me), 6.74 (1 H, s, PhCH=), and 7.10—8.00 (5 H, ArH) (Found: C, 64.4; H, 4.8. $C_{14}H_{12}O_5$ requires C, 64.6; H, 4.65%). Yields of these isomers [E-(**44**) and Z-(**44**)] could have been increased by adding the triphenylphosphine in benzene dropwise to the stirred boiling solution of the bromo compound (**43**) in benzene and by isolating the inner salt in the pure state by washing out the methyltriphenylphosphonium bromide [see preparation of the inner salt (**15**)].

(Z)-5-*Benzylidene*-4-*hydroxyfuran*-2(5H)-*one* (**37**).—A suspension of the foregoing (*Z*)-furan-2(5*H*)-one *Z*-(**44**) (1.1 g) in aqueous sodium hydroxide (0.5M; 200 ml) was stirred for 30 min at ambient temperature. The resultant solution was set aside for 2 days, acidified with hydrochloric acid (5M) and then extracted thrice with ether. The combined organic phases were washed with brine and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residual solid (880 mg) was recrystallised from benzene to give *Z*-5-benzylidene-4-hydroxyfuran-2(5*H*)-one (**37**) (512 mg), m.p. 167—171 °C (lit.,[20] m.p. 165 °C), $\lambda_{max.}$ 306 nm (ε 26 600); $\nu_{max.}$ 1 716 cm^{-1}; δ [$(CD_3)_2CO$] 5.21 (1 H, s, 3-H), 6.29 (1 H, s, PhCH=), and 7.10—8.00 (5 H, ArH) (Found: C, 70.1; H, 4.35. $C_{11}H_8O_3$ requires C, 70.2; H, 4.3%).

(Z)-5-*Benzylidene*-4-*isobutyryloxy*-3-*phenylfuran*-2(5H)-*one* (**45**).—Isobutyric anhydride (12 ml) was added to a solution of (*Z*)-pulvinone *Z*-(**9a**) (3 g) in pyridine (12 ml) and the mixture set aside for 24 h. The mixture was poured into water (100 ml) at 0 °C and the precipitated solid was filtered off, dried, redissolved in methylene chloride and the solution passed through a short column of silica. Elution with methylene chloride furnished the major component (t.l.c.) which was recrystallised from methylene chloride–methanol to give the *isobutyryloxy ester* (**45**) (2.8 g) as yellow needles, m.p. 128—129 °C; $\lambda_{max.}$ 340 nm (ε 25 000); $\nu_{max.}$ 1 768, 1 658, and 1 640 cm^{-1}; δ 1.38 [6 H, d, *J* 7 Hz, Me_2CH], 2.87 [1 H, sept, *J* 7 Hz, $(Me)_2CH$], 5.98 (1 H, s, PhCH=C), and 7.20—8.00 (10 H, ArH) (Found: C, 75.25; H, 5.45. $C_{21}H_{18}O_4$ requires C, 75.45; H, 5.45%).

(Z)-5-*Benzylidene*-3-*phenyl*-4-*pivaloyloxyfuran*-2(5H)-*one* (**46**).—(*Z*)-Pulvinone *Z*-(**9a**) (2.5 g) was added to a solution of pivaloyl chloride (2.4 ml) in pyridine (12 ml) and the mixture set aside for 24 h at ambient temperature. Isolation and recrystallisation by the procedures described above furnished the *pivalate* (**46**) (2.6 g) as yellow needles, m.p. 173—174.5 °C; $\lambda_{max.}$ 338 nm (ε 25 900); $\nu_{max.}$ 1 773, 1 654, and 1 631 cm^{-1}; $\nu_{max.}$ (CH_2Cl_2) 1 783 cm^{-1}; δ 1.38 [9 H, s, Me_3C], 5.93 (1 H, s, PhCH=C), and 7.20—8.00 (10 H, ArH) (Found: C, 75.65; H, 5.65. $C_{22}H_{20}O_4$ requires C, 75.85; H, 5.8%).

(Z)-4-*Benzoyloxy*-5-*benzylidene*-3-*phenylfuran*-2(5H)-*one* (**47**).—Benzoyl chloride (2 ml) was added dropwise to a solution of (*Z*)-pulvinone *Z*-(**9a**) (2 g) in pyridine (10 ml) at 5 °C and the mixture was set aside for 20 h. Isolation by the procedure described above and recrystallisation from acetone gave the *benzoate* (**47**) (2.26 g) as yellow needles, m.p. 216—218 °C; $\lambda_{max.}$ 235 (ε 21 000) and 342 nm (ε 26 000); $\nu_{max.}$ 1 765 and 1 740 cm^{-1}; $\nu_{max.}$ (CH_2Cl_2) 1 760 cm^{-1}; δ 6.10 (1 H, s, PhCH=C) and 7.20—8.35 (15 H, ArH) (Found: C, 78.0; H, 4.35. $C_{24}H_{16}O_4$ requires C, 78.25; H, 4.4%).

(Z)-5-*Benzylidene*-4-*allyloxy*-3-*phenylfuran*-2(5H)-*one* (**48**).—(*Z*)-Pulvinone *Z*-(**9a**) (2 g), allyl bromide (2 ml) and potassium carbonate (1 g) in acetone (100 ml) were heated under reflux with stirring in an atmosphere of nitrogen for 1 h. The mixture was cooled, filtered and the filtrate evaporated to dryness under reduced pressure. The residual solid (2 g) was dissolved in hexane and chromatographed on silica. The fractions eluted with toluene were recrystallised from a small volume of n-pentane at −60 °C to give the allyl ether (**48**) (670 mg) as needles, m.p. 60—63 °C; $\lambda_{max.}$ 315 (ε 25 600) and 326 nm (ε 24 200); $\nu_{max.}$ 1 800, 1 735 and 1 645 cm^{-1}; $\nu_{max.}$ (CH_2Cl_2), 1 814, 1 740, and 1 640 cm^{-1}; δ 2.99 (2 H, d, *J* 6 Hz, CH_2=$CHCH_2$), 5.00—6.00 (3 H, m, CH_2=$CHCH_2$), 6.71 (1 H, s, PhCH=C), and 7.20—8.00 (10 H, ArH) (Found: C, 79.2; H, 5.45. $C_{20}H_{16}O_3$ requires C, 78.9; H, 5.3%).

(Z)-5-*Benzylidene*-4-*ethoxycarbonylmethoxy*-3-*phenylfuran*-2(5H)-*one* (**49**).—(*Z*)-Pulvinone *Z*-(**9a**) (1.5 g), ethyl bromoacetate (1.5 ml) and potassium carbonate (0.8 g) in acetone (75 ml) were heated under reflux with stirring in an atmosphere of nitrogen for 1 h. The mixture was cooled, filtered and the filtrate evaporated to dryness under reduced pressure. The residual solid was dissolved in methylene chloride and the solution passed through a short silica column. Elution with methylene chloride and removal of the solvent afforded a crystalline solid which was suspended in boiling ether (50 ml) for a few min. The solvent was reduced to *ca.* one half of the volume and the mixture was cooled and filtered to afford the *ethoxycarbonylmethyl ether* (**49**) (1.34 g) as needles, m.p. 122—124 °C; $\lambda_{max.}$ 328 nm (ε 32 100); $\nu_{max.}$ 1 760, 1 635, and 1 595 cm^{-1}; $\nu_{max.}$ (CH_2Cl_2), 1 760, 1 636, and 1 597 cm^{-1}; δ 1.17 (3 H, t, *J* 7 Hz, $MeCH_2CO_2$), 4.10 (2 H, q, *J* 7 Hz, $MeCH_2CO_2$), 4.58 (1 H, s, $EtCO_2CH_2$), 6.45 (1 H, s, PhCH=C), and 7.25—8.10 (10 H, ArH) (Found: C, 71.95; H, 5.3. $C_{21}H_{18}O_5$ requires C, 72.0; H, 5.2%).

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