The chemical behavior of 2-methylene-2,3-dihydro-3-furanones
14.* 5-Aryl-2-methoxycarbonylmethylene-2,3-dihydro-3-furanones in the [2+2]-cycloaddition of diphenylketene

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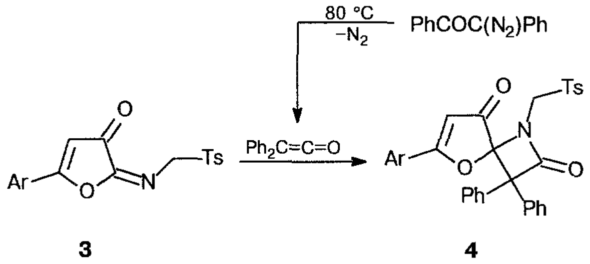
Diphenylketene undergoes regioselective thermal [2+2]-cycloaddition to the heterocyclic C(3)=O carbonyl group of 5-aryl-2-methoxycarbonylmethylene-2,3-dihydrofuran-3-ones and 5-phenyl-2,3-dihydrofuran-2,3-dione to give the corresponding 3-diphenylmethylene derivatives of 2,3-dihydrofuran.

Key words: 5-aryl-2-methoxycarbonylmethylene-2,3-dihydrofuran-3-ones, 5-phenyl-2,3-dihydrofuran-2,3-dione, diphenylketene, [2+2]-cycloaddition reaction, 5-aryl-3-diphenylmethylene-2,3-dihydrofurans.

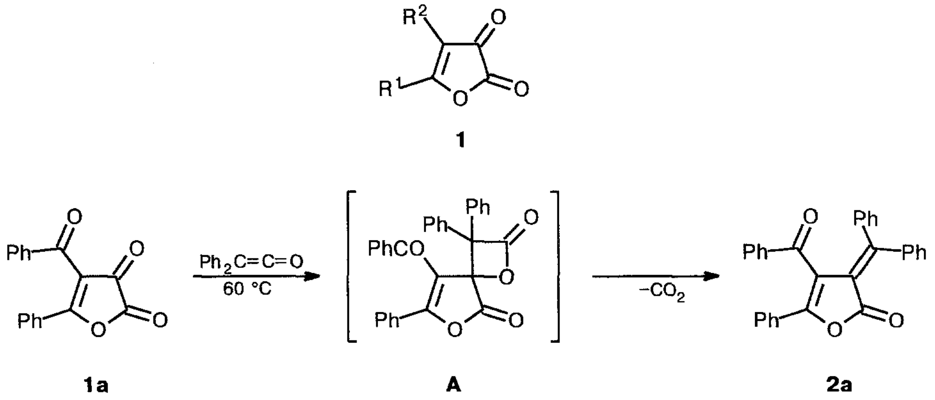
It is known that 2,3-dihydrofuran-2,3-diones (**1**) are easily transformed into highly-reactive acylketenes $R^1CO—C(R^2)=C=O$ and, therefore, readily undergo [4+2]-cycloaddition to various reagents containing double bonds, namely, olefins, carbonyl compounds, imines, amidines, nitriles, heterocumulenes, and ylides to give various heterocyclic systems.[2,3] 4-Benzoyl-5-phenyl-2,3-dihydrofuran-2,3-dione (**1a**) can be involved, skipping the step of decarbonylation into dibenzoylketene, in the thermal $[_{\pi}2_s+_{\pi}2_a]$-cycloaddition of diphenylketene to the carbonyl group at ring position 3 to eventually give 4-benzoyl-3-diphenylmethylene-5-phenyl-2,3-dihydro-2-furanone (**2a**).[4] It has been assumed that this reaction involves the formation of unstable spiro(furan-oxetanone) (**A**)[4] as an intermediate (Scheme 1).

There is also a report on the [2+2]-cycloaddition of diphenylketene to the 2-exocyclic C=N bond to give stable substituted spiro(furan-azetidinones) (**4**) instead of the addition to the C(3)=O carbonyl of 2-imino derivatives, *viz.*, 5-aryl-2-tosylmethylimino-2,3-dihydro-3-furanones (**3**), which are closely related to 2,3-furandiones[5] (Scheme 2).

Scheme 2



Scheme 1



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* For communication 13, see Ref. 1.

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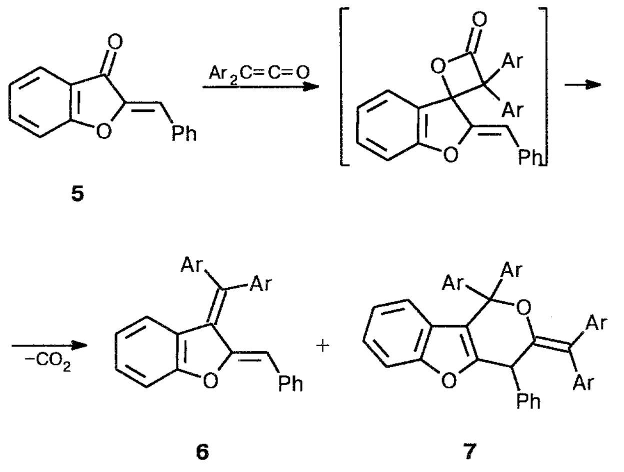
Scheme 3



No data has been reported in the literature on the cycloaddition of ketenes to monocyclic 2-ylidene derivatives of five-membered 3-oxoheterocycles. There is only spotty information that 2-benzylidene-2,3-dihydro-3-benzo[*b*]furanone (**5**) reacts with diarylketenes. As a result, both the products of thermal [2+2]-cycloaddition to the C(3)=O carbonyl, namely, 3-diarylmethylene-2-benzylidene-2,3-dihydro-3-benzo[*b*]furanones (**6**), and the products of subsequent [4+2]-cycloaddition (**7**) to the 1,3-butadiene system of the bis-olefin formed (**6**) have been obtained.[6,7]

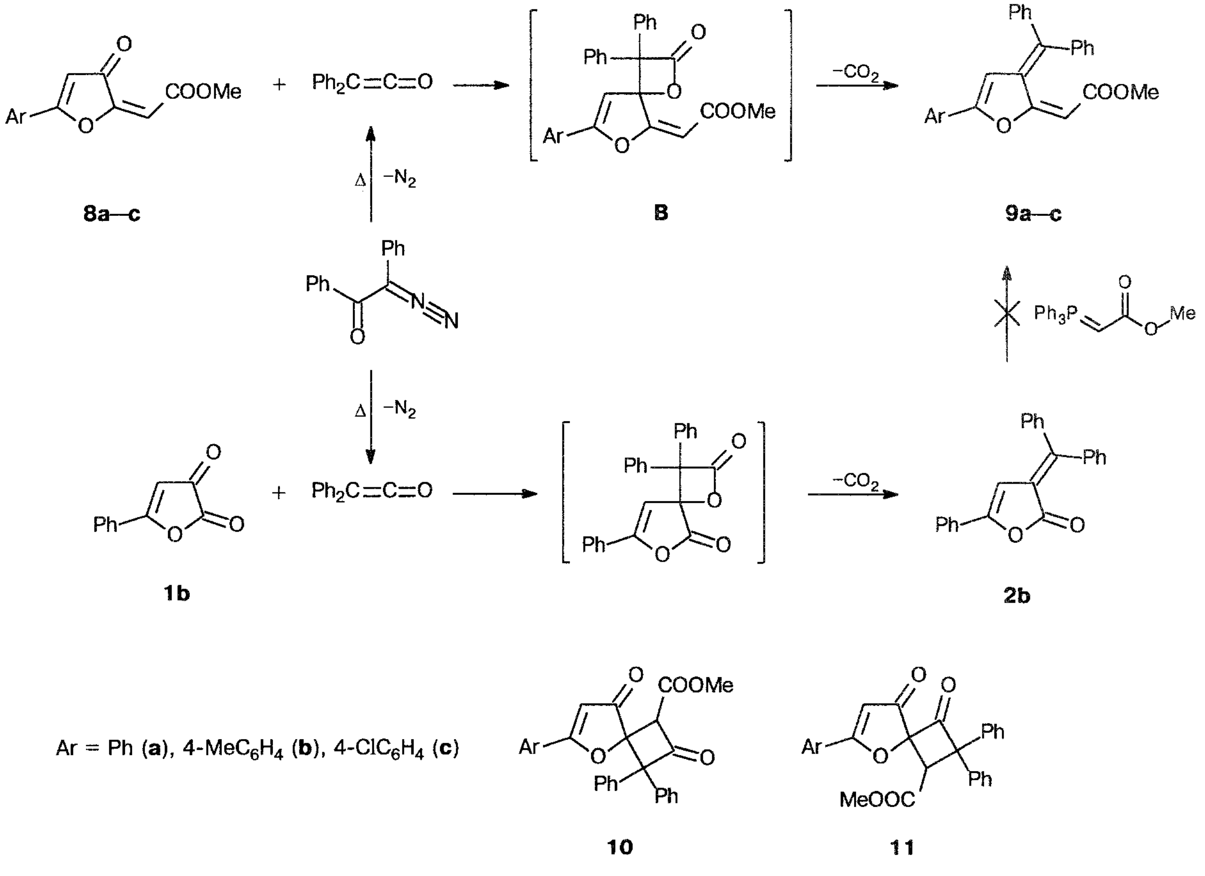
Thus, the available data demonstrate the very diverse chemical behavior of 2-oxo- and 2-ylidene-substituted 2,3-dihydro-3-furanones and their homologs in reactions with diphenylketene.

In this context, it was of interest to study the [2+2]-cycloaddition reactions of 2-acylmethylene-2,3-dihydro-3-furanones[8—10] and to determine whether both the 2-ethylene and 3-oxo fragments of the molecule can be involved in these reactions.

We have found that diphenylketene generated by thermolysis of phenylbenzoyldiazomethane[11] in boiling toluene reacts with 5-aryl-2-methoxycarbonylmethylene-2,3-dihydro-3-furanones (**8a—c**) to give eventually the products of the replacement of the oxygen atom in the C(3)=O carbonyl by a diphenylmethylene moiety, 5-aryl-3-diphenylmethylene-2-methoxycarbonylmethylene-2,3-dihydrofurans (**9a—c**)* in 31—56 % yields.

The spiro(furan-oxetanone) (**B**), which is formed as an intermediate due to [2+2]-cycloaddition, probably undergoes decarboxylation under the reaction conditions to give 1,3-dienes **9a—c**. This does not contradict the reported data[4,6,7] (Scheme 4).

Scheme 4



Ar = Ph (**a**), 4-MeC$_6$H$_4$ (**b**), 4-ClC$_6$H$_4$ (**c**)

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* For the preliminary communications, see Refs. 12, 13.

An attempt to perform an independent synthesis of compound **9a** by the Wittig reaction from methoxycarbonylmethylenetriphenylphosphorane and 3-diphenylmethylene-5-phenyl-2,3-dihydro-2-furanone **2b** (obtained by treatment of 5-phenyl-2,3-dihydro-2,3-furandione with diphenylketene) failed. TLC data suggest that the reaction does not occur even when a mixture of the reagents in xylene is boiled for a long period of time.

The spectral characteristics of compounds **2b** and **9a—c** agree with the assumed structure and with the data reported for their structural analogs.[4,6,7]

The position of the high-frequency stretching band of the lactone carbonyl group at 1768 cm^{-1} in the IR spectrum of 2,3-dihydro-2-furanone **2b** is in good agreement with the data known for lactones.[4,10,14]

The band of stretching vibrations of the ester carbonyl in the IR spectra of compounds **9a—c** (1712—1720 cm^{-1}) is observed at lower frequencies (by 10—20 cm^{-1}) than those in the spectra of the starting 5-aryl-2-methoxycarbonylmethylene-2,3-dihydro-3-furanones **8a—c**,[8,15] which attests to the lengthening of the conjugation system involving the ester carbonyl.

The absence of the stretching band of the C(3)=O group in the IR spectra of compounds **9**, which is located around 1672—1710 cm^{-1} for 3-furanones,[1,8—10] the presence of an intense band at 1644—1661 cm^{-1} corresponding to the vibrations of exocyclic double bonds, and a bright orange color allowed us to rule out the alternative structures of spiro-compounds **10** and **11**, whose formation seemed possible, judging by the literature data.[5] This assumption is further supported by the absence of the $[M-CO]^+$, $[M-Ph_2C=C=O]^+$, and $[Ph_2C=C=O]^+$ peaks (*m/z* 194) in the mass spectra of compounds **9a,b**. Figure 1 sketches the mass spectrum of compound **9a**.

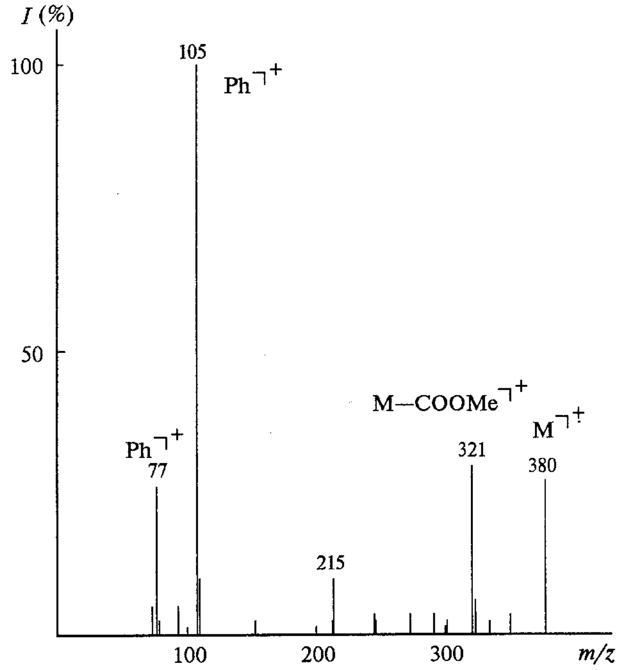

Fig. 1. Mass spectrum of 3-diphenylmethylene-2-methoxycarbonylmethylene-5-phenyl-2,3-dihydrofuran (**9a**).

Thus, diphenylketene undergoes regioselective thermal [2+2]-cycloaddition to the C(3)=O carbonyl group of the ring rather than to the 2-*exo*-ethylene fragment in 5-aryl-2-methoxycarbonylmethylene-2,3-dihydro-3-furanones (**8**). As a result, derivatives of 2,3-bis-methylene-2,3-dihydrofurans **9** are formed.

The compounds **9** obtained exhibit pronounced antibacterial activity against standard strains of *Staphylococcus aureus* P-209 and *Escherichia coli* M_{17} (see Refs. 12,13).

Experimental

IR spectra of compounds **2a** and **9a—c** were recorded in vaseline oil on UR-20 and Specord M-80 spectrometers. ^1H NMR spectra were obtained on a RYa-2310 spectrometer (60 MHz) in $CDCl_3$ (compounds **9a—c**) or in DMSO-d_6 (compound **2b**) using HMDS as the internal standard. Mass spectra (*m/z*, *I* (%)) were recorded on a Varian MAT-311A spectrometer with direct injection of samples into the ion source, emission current 1000 μA, energy of ionizing electrons 70 eV. The course of the reactions and the purity of the compounds were monitored on Silufol UV-254 plates in a benzene—ether— acetone system (10 : 9 : 1). Chromatograms were visualized by iodine. The starting 5-aryl-2-methoxycarbonylmethylene-2,3-dihydro-3-furanones (**8a—c**) were obtained by the method previously reported.[8,10,15] Diphenylketene was obtained using a known procedure.[11] 5-Phenyl-2,3-dihydro-2,3-furandione (**1b**) was synthesized using a modified procedure from Ref. 10. Methoxycarbonylmethylenetriphenylphosphorane was obtained by a known procedure.[16]

5-Aryl-3-diphenylmethylene-2-methoxycarbonylmethylene-2,3-dihydrofurans (9a—c). A mixture of 5-aryl-2-methoxycarbonylmethylene-2,3-dihydro-3-furanone **8a—c** (5 mmol) and phenylbenzoyldiazomethane (1.11 g, 5 mmol) was refluxed in xylene (70 mL) for a period from 40 min to 2 h (TLC monitoring). The solvent was evaporated and the residue was recrystallized from ethanol (compounds **9a,c**) or acetonitrile (compound **9b**).

Compound 9a. Yield 1.10 g (57 %), m.p. 179—180 °C. IR, ν/cm^{-1}: 1720 ($\underline{C}OOMe$), 1645—1655 (C=C). ^1H NMR ($CDCl_3$), δ: 3.62 (s, 3 H, OMe); 4.92 (s, 1 H, CH_{exo}); 6.56 (s, 1 H, C(4)H); 7.33—7.80 (m, 15 H, 3 Ph). MS (Fig. 1), *m/z* (*I* (%)), peaks with $I > 2$ %: 380 (27) $[M]^+$, 349 (3) $[M-MeO]^+$, 337 (2), 322 (7), 321 (29) $[M-COOMe]^+$, 303 (2) $[M-Ph]^+$, 289 (4), 276 (4), 244 (2), 243 (5), 215 (12) $[M-Ph(C_6H_4)C]^+$, 213 (3), 151 (2), 106 (9), 105 (100) $[PhC{\equiv}O]^+$, 91 (5), 78 (2), 77 (27) $[Ph]^+$, 69 (5). Found (%): C, 82.28; H, 5.37. $C_{26}H_{20}O_3$. Calculated (%): C, 82.09; H, 5.29. Mol. weight 380.44.

Compound 9b. Yield 1.00 g (51 %), m.p. 192—193 °C. IR, ν/cm^{-1}: 1718 ($\underline{C}OOMe$), 1650—1660 (C=C). ^1H NMR ($CDCl_3$), δ: 2.25 (s, 3 H, Me); 3.62 (s, 3 H, OMe); 4.88 (s, 1 H, CH_{exo}); 6.48 (s, 1 H, C(4)H); 7.10—7.70 (m, 14 H, 2 Ph, C_6H_4). MS, *m/z* (*I* (%)), peaks with $I > 3$ %: 394 (49) $[M]^+$, 363 (5) $[M-MeO]^+$, 335 (41) $[M-COOMe]^+$, 334 (50) $[M-COOMe-H]^+$, 303 (6) $[M-MeC_6H_4]^+$, 289 (20), 276 (6), 243 (4), 216 (11), 215 (41), 189 (6), 119 (100) $[p\text{-}MeC_6H_4-C{\equiv}O]^+$, 91 (33) $[p\text{-}MeC_6H_4-]$. Found (%): C, 82.07; H, 5.81. $C_{27}H_{22}O_3$. Calculated (%): C, 82.21; H, 5.62. Mol. weight 394.47.

Compound 9c. Yield 0.64 g (31 %), m.p. 200—202 °C. IR, ν/cm^{-1}: 1712 ($\underline{CO}$OMe), 1645—1660 (C=C). ^{1}H NMR ($CDCl_3$), δ: 3.59 (s, 3 H, OMe); 4.84 (s, 1 H, CH_{exo}); 6.43 (s, 1 H, C(4)H); 7.07—7.68 (m, 14 H, 2 Ph, C_6H_4). Found (%): C, 77.79; H, 4.28; Cl, 7.36. $C_{26}H_{19}ClO_3$. Calculated (%): C, 78.02; H, 4.10; Cl, 7.60. Mol. weight 466.78.

3-Diphenylmethylene-5-phenyl-2,3-dihydro-2-furanone (2b). A mixture of 5-phenyl-2,3-dihydro-2,3-furandione (1.74 g, 10 mmol) and phenylbenzoyldiazomethane (2.22 g, 10 mmol) in benzene (50 mL) was refluxed for 1 h (TLC monitoring). The solvent was evaporated, and the residue was triturated with ether (100 mL) and recrystallized from acetonitrile. Yield 1.75 g (54 %), m.p. 178—179 °C. IR, ν/cm^{-1}: 1768 (CO lactone), 1625 (C=C). ^{1}H NMR (DMSO-d_6), δ: 6.51 (s, 1 H, C(4)H); 7.32—7.60 (m, 15 H, 3 Ph). Found (%): C, 85.40; H, 4.73. $C_{23}H_{16}O_2$. Calculated (%): C, 85.16; H, 4.97. Mol. weight 324.38.

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