Photosensitized Oxidation of Furans. Part 2.[1] Comparison between Triplet and Singlet Molecular Oxygen Oxidation of Methyl 2-Methyl-5-phenylfuran-3-carboxylate

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Unsensitized photo-oxidation of the furan (1) yields the acrylate (4) as the major product. This reaction and that with singlet oxygen proceed through completely independent routes. Oxidation of (1) by triplet oxygen has also been studied using AIBN as a free-radical initiator; in addition to (4) the product (12), incorporating the isobutyronitrile radicals, was formed.

THE reaction of methyl 2-methyl-5-phenylfuran-3-carboxylate (1) with singlet molecular oxygen has recently been shown to yield quantitatively the furan endo-peroxide (2), which is stable at −15 °C under strictly anhydrous conditions. At room temperature in the absence of solvent, within 15—20 days it gives the epoxide (3) as the major product (62%).[1]

In this paper we describe the behaviour of the furan (1) towards triplet molecular oxygen. This oxidation afforded methyl (E)-2-acetyl-3-benzoylacrylate (4) as the major product. Neither the endo-peroxide (2) nor epoxide (3) were formed.

RESULTS AND DISCUSSION

The furan (1) was unchanged by treatment with triplet oxygen in refluxing benzene or upon irradiation with a halogen-superphot lamp (Osram 650 W). Irradiation of a benzene solution of (1) with a low-pressure mercury lamp (Hanovia 4 W) at room temperature, dry oxygen being bubbled through during the irradiation, slowly gave as identifiable products the acrylates (4) and (5), and trace amounts of methyl 2-formyl-5-phenylfuran-3-carboxylate (6). After 24 h the composition of the reaction mixture, deduced on the basis of the [1]H n.m.r. spectrum, was confirmed by silica gel chromatography which allowed the isolation of a mixture of (4) and (5), and of (6), as well as a mixture of gummy materials and unchanged furan (1) (71%). It should be noted that, when the photo-oxidation of (1) was carried out in hexadeuteriobenzene, the [1]H n.m.r. spectrum of the reaction mixture recorded after 8 h showed, in addition to the signals of (1), the signals previously assigned to the E-isomer (4).[1] Therefore the Z-isomer (5) was evidently formed by isomerization of the initially formed E-isomer (4) which partly converts into (5) by standing at room temperature or on contact with silica gel.[1] Acrylates (4) and (5) were identified by comparison of their i.r. and [1]H n.m.r. spectra with those of authentic samples.[1] Structure (6) was assigned on the basis of the elemental analyses and spectral data detailed in the Experimental section. The free-radical nature of the photo-oxidation of the furan (1) with triplet oxygen, which could be deduced on the basis of the above and previous [2] results, was confirmed by the observation that the photo-

oxidation process was completely stopped when a radical trap, such as 2,6-di-t-butyl-p-cresol (DTBC),[3] was added to the oxidation mixture. An overall view of the results is summarized in the Table.

The mechanistic origin of (4) can be explained assuming that the u.v. light excites the furan (1) which is then susceptible to attack by ground-state oxygen to yield the diradical (7) † which could react with another mole-

TABLE
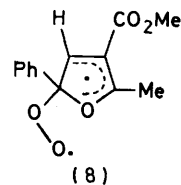
Oxidation of furan (1) by triplet oxygen

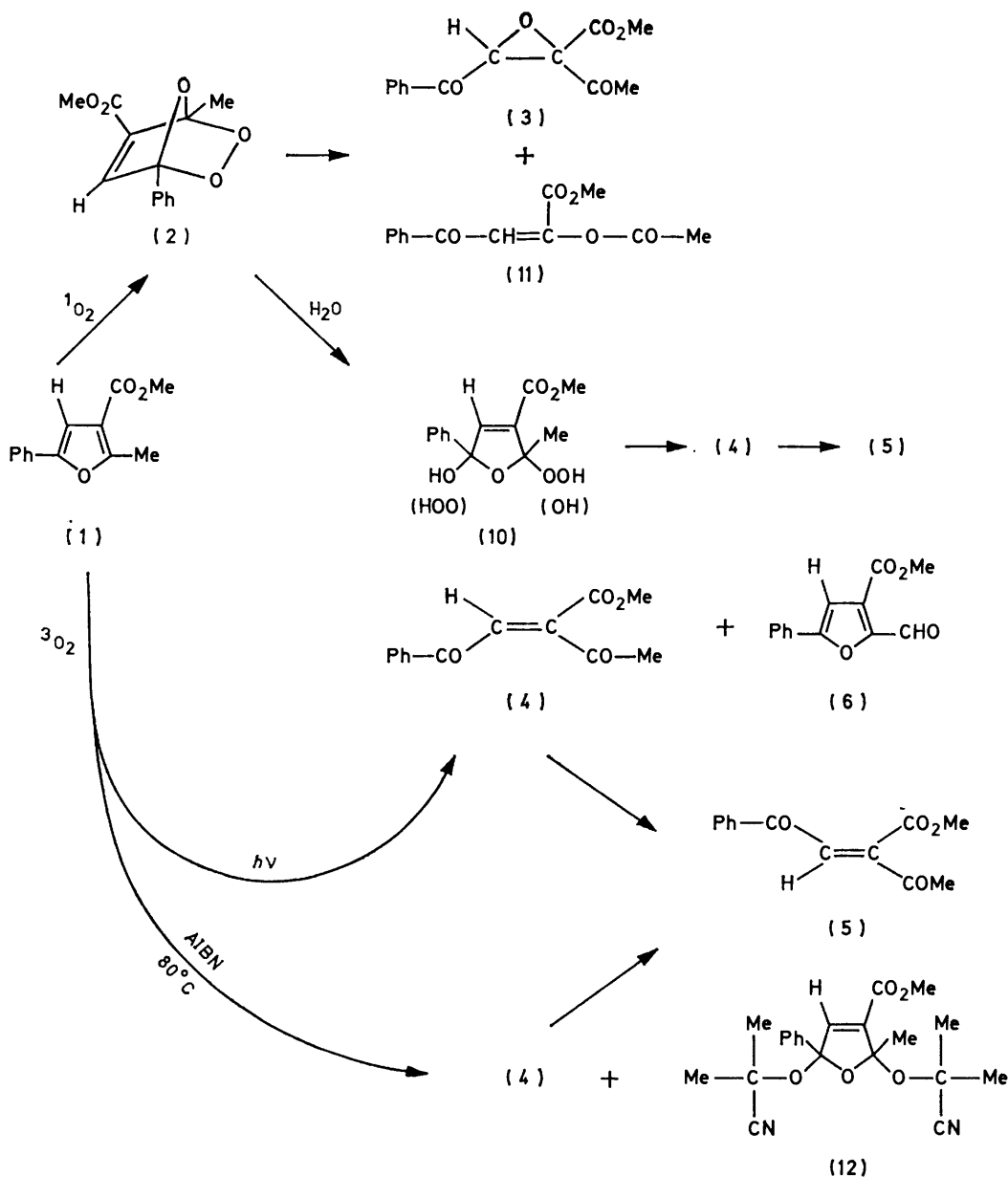| Reaction conditions [a]	Reaction time/h	Oxidation [b] (%)	Yield (%) [c]		
			(4) + (5)	(6)	(12)
80 °C	24[d]	0			
15—20 °C, irradiation (HSL) [e]	24[d]	0			
15—20 °C, irradiation (LPHL) [f]	24[d]	29	40	4	
15—20 °C, irradiation (LPHL),[f] DTBC [g]	24[d]	0			
80 °C, AIBN [h]	8[d]	16	32		15
80 °C, AIBN [i]	8	100	30		21

[a] Using a 2% benzene solution. [b] Deduced on the basis of the [1]H n.m.r. spectrum of the reaction mixture and confirmed by silica gel chromatography. [c] Calculated on the basis of recovered (1). [d] Standard time used. [e] Halogen-superphot lamp (Osram 650 W). [f] Low-pressure mercury lamp (Hanovia 4 W). [g] Molar ratio furan (1) : DTBC of 3 : 1. [h] Molar ratio furan (1) : AIBN of 10 : 1. [i] Molar ratio furan (1) : AIBN of 1 : 1.

cule of (1) to give the diradical (9). The latter would generate (4) by peroxide bond fission. The proposed mechanism is similar to those previously suggested in similar cases.[2,4]

The results obtained by singlet and triplet oxygen oxidation of fully substituted alkoxyoxazoles have been rationalized in terms of the equilibrium between diradicals like (7) and endo-peroxides like (2).[2] The equili-

† The increased electron-delocalization in (7) with respect to (8) is consistent with the proposed intermediate.

(8)

MeO₂C ... O ... Me
(2)

H ... O ... CO₂Me
Ph—CO—C—C—COMe
(3)

+

CO₂Me
Ph—CO—CH=C—O—CO—Me
(11)

¹O₂ / H₂O

H CO₂Me
Ph— —Me
O
(1)

H CO₂Me
Ph—Me
HO O OOH
(HOO) (OH)
(10)

⟶ (4) ⟶ (5)

³O₂

H CO₂Me
C=C
Ph—CO CO—Me
(4)

+

H CO₂Me
Ph— —CHO
O
(6)

hv

Ph—CO CO₂Me
C=C
H COMe
(5)

AIBN 80°C

(4) +

H CO₂Me
Me Ph Me Me
Me—C—O O O—C—Me
CN CN
(12)

brium was also postulated in the photosensitized oxidation of 2-methyl-4,5-diphenylimidazole.[5] In order to ascertain whether the *endo*-peroxide (2) plays a role in the autoxidation of (1) or not, an investigation on the behaviour of (2) was undertaken. Thus, we have established that the *endo*-peroxide (2), prepared as previously described,[1] upon irradiation in benzene after 24 h was completely transformed. The ¹H n.m.r. spectrum of the irradiation mixture showed, in addition to the signals of polymeric materials[1] and of (4), (5), and hydroxy-hydroperoxy-compounds (10), evidently formed from the extremely hydrolysis-sensitive (2),[1] the signals of the epoxide (3) and of methyl 2-acetoxy-4-oxo-4-phenylbutenoate (11),* which might result from a Baeyer-Villiger type of rearrangement of the *endo*-peroxide (2), as previously suggested in similar cases.[6] The identification of the above products was confirmed

by comparison of their chromatographic, spectral, and chemical properties with those previously reported.[1,7] Since by unsensitized photo-oxidation of the furan (1) neither epoxide (3) nor enol ether (11) were detected, the above results demonstrate that, in this case, other reactions occur within (7) in preference to, and probably faster than, the spin-inversion-dependent cyclization into the *endo*-peroxide (2). If the hypothesized mechanism for the oxidation of the furan (1) by triplet oxygen is actual, not even the conversion (2) ⟶ (7) takes place; in fact, irradiation of equimolar quantities of (1) and (2) in benzene left the furan (1) completely unchanged. On the basis of the above results it can be concluded that,

* In the light of the present results, we re-examined the thermal conversion of (2) at room temperature;[1] in this case also small amounts of (11) were detected in the reaction mixture.

in the case of the furan (1), the oxidations by triplet and singlet oxygen proceed through completely independent routes, different from the fully substituted alkoxy-oxazoles.[2]


(7)

(4) ← (9)
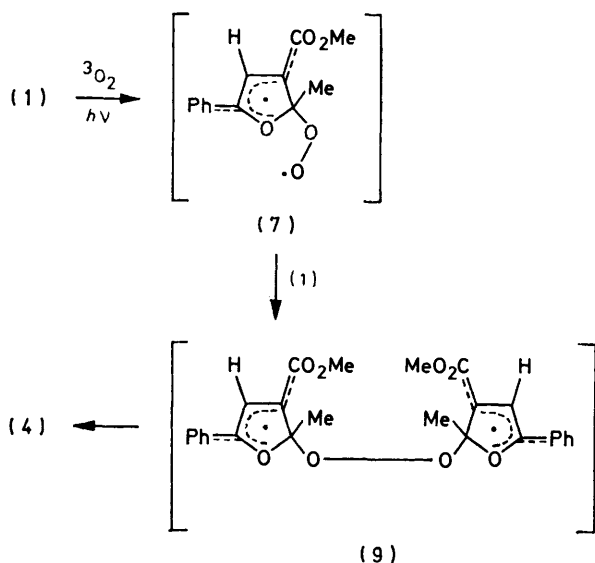
Oxidation of the furan (1) also occurred refluxing a benzene solution of (1) and the free-radical initiator azobisisobutyronitrile (AIBN),[8] dry oxygen being

addition to 84% of recovered starting material. With a molar ratio (1) : AIBN of 1 : 1, the reaction was complete after 8 h; in this case (4), (5), and methyl 2,5-bis-(1-cyano-1-methylethoxy)-2-methyl-5-phenyl-2,5-dihydrofuran-3-carboxylate (12) as identifiable products. Structure (12) was assigned on the basis of the elemental analyses and spectral data detailed in the Experimental section; the stereochemistry has not been investigated. A reasonable sequence for the formation of (12) is initial bond formation between the peroxy-radical (13)[9] and the furan (1) to give the radical (14). Cleavage of this species to acrylate (4) and alkoxy-radical (15) would be a possible step. The radical (15) could react with another molecule of (1) to give the radical (16) and finally the dihydrofuran (12). When the oxidation was carried out in hexadeuteriobenzene, after 90 min the ^{1}H n.m.r. spectrum of the reaction mixture showed the presence of (4) but not of (5), thus supporting the postulated mechanism.

EXPERIMENTAL

M.p.s are uncorrected. I.r. spectra were measured with chloroform as solvent on a Perkin-Elmer 399 spectrophotometer. ^{1}H N.m.r. spectra were recorded with deuteriochloroform as solvent, unless otherwise stated, on a Perkin-Elmer R 12 A or on a Bruker WH 270 with tetramethylsilane as internal standard. ^{13}C N.m.r. spectra were recorded on a Bruker WH 270 in deuteriochloroform

(13)

(14) → (4) + (15)

(15) + (1) → (16) → (12)
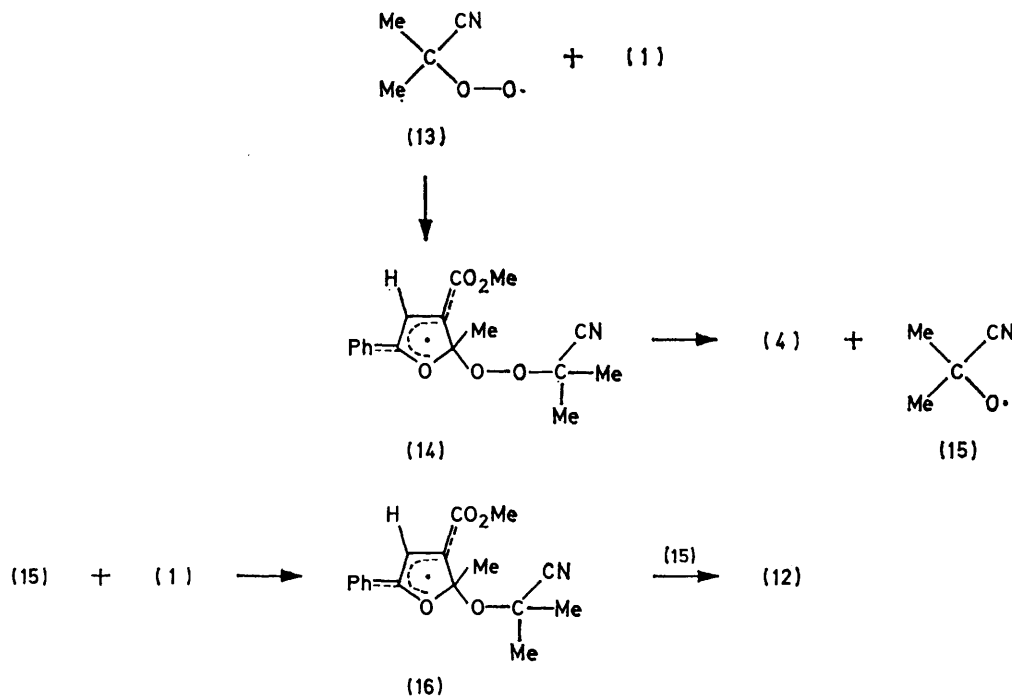
bubbled through during the heating. When the molar ratio (1) : AIBN was 10 : 1 the oxidation occurred slowly and after 8 h yielded, as identifiable products, the acrylates (4) and (5) and a small amount of a product (12) incorporating the isobutyronitrile radicals, in

solution with tetramethylsilane as internal standard. Silica gel 0.05—0.20 mm (Merck) and light petroleum, b.p. 30—50 °C, were used for column chromatography.

Photo-oxidation of the Furan (1).—A 2% solution of (1)[1] (910 mg, 4.21 mmol) in dry benzene was irradiated with a

low-pressure mercury lamp (Hanovia 4 W) placed in a water-cooled quartz immersion well. During the irradiation dry oxygen was bubbled through the solution. After 24 h the reaction was stopped and the solvent was removed *in vacuo*. Inspection of the ^{1}H n.m.r. spectrum showed the presence of (1), (4), (5), and (6) as identifiable products. The mixture was chromatographed on silica gel (45 g). Elution with light petroleum–ether (19 : 1, 9 : 1, and 4 : 1 v/v) gave successively unchanged (1) (635 mg, 71%), (6) (7 mg, 4%), and (4) + (5) (114 mg, 40%). Elution with ether gave gummy materials (160 mg). The acrylates (4) and (5) were identified by comparison of i.r. and ^{1}H n.m.r. spectra with those of the authentic samples.[1]

Furan (6) is a white solid, m.p. 111—113 °C (Found: C, 67.35; H, 4.5. $C_{13}H_{10}O_4$ requires C, 67.82; H, 4.38%); $\nu_{max.}$ 2 735, 1 728, and 1 678 cm^{-1}; δ_H 3.92 (3 H, s, CO$_2$Me), 7.01 (1 H, s, CH), 7.30—7.95 (5 H, m, aromatic), and 11.12 (1 H, s, CHO); δ_C 52.90 (q, OMe), 99.07 (s, C-3), 107.44 (d, C-4), 125.43 (d, C-3 and C-5 of Ph group), 128.22 (s, C-1 of Ph group), 129.02 (d, C-2 and C-6 of Ph group), 130.14 (d, C-4 of Ph group), 151.16 and 158.04 (2 s, C-2 and C-5), 162.07 (s, CO$_2$), and 178.32 (d, CO).

When the photo-oxidation was carried out in hexadeuteriobenzene, after 8 h the ^{1}H n.m.r. spectrum showed the presence of (1) and (4) as identifiable products.

The photo-oxidation of (1) in the presence of DTBC (molar ratio 3 : 1) was completely inhibited. After 24 h (1) was recovered quantitatively.

Photo-decomposition of the endo-*Peroxide* (2).—A 2% solution of (2)[1] (175 mg, 0.81 mmol) in dry benzene was irradiated with a low-pressure mercury lamp (Hanovia 4 W) placed in a water-cooled quartz immersion well. After 24 h (2) was completely transformed (^{1}H n.m.r.) and the solvent was removed *in vacuo*. Inspection of the ^{1}H n.m.r. spectrum showed the presence of (3), (4), (5), (10), (11), and polymeric materials. The mixture was chromatographed on silica gel (10 g). Elution with light petroleum–ether (4 : 1 v/v) gave successively (11) (11 mg, 5%), (4) + (5) (52 mg, 28%), an unidentified compound (6 mg), and (3) (38 mg, 19%). Elution with ether gave gummy materials (68 mg).

To the solution obtained by irradiation of (2) (248 mg, 1 mmol), diethyl sulphide[1] (0.1 ml, 1 mmol) was added; after 3 h the solvent and the unchanged diethyl sulphide were removed *in vacuo*. Silica gel chromatography of the reaction mixture allowed the isolation of (11) (12 mg, 5%), (4) + (5) (102 mg, 44%), an unidentified compound (5 mg), (3) (44 mg, 18%), and gummy materials (38 mg).

Compounds (3), (4), and (5) were identified by comparison of i.r. and ^{1}H n.m.r. spectra with those of authentic samples.[1] Enol ether (11), which has been reported[7] but not fully characterized, is a colourless liquid; $\nu_{max.}$ 1 773, 1 732, 1 680, and 1 625 cm^{-1}; δ_H (CCl$_4$)[7] 2.10 (3 H, s, COMe), 3.84 (3 H, s, CO$_2$Me), and 7.32 and 7.25—7.80 (6 H, s and m, CH and aromatic); δ_C 20.32 (q, Me), 53.24 (q, OMe), 121.36 (d, C-3), 128.71 and 128.88 (2 × d, C-2, C-6 and C-3, C-5 of Ph group), 133.94 (d, C-4 of Ph group), 137.00 (s, C-1 of Ph group), 144.46 (s, C-2), 162.12 (s, C-1), 168.17 (s, C=O of Ac group), and 188.98 (s, C-4).

The photo-decomposition of (2) was also carried out in the presence of (1) (molar ratio 1 : 1); after 24 h the mixture was chromatographed on silica gel, and the furan (1) was quantitatively recovered.

Oxidation of the Furan (1) *in the Presence of AIBN*.—To a 2% benzene solution of (1) (620 mg, 2.87 mmol) was added AIBN (470 mg, 2.87 mmol). The solution was refluxed, oxygen being bubbled through during the heating. The reaction was complete within 8 h (^{1}H n.m.r.). After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel (50 g). Elution with light petroleum–ether (9 : 1 v/v) gave AIBN and impurities deriving from it. Elution with light petroleum–ether (4 : 1 v/v) yielded successively (4) + (5) (196 mg, 30%) and (12) (232 mg, 21%). Elution with ether gave gummy materials (236 mg).

Dihydrofuran (12) is a white solid, m.p. 83—85 °C (Found: C, 65.5; H, 6.3; N, 7.25. $C_{21}H_{24}N_2O_5$ requires C, 65.61; H, 6.29; N, 7.29%); $\nu_{max.}$ 2 221, 1 730, and 1 658 cm^{-1}; δ_H 1.54, 1.57, 1.62, and 1.65 (12 H, 4 × s, 4 × Me), 2.15 (3 H, s, Me on C-2), 3.78 (3 H, s, OMe), 7.08 (1 H, s, CH), and 7.30—7.80 (5 H, m, aromatic); δ_C 23.62, 25.09, 25.25, 29.04, and 30.46 (5 × q, 5 × Me), 52.15 (q, OMe), 67.81 and 75.77 (2 × s, 2 × C–O), 112.66 and 115.17 (2 × s, C-2 and C-5), 120.18 and 121.87 (2 × s, 2 × CN), 126.80 and 128.63 (2 × d, C-2, C-6 and C-3, C-5 of Ph group), 129.94 (d, C-4 of Ph group), 136.01 (s, C-3), 139.12 (d, C-4), 139.26 (s, C-1 of Ph group), and 161.68 (s, C=O).

When the above oxidation was carried out in hexadeuteriobenzene, after 90 min the ^{1}H n.m.r. spectrum of the reaction mixture showed the presence of (1), (4), and AIBN as identifiable products.

When the oxidation of (1) (600 mg, 2.78 mmol) was carried out under the above conditions but in the presence of 45 mg (0.28 mmol) of AIBN, after 8 h the ^{1}H n.m.r. spectrum of the reaction mixture showed the presence of much unchanged (1). The reaction was stopped, the solvent was removed *in vacuo*, and the residue chromatographed on silica gel (50 g). Elution with light petroleum–ether (19 : 1 v/v) yielded unchanged (1) (500 mg, 84%). The acrylates (4) + (5) (34 mg, 32%), the dihydrofuran (12) (28 mg, 15%), and gummy materials (45 mg) were also isolated.

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