

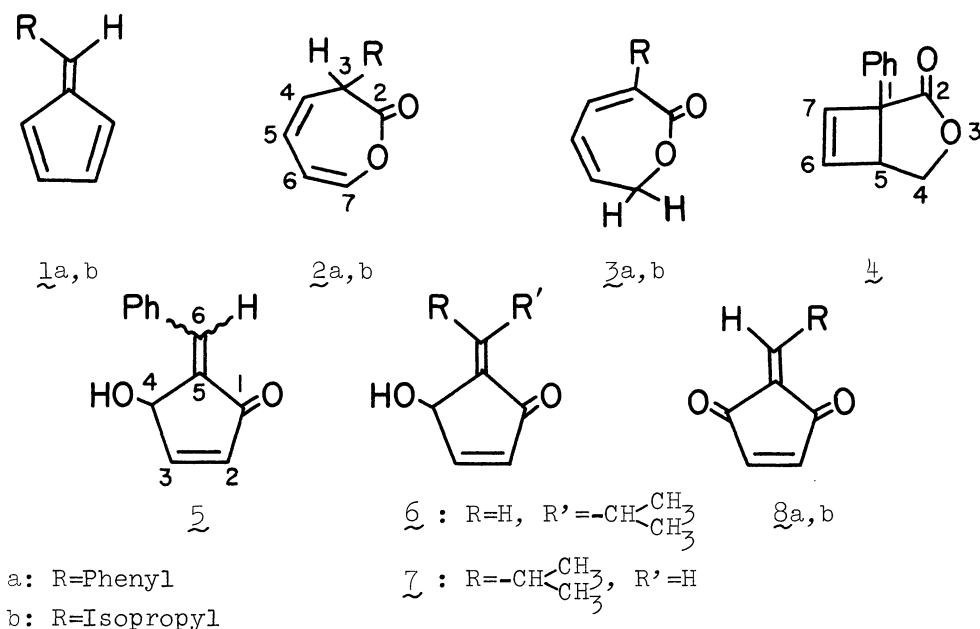
2(7H)-OXEPINONES: PHOTOCHEMICAL OXIDATION OF
6-MONOSUBSTITUTED FULVENES

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The photooxidation of 6-phenylfulvene gave a mixture of oxepinone derivatives, from which the more stable 3-phenyl-2(7H)-oxepinone was obtained in pure form. On the other hand, 6-isopropylfulvene afforded 3-isopropyl-2(3H)-oxepinone or an inseparable mixture with 3-isopropyl-2(7H)-oxepinone. 4-Hydroxy-2-cyclopentenone derivatives were preferentially produced from both fulvenes when the reaction was conducted in methanol using Rose Bengal as a sensitizer.

In connection with studies on the photochemical oxidation of 6,6-disubstituted fulvene derivatives,^{1,2,3,4} we have investigated the photooxidation of 6-mono-substituted fulvenes 1 under various conditions in order to gain further insight about this reaction and to extend it to yield hitherto unknown 2(7H)-oxepinone derivatives.

Direct and sensitized photooxidations of 6-phenylfulvene (1a)⁵ were carried out in the manners as summarized in Table 1. In each case the lactone fraction of the crude photolysate contained two oxepinones, the original product 2a and its isomerized one 3a, which were apparently separable by column or preparative layer



chromatography on silica gel with ether - petroleum ether. However, each eluted fraction, especially the fraction supposed to be 2a (see below), was shown to be again a mixture of 2a and 3a. Isolation of pure 3a, 3-phenyl-2(7H)-oxepinone, mp 102.0 ~ 102.5°, ⁶ was achieved by recrystallization of the fraction of 3a from ethyl acetate - petroleum ether. The spectral data⁷ were in accord with the assigned structure: ir (CCl₄) 1720 cm⁻¹ (conjugated lactone); uv (EtOH) λ_{\max} 289 nm (log ϵ = 3.89); nmr (100 MHz, C₆D₆) δ 3.90 (2 H, d, J₆₋₇ = 5.9 Hz, C-7 methylene), 5.73 (1 H, dt, J₅₋₆ = 10.1 Hz, H-6), 5.92 (1 H, dd, J₄₋₅ = 5.3 Hz, H-5), 6.23 (1 H, d, H-4), 7.51 (2 H, m) and 7.17 ppm (3 H, m) (phenyl). The chemical-shift assignments and couplings were verified by a double resonance experiment. Uv irradiation (500-W high-pressure mercury lamp, Vycor filter) of an ethereal solution of 3a at room temperature for 2.5 hr gave 1-phenyl-3-oxabicyclo[3.2.0]hept-6-en-2-one (4) in 45 % yield: ir (neat) 1760 cm⁻¹ (γ -lactone); nmr (100 MHz, CCl₄) δ 3.49 (1 H, dd, J₄₋₅^{cis} = 6.6 and J₄₋₅^{trans} = 2.3 Hz, H-5), 4.16 (1 H, dd of A part, J_{AB(gem)} = 9.7 Hz, H-4 ^{trans} to H-5), 4.33 (1 H, dd of B part, H-4 ^{cis} to H-5), 6.45 and 6.55 (1 H each, AB type q, J = 2.6 Hz, two olefinic protons), and 7.27 ppm (5 H, s, phenyl). Thus, the compound 3a is the first example of 2(7H)-oxepinone derivative as expected, and it should be noted that the sensitized photooxidation of 1a conducted in chloroform at low temperature using Methylene Blue as a sensitizer is most promising in practice for the preparation of the oxepinone 3a (see Table).

On the other hand, the originally produced oxepinone 2a could not be isolated in pure state, because of a facile isomerization to 3a in solution; the ratio of 2a and 3a in the fraction of 2a, separated by preparative tlc, was initially about 3 : 1 and changed to about 2 : 3 after 24 hr.⁸ Spectral analysis of a mixture of 2a and 3a by comparison with the spectra of 3a and 3,3-dimethyl-2(3H)-oxepinone^{1,2} leads to the structure of 2a, 3-phenyl-2(3H)-oxepinone: ir (neat) 1760 cm⁻¹ (lactone); nmr (100 MHz, CCl₄) δ 3.65 (1 H, br.d, J₃₋₄ = ca. 5.2 and J₃₋₅ = ca. 2.0 Hz, H-3), 5.81 (1 H, dd, J₄₋₅ = 9.5 Hz, H-4), 5.86 (1 H, dd, J₅₋₆ = 5.8 and J₆₋₇ = 6.3 Hz, H-6), 6.23 (1 H, ddd, H-5), 6.58 ppm (1 H, d, H-7), and aromatic protons.

When the photooxidation of 1a was conducted in methanol employing Rose Bengal, an isomer of 5-benzylidene-4-hydroxy-2-cyclopentenone (5), mp 160°: ir (KBr) 3350 (OH), and 1670 and 1620 cm⁻¹ (doubly conjugated five-membered ring ketone); nmr (100 MHz, d₆-DMSO) δ 5.50 (1 H, br.s, H-4), 6.57 (1 H, dd, J₂₋₃ = 6.1 and J₂₋₄ = 1.0 Hz, H-2), 7.35 (1 H, br.s, H-6), 7.83 (1 H, dd, J₃₋₄ = 2.5 Hz, H-3), and around 7.58 and 7.98 ppm (total 5 H, m, phenyl), was obtained as the major product, analogous to the result observed in the case of 6,6-dimethylfulvene.³ Jones oxidation⁹ of 5 afforded quantitatively the known 4-benzylidene-cyclopentene-3,5-dione (8a),¹⁰ whose physical properties were in accord with the reported values. Compound 5 was a sole product of two possible isomers in respect of the geometry at C-6. At present, the geometry at C-6 in 5 is unknown.

Similarly, the photooxidation of 6-isopropylfulvene (1b),⁵ an alkyl analogue of 1a, gave the comparable results with those in the case of 1a, which were shown in Table 2. From the run in tert-butyl alcohol, although the yield was very low (6 %), almost pure original oxepinone, 3-isopropyl-2(3H)-oxepinone (2b), was obtained: ir (CCl₄) 1760 cm⁻¹; nmr (100 MHz, CCl₄) δ 1.07 (3 H, d, J = 7.1 Hz) and 1.09 (3 H, d, J = 7.1 Hz) (isopropyl methyls), 2.0 2.4 (2 H, m, H-3 and isopropyl

Table 1. Photooxidation of 6-Phenylfulvene (1a)

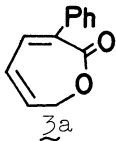
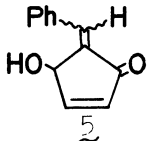
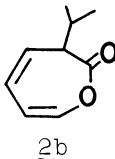
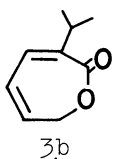
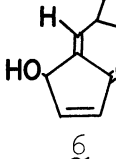
Conditions ^a				Products (Yield) ^b	
Direct or Sensitized Filter Sensitizer	Solvent	Temp.	Time	 <u>2a</u>	 <u>5</u>
Direct Pyrex	Benzene	r.t.	16 ^{hr}	17 %	c %
"	Ether	-65° ~ -40°	10	10	c
Sensitized Methylene Blue	Chloroform	-70°	1	44 ^d	
Rose Bengal	Methanol	r.t.	2.5	1 ~ 2	13

Table 2. Photooxidation of 6-Isopropylfulvene (1b)

				 <u>2b</u>	 <u>6</u>	 <u>7</u>
Direct Pyrex	Benzene	r.t.	2 ^{hr}	22 %	c %	
Sensitized Methylene Blue	Chloroform	r.t.	1.7	47 ^d		
"	"	-70°	2	74 ^e		
Rose Bengal	Methanol	r.t.	4.5	c	25	25
"	<u>t</u> -Butyl Alcohol	r.t.	1.8	6	8	8

- a) A 500-W high-pressure mercury lamp was used for the direct photooxidation, and a 200-W tungsten lamp for the sensitized one. A finely dispersed stream of oxygen was bubbled through the reaction mixture during irradiation.
- b) Products were isolated by column or preparative layer chromatography on silica gel and then purified by recrystallization or evaporative distillation.
- c) No detectable amount was isolated.
- d) Nmr or glc analysis indicated that the oxepinone(s) was a sole product.
- e) Crude yield before distillation.

methine), 5.58 (1 H, dd, $J_{3-4} = 5.2$ and $J_{4-5} = 9.3$ Hz, H-4), 5.81 (1 H, dd, $J_{5-6} = 5.3$ and $J_{6-7} = 6.8$ Hz, H-6), 6.19 (1 H, ddd, $J_{3-5} = 1.9$ Hz, H-5), and 6.52 ppm (1 H, d, H-7). In the other cases, always a mixture of 2b and the isomeric oxepinone, 3-isopropyl-2(7H)-oxepinone (3b), which could not be separated either by preparative glc or tlc, was obtained in the ratio of about 4 : 1 as indicated by carbonyl bands at 1760 (strong) and 1710 cm^{-1} (weak) in ir and chemical-shift values, coupling patterns, and peak areas in nmr. Therefore, the lactone carbonyl group would not be so effective to the conjugation with the double bonds in a 2-oxepinone ring system, in contrast with the large contribution of a phenyl substituent at C-3 for the conjugation. Among the oxepinones from both 1a and 1b the existence of an isomeric 2(5H)-oxepinone derivative could not be observed.

Sensitized photooxidation of 1b in methanol again resulted in preferential formation of 4-hydroxy-2-cyclopentenone derivatives, two separable geometric isomers of 5-isobutylidene-4-hydroxy-2-cyclopentenone 6 and 7, in equal amounts. Structural assignments of 6 and 7 were supported by close resemblance of the absorption bands in ir and the splitting pattern of ring protons in nmr with those of 5-isopropylidene analogue^{1,2} and conversion to 4-isobutylidene-cyclopentene-3,5-dione (8b), mp 24~26°. In the nmr spectra of 6 and 7, contrary to the equivalency of the isopropyl methyls in 6 (doublet at δ 1.10 ppm, $J = 6.7$ Hz), the isopropyl methyls of 7 reveal four lines around δ 1.02 ppm, undoubtedly owing to the effect of a closely disposed asymmetric carbon atom, C-4, which provides the evidence to the respective geometry of the isobutylidene side-chain in 6 and 7 as formulated.

From the present studies the photooxidation of 6-arylfulvenes would serve as a useful method for the synthesis of 3-aryl-2(7H)-oxepinone derivatives.¹¹

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References

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- 4) N. Harada, S. Suzuki, H. Uda, and H. Ueno, Chemistry Lett., submitted for publication.
- 5) Improved procedure for the preparation of the fulvenes 1 will be reported elsewhere.
- 6) All new compounds gave satisfactory elemental analyses.
- 7) The spectra were taken immediately after the solutions were prepared.
- 8) The equilibrated ratio of 2a and 3a in CDCl_3 starting from pure 3a was about 1 : 6 as determined by nmr.
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- 11) In the present studies, any of the intermediates including the 1,4-epidioxides could not be isolated or even detected spectroscopically.

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