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ON THE PHOTOCHEMISTRY OF 6-epi-α-SANTONIN, 6-epi-LUMISANTONIN AND RELATED COMPOUNDS[1,2]

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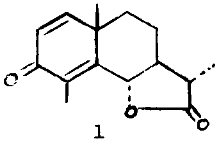
One aspect of the photochemistry of dienones[4] that has remained puzzling is that several dienones give significant yields of phenolic and certain rearranged ketonic products on photolysis in solvents such as dioxane, methanol, and glacial or aq. acetic acid,[5] while analogous products have not been detected from irradiation of α-santonin (1) in similar media.[4] Kropp[5a,6] has proposed that such products would arise from α-santonin via the spiro intermediate 2, containing a "highly strained" trans fusion of two five-membered rings, and that therefore other lower energy paths are preferred, particularly that leading to the linearly conjugated dienone 3. Acid-catalyzed dienone-phenol rearrangements of α-santonin (1) or 6-epi-α-santonin (4)[8] give 5[9], which has a cis-fused lactone ring,[10] while an acid-catalyzed rearrangement through a spiro intermediate occurs with a dienone containing a cis-fused lactone ring.[11]

As a test of Kropp's hypothesis,[5a,6] the photochemistry of 6-epi-α-santonin (4)[8] has been studied, and some significant preliminary results are now reported.

Irradiation of 4 in dioxane at 2537 A° (low pressure



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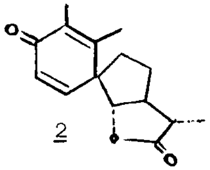

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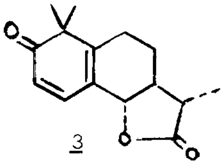

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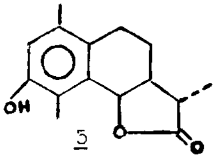

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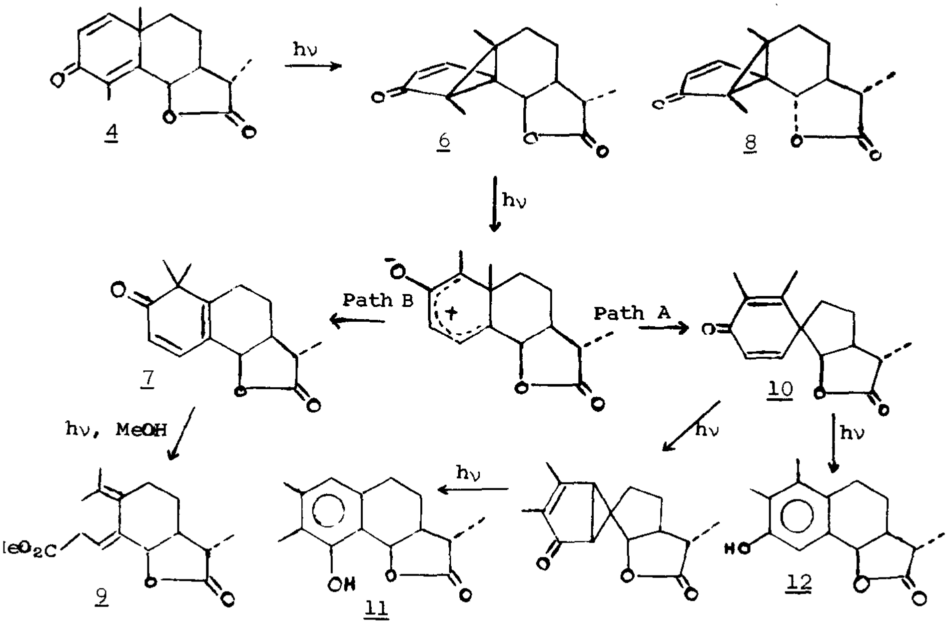
mercury arc)[5,6] gave 6-epi-lumisantonin (6), m.p. 138-140°, isolated by silica gel chromatography.[12] Spectral data for 6: IR (CHCl$_3$), 1780, 1710 cm^{-1}; $\lambda_{max}^{95\%\ EtOH}$ 241 mu, ε 4160; NMR (ppm relative to internal TMS) 5.95 and 7.35 (doublets, J_{AB}=5 cps), each 1 H, and 5.35 (doublet, 1H). The latter resonance (C-6 H) is characteristic of the 6-epi series (C-6 H for lumisantonin (8) appears at 3.9 ppm). Dihydro product of 6:[12] m.p. 178-178.5°, IR 1780 and 1715 cm^{-1}, no vinyl protons in nmr. Irradiation of 4 in neutral media (benzene, acetone or dioxane), using a 450-watt Hanovia high-pressure mercury arc (Pyrex filter) gave two products detectable by gas liquid partition chromatography (glpc)[13]. One product was 6, and the other was an isomeric dienone 7, shown by direct comparison with an independently synthesized sample.[14] 7 could also be obtained from photolysis of 6. The yield of 7 from either 4 or 6 was 10-25%, as the major product (40-50% yield) was a high-melting base-insoluble material. Photolysis of 7 in benzene (same conditions as for 4 and 6) gave no detectable reaction in the time required for complete disappearance of 4 and 6 (about 2 hrs.), thus eliminating photo-dimerization or polymerization of 7 as the source of the high-melting material. There is no evidence (glpc, spectra, base solubility) for formation of phenols in any of the above reactions.

FIGURE 1



Irradiation of lumisantonin 8 in 45% aqueous acetic acid at 0° is reported to give photosantonic acid in better than 90% yield,[15] a result which was easily verified. Under the same conditions, 6-epi-lumisantonin 6 gave a complex mixture of products, (glpc and tlc), 50% of which was extractable into aq. bicarbonate. Column chromatography of the "acid" fraction did not cleanly give the expected 6-epi-photosantonic acid but rather a complex mixture (nmr, glpc, tlc). Somewhat cleaner results were obtained by photolysis of 6 in methanol and 7 in benzene-methanol. Again mixtures were obtained including several methyl esters (NMR resonances at 3.9 ppm.), one component of which seems to be methyl 6-epi-photosantonate (9) (from comparison with NMR spectra of photosantonic acid). The source of these added unexpected complexities in the photochemistry of 7 in comparison with 3 is not clear at this time.

More definitive results were obtained from analysis of the "neutral" portion from photolysis of 6 in cold aq. HOAc. Chromatography afforded a new isomeric ketone, m.p. 146-148° (15% yield), assigned structure 10[12]. Spectral evidence: IR, 1780, 1660, 1630 and 830 cm^{-1}; $\lambda_{max}^{dioxane}$ 239 mu, ϵ 14,100; NMR (ppm in $CDCl_3$), 6.8 and 6.2 (doublets, J_{AB}=10 cps), each 1H, 4.9 doublet (1 H), 2.15 singlet (3 H) and 2.05 singlet (3 H).[16] Tetrahydro-derivative: IR 1780, 1720 cm^{-1}; nmr, no vinyl hydrogens, methyls shifted to 1.0-1.5 ppm. Further chromatography gave a phenol (2%) isolated as an oil, with the following spectral properties: IR, 3520, 3300, 1780, 1650 and 1150 cm^{-1}; UV, $\lambda_{max}^{dioxane}$ 280 (ϵ 900) and 225 mu (ϵ 3620); NMR, 6.68 singlet (1 H). The data are consistent with structures 11 or 12, but final assignment has not been made as yet. The phenol is strikingly similar in its properties to 5[9] (spectra, solubility in base, glpc retention time). Other minor unidentified products have also been isolated from the "neutral" fraction.

The formation of the spiro ketone 10 and a phenol on photolysis of 6 in cold aq. HOAc indicates that route A (Fig. 1) competes with route B when the lactone fusion is changed from *trans* to *cis*, supporting the steric control argument proposed by Kropp[5a,6].

The efficiency of these photochemical reactions has been determined initially with competition experiments. Irradiation of a mixture of α-santonin (1) and 6-epi-α-santonin (4) in benzene was followed by glpc, using conditions such that the disappearance of **1** and **4**, as well as the appearance of the corresponding lumiproducts **8** and **6** and dienones **3** and **7** (the latter are not separated) could be followed. **1** and **4** disappeared initially at the same rate, but after about 15 minutes it was clear that **1** was disappearing faster than **4**. Apparently, one of the products acts as a quencher for **4**, but not for **1**. A mixture of the two lumiproducts **8** and **6** was irradiated in benzene, and no substantial changes in the ratio **8**/**6** occurred during the photolysis (by glpc). Thus, the initial quantum yields for the 6-epi-isomers are virtually the same as those for santonin[7b] and lumisantonin.

FOOTNOTES AND REFERENCES

1. Part IX of a series on the photochemistry of unsaturated ketones in solution. Part VIII: D. I. Schuster and I. S. Krull, submitted for publication.
2. Supported in part by the U. S. Army Research Office (Durham), Grant No. DA-ARO(D)-31-124-G425.
3. American Cyanamid Corp. Summer Research Fellow, 1965.
4. For reviews see: (a) N. J. Turro, "Molecular Photochemistry", W. A. Benjamin, Inc., New York, N. Y., 1965; (b) O. L. Chapman, *Advan. Photochem.*, **1**, 323 (1963); (c) H. E. Zimmerman, *ibid*, **1**, 183 (1963).
5. (a) P. J. Kropp and W. F. Erman, J. Am. Chem. Soc., **85**, 2456 (1963); (b) C. Ganter, E. C. Utzinger, K. Schaffner, and O. Jeger, Helv. Chim. Acta, **45**, 2403 (1962); (c) H. Dutler, C. Ganter, H. Ryf, E. C. Utzinger, K. Weinberg, K. Schaffner, D. Arigoni and O. Jeger, *ibid*., **45**, 2346 (1962).
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7. (a) O. L. Chapman and L. F. Englert, *ibid*., **85**, 3028 (1963); (b) M. H. Fisch and J. H. Richards, *ibid*., **85**, 3029 (1963).
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10. Huang Minlon, J. Am. Chem. Soc., 70, 611 (1948); D. H. R. Barton, J. Org. Chem., 15, 467 (1950).

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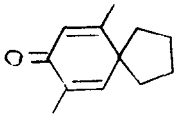
12. All new compounds gave satisfactory elemental analyses.

13. Columns used were Apiezon L, DC-11, or SE 30 on Chrom W A/W DMCS. Operating temperature varied from 200-220° on an F and M 810 dual column instrument equipped with a flame detector.

14. E. E. van Tamelen, S. H. Levin, G. Brenner, J. Wolinsky and P. E. Aldrich, J. Am. Chem. Soc., 81, 1666 (1959).

15. D. H. R. Barton, P. de Mayo and M. Shafiq, Proc. Chem. Soc., 205 (1957); J. Chem. Soc., 140 (1958).

16. These data compare with those for 13: UV, λ_{max} 246 mu (ϵ 15,600); IR, 1625, 1660 cm^{-1}, NMR: 6.72, 6.10, 1.96 and 1.88 ppm: P. J. Kropp, Tetrahedron 21, 2183 (1965).



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