5'-hydroxyl group is free, with dicyclohexylcarbodiimide (or with related compounds such as diisopropylcarbodiimide) and phosphoric acid or pyridinium phosphate in anhydrous dimethyl sulfoxide leads to a rapid and selective oxidation to the aldehyde.[1] We have now applied this reaction to the oxidation of a considerable number of other primary and secondary alcohols. Thus, addition of dicyclohexylcarbodiimide (3 mmoles) to a solution of p-nitrobenzyl alcohol (1 mmole) and anhydrous phosphoric acid (0.5 mmole) in dry dimethyl sulfoxide leads to the quantitative (thin layer chromatography) formation of p-nitrobenzaldehyde, which was isolated in 92% yield as the dinitrophenylhydrazone (m.p. 316–317°). In a similar fashion oxidation of 1-octanol gave octylaldehyde isolated in 70% yield as its crystalline dinitrophenylhydrazone (m.p. 104–105°). Optimal reaction conditions have been determined using the oxidation of testosterone to Δ^4-androstene-3,17-dione as a model and following the course of the reaction by quantitative thin layer chromatography. It has thus been shown that acids such as phosphoric acid, phosphorous acid, cyanoacetic acid, or pyridinium phosphate promote a rapid oxidation within a few hours at room temperature. On the other hand, stronger acids such as trifluoroacetic acid serve only poorly and mineral acids such as hydrogen chloride or sulfuric acid lead to no oxidation. All three of these, however, function well as their pyridine salts. A considerable variation in the amounts of acid (0.1–2.0 mole equiv.) and of carbodiimide (2–5 mole equiv.) can be used and the sulfoxide (tetramethylene sulfoxide is entirely suitable) may be diluted to the extent of 90% with an inert solvent if required. Thus, overnight reaction at room temperature of testosterone (2 mmoles), pyridinium trifluoroacetate (1 mmole), and dicyclohexylcarbodiimide (6 mmoles) in anhydrous dimethyl sulfoxide (5 ml.) results in quantitative oxidation to Δ^4-androstene-3,17-dione (m.p. 169–170°), which was isolated by direct crystallization in 92% yield.

In similar fashions, the oxidation of various types of steroidal alcohols have been studied, the nature of the acid catalyst being given in parentheses. The products were usually isolated by chromatography on silicic acid or by direct crystallization.[2] Cholane-24-ol (H_3PO_4) gave cholane-24-al (hydrate, m.p. 95°) in 85% yield. Cholestanol (H_3PO_4) gave cholestanone (m.p. 129°) in 68% yield. 3β-Acetoxy-Δ^5-androstene-17-one-19-ol (pyridinium trifluoroacetate) gave the pure 19-aldehyde (m.p. 141–143°) in 53% yield. Δ^5-Androstene-3-β-ol-17-one (pyridinium trifluoroacetate) was converted to the extent of 90% into the unconjugated ketone Δ^5-androstene-3,17-dione as judged by thin layer chromatography and ultraviolet spectra before and after mild acidic treatment, but partial migration of the double bond into conjugation occurred on attempted column chromatography. The pure Δ^5-3-one, λ_{max} 240 and 290 mμ; Σ_{max} 47 and 40 in methanol (m.p. 167–169° with migration of the double bond on heating[3]), was isolated in 55% yield by direct crystallization from acetone. The equatorial hydroxyl group of 11α-hydroxyprogesterone (pyridinium trifluoroacetate) was smoothly oxidized giving 11-keto-progesterone[4]

(m.p. 175–177°) in 68% yield. On the other hand, the axial 11β-hydroxyl of corticosterone-21-acetate was completely inert using pyridinium trifluoroacetate and was only partially dehydrated (22%) to 21-acetoxy pregna-4:9(11)-diene-3,20-dione[5] (22%) (m.p. 157–159°) using phosphoric acid. A similar pattern obtains with 11β-hydroxyprogesterone. The much less hindered pair of epimeric 3α- and β-hydroxy-5β-pregn-16-ene-20-ones, however, were oxidized at remarkably similar rates using either phosphoric acid or pyridinium trifluoroacetate to the 3-ketone and an anhydro compound (presumably Δ^2) in a ratio of 6:1 as determined by quantitative thin layer chromatography. The oxidation of hydroxy compounds containing strongly basic functions requires the addition of a molar excess of acid relative to the base for satisfactory oxidation. Thus, spegazzinidine dimethyl ether[6] is smoothly oxidized in the presence of 1.5 mole equiv. of phosphoric acid to give 3-dehydrospegazzinidine dimethyl ether[6] in 83% yield.

This method of oxidation thus appears to be of rather general utility and is particularly suited for use with otherwise labile compounds. The completely selective oxidation of primary alcohols to aldehydes with no trace of the corresponding acid is to be particularly noted. Further studies on this reaction, which somewhat resembles the Kornblum oxidation of alkyl halides or tosylates,[7] and a discussion of its probable mechanism will be presented shortly.

(5) R. Casanova, C. W. Shoppee, and G. H. R. Summers, J. Chem. Soc., 2983 (1953).

(6) C. Djerassi, H. W. Brewer, H. Budzikiewicz, O. O. Orazi, and R. A. Corrall, J. Am. Chem. Soc., 84, 3480 (1962).

(7) N. Kornblum, W. J. Jones, and G. J. Anderson, ibid., 81, 4114 (1959).

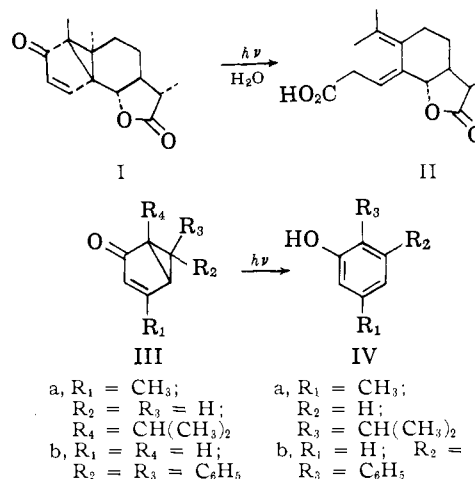CONTRIBUTION No. 10   K. E. PFITZNER
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A Mechanistically Significant Intermediate in the Lumisantonin to Photosantonic Acid Conversion[1]

Sir:

We wish to report the isolation and identification of a mechanistically significant intermediate in the lumisantonin (I) to photosantonic acid (II) conversion.[2,3] This intermediate points to a clear relationship between the conversion of I to II and the photoisomerization of

I   II

III   IV

a, $R_1 = CH_3$;
  $R_2 = R_3 = H$;
  $R_4 = CH(CH_3)_2$
b, $R_1 = R_4 = H$;
  $R_2 = R_3 = C_6H_5$

a, $R_1 = CH_3$;
  $R_2 = H$;
 $R_3 = CH(CH_3)_2$
b, $R_1 = H$; $R_2 =$
  $R_3 = C_6H_5$

(1) Part VIII of the Photochemical Transformations Series. For Part VII see O. L. Chapman, H. G. Smith, R. W. King, D. J. Pasto, and M. R. Stoner, J. Am. Chem. Soc., 85, 2031 (1963).

(2) D. H. R. Barton, P. de Mayo, and M. Shafiq, Proc. Chem. Soc., 345 (1957); J. Chem. Soc., 3314 (1958).

(3) E. E. van Tamelen, S. H. Levin, G. Brenner, J. Wolinsky, and P. Aldrich, J. Am. Chem. Soc., 80, 501 (1958); ibid., 81, 1666 (1959).

(1) K. E. Pfitzner and J. G. Moffatt, J. Am. Chem. Soc., 85, 3027 (1963).

(2) All compounds gave satisfactory elemental analyses and ultraviolet and infrared spectra.

(3) C. Djerassi, R. R. Engle, and A. Bowers, J. Org. Chem., 21, 1547 (1956); and W. R. Nes, E. Loeser, R. Kirdani, and J. Marsh, Tetrahedron, 19, 299 (1963), report m.p. 119–125° while A. Butenandt and J. Schmidt–Thome; Ber., 69, 882 (1936), report 158°. We have been able to detect only the faintest transition at 125° and have positively identified the melted product as the rearranged Δ^4-3-one.

(4) D. H. Peterson, H. C. Murray, S. H. Eppstein, L. M. Reineke, A. Weintraub, P. D. Meister, and H. M. Leigh, J. Am. Chem. Soc., 74, 5933 (1952).

the related ketones IIIa[4] and IIIb[5] to phenols IVa and IVb. The ketene–carbene mechanism previously suggested to account for the conversion of I to II[2,3] fails to account for the conversion of IIIa and IIIb to the corresponding phenols. The polar state concept[6-8] provides a smooth rationalization of both processes and in addition implicates a potentially isolable intermediate V between I and II.[9] Photochemical conver-

I

II V

IIIa IVa
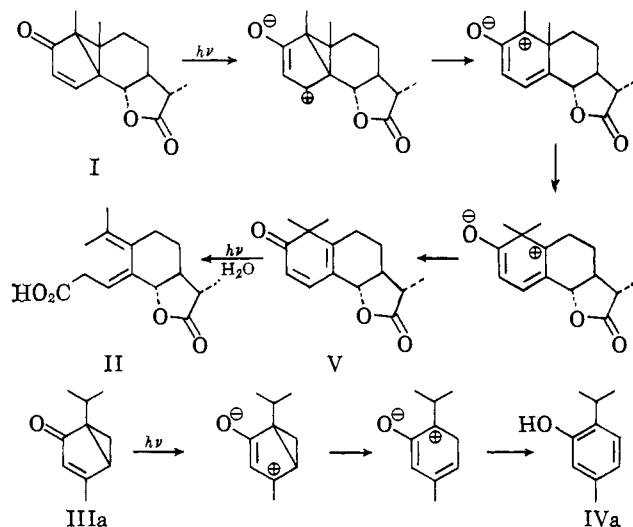
sion of a 2,4-cyclohexadienone such as V to an unsaturated acid such as II is a well documented process.[7,10]

Irradiation[11] of lumisantonin (I) in anhydrous ether leads to formation of an oily product identified as V by the following observations. The intermediate, purified by vapor phase chromatography, shows infrared absorption at 5.62 (lactone carbonyl), 6.03 (conjugated carbonyl), and 6.13 μ (double bonds) and ultraviolet absorption at 308 mμ in accord with expectation. The n.m.r. spectrum of V shows two olefinic protons as a pair of doublets (J_{AX} = 9.9 c.p.s.) at 2.85 and 4.00 τ.[12]

Treatment of V under mild conditions with 2,4-dinitrophenylhydrazine in phosphoric acid gives the 2,4-dinitrophenylhydrazone of V,[13] m.p. 252–254°. Treatment of V with 2,4-dinitrophenylhydrazine in ethanolic sulfuric acid gives an isomeric 2,4-dinitrophenylhydrazone, m.p. 228–230°, identical with the 2,4-dinitrophenylhydrazone of VI prepared previously.[3] It seems reasonable that the more vigorous acid condi-

VI
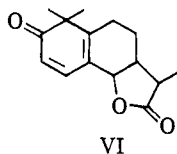
(4) J. W. Wheeler and R. H. Eastman, *J. Am. Chem. Soc.*, **81**, 236 (1959);

(5) H. E. Zimmerman and D. I. Schuster, *ibid.*, **84**, 4527 (1962).

(6) O. L. Chapman and S. L. Smith, *J. Org. Chem.*, **27**, 2291 (1962).

(7) D. H. R. Barton and G. Quinkert, *J. Chem. Soc.*, 1 (1960).

(8) C. Ganter, R. Warszawski, H. Wehrli, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **46**, 320 (1963).

(9) The possibility of an intermediate such as V between I and II has been considered previously. See footnote 53 of ref. 5 and K. Weinberg, E. C. Utzinger, D. Arigoni, and O. Jeger, *Helv. Chim. Acta*, **43**, 236 (1960).

(10) W. G. Dauben, D. A. Lightner and W. K. Hayes, *J. Org. Chem.*, **27**, 1897 (1962).

(11) A General Electric UA-3 mercury arc lamp was used. Irradiation was carried out in a Pyrex vessel.

(12) This value for the olefinic coupling constant is in accord with expectation for *cis*-vinyl protons in a six-membered ring (O. L. Chapman, *J. Am. Chem. Soc.*, **85**, 2014 (1963); G. V. Smith and H. Kriloff, *ibid.*, **85**, 2016 (1963); P. Laszlo and P. von R. Schleyer, *ibid.*, **85**, 2017 (1963). The low field position of the β-olefinic proton is consistent with the deshielding effect of the carbonyl group and the second double bond.

(13) This derivative is identical in melting point and infrared absorption with a sample prepared by Prof. J. Richards and co-workers, *J. Am. Chem. Soc.*, **85**, 3029 (1963).

tions epimerize C-6 giving the more stable fusion of the lactone ring.

The intermediate V is rapidly converted to photosantonic acid in the presence of light and water. The ultraviolet absorption of V is not observed in the conversion of lumisantonin (I) to photosantonic acid (II) in aqueous organic solvents because the rate of destruction of the intermediate is greater than the rate of formation. Irradiation[11] of lumisantonin (II) in anhydrous ether in a Pyrex vessel required 2.5 hr. to achieve the maximum concentration of V. Addition of 2% water and continued irradiation under identical conditions leads to complete disappearance of V in less than 45 min.

The isolation of V as an intermediate in the conversion of I to II emphasizes the dangers inherent in interpretation of photochemical processes without a detailed knowledge of the nature and number of discrete photochemical reactions involved.

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The Mechanism of the Photoconversion of Santonin

Sir:

The photochemistry of santonin has an illustrious history which has dealt, in the main, with the isolation, characterization, and interrelation of the manifold products formed on exposure of santonin to light in various media.[1] The established course of the reaction in certain media is from santonin (I) to lumisantonin (II) and thence to photosantonic acid (IV).[2,3]

I II

III IV
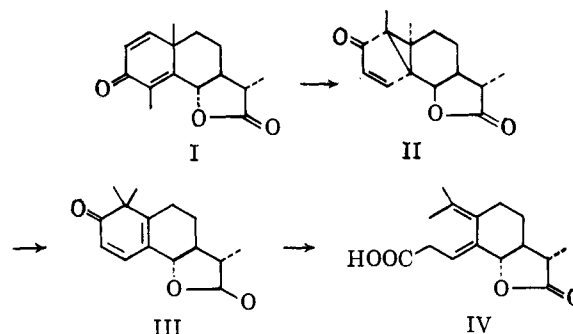
We should like to report evidence that the photoconversions of santonin and lumisantonin involve as intermediates the triplet states of the respective substances and that there exists an important intermediate (III)[4] between lumisantonin and photosantonic acid.

The evidence relative to the first assertion is the demonstration that in appropriate systems there is a transfer of triplet character and energy from photo-

(1) D. Arigoni, H. Bosshard, H. Bruderer, G. Büchi, O. Jeger, and L. J. Krebaum, *Helv. Chim Acta*, **40**, 1732 (1957).

(2) D. H. R. Barton, P. de Mayo, and M. Shafiq, *J. Chem. Soc.*, 3314 (1958).

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

(4) The presence of III as an intermediate in the photoconversion of lumisantonin to photosantonic acid has been previously suggested. [K. Weinberg, E. C. Utzinger, D. Arigoni, and O. Jeger, *Helv. Chim. Acta*, **43**, 236 (1960); H. E. Zimmerman and D. I. Schuster, *J. Am. Chem. Soc.*, **84**, 4527 (1962).]