removed *in vacuo*. One gram (28.9%) of product was obtained which was purified by sublimation, m.p. 147–148°.

Anal. Calcd. for C_5H_9ON: C, 60.58; H, 9.15. Found: C, 60.40; H, 9.16.

Attempted Preparation of 2-Methylcyclopropane-1,1-dicarboxamide.—The procedure recommended[51] for diesters was used. From 500 ml. of methanol, 0.23 g. (0.01 g. atom) of sodium and 20 g. (0.10 mole) of diethyl 2-methylcyclopropane-1,1-dicarboxylate[52] there was obtained, after removal of ammonia and methanol *in vacuo*, 15 g. of water-soluble material. Recrystallization from benzene gave 12 g. (76%) of white crystals, m.p. 72–73°, whose elemental composition suggests that the compound may be **methyl 2-methylcyclopropane-1-carboxamide-1-carboxylate**.

Anal. Calcd. for $C_7H_{11}NO_3$: C, 53.49; H, 7.05; N, 8.91. Found: C, 53.01; H, 6.95; N, 10.13.

2-Methylcyclopropane-1,1-dicarbonyl Chloride.—A mixture of 45 g. (0.31 mole) of 2-methylcyclopropane-1,1-dicarboxylic acid[52] and 60 g. (0.5 mole) of thionyl chloride was stirred at room temperature for 1 hour and then heated at 65–80° for 2 hours. After standing overnight, distillation yielded 23 g. (40%) of a light yellow oil, b.p. 76–82° (15 mm.).

Anal. Calcd. for $C_6H_6O_2Cl_2$: Cl, 39.17. Found: Cl, 38.79.

1,1-Dibenzoylethylene.—A mixture of 12.7 g. (0.05 mole) of dibenzoylmethane, 20 ml. of diethylamine and 35 ml. of ether was cooled in an ice-bath. To the mixture there was added 8 g. (0.1 mole) of 37.3% formalin solution. After standing overnight, the white solid which had crystallized from the reaction mixture was collected, weight 11.6 g. (98%). It was recrystallized from ethanol, m.p. 178–179°. It had infrared bands at 1692 (C=O) and 1667 cm.$^{-1}$ (C=C).

Anal. Calcd. for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found: C, 81.33; H, 5.56.

1-Acetyl-2-nitro-2,3,3-trimethylcyclopropane 2,4-dinitrophenylhydrazone was reported by Smith and Kohlhase[53] with a molecule of methanol of crystallization. The 2,4-dinitrophenylhydrazone prepared in the present work by the procedure of Brady[41] melted at 161–162° after recrystallization from ethanol. Its analysis indicates the absence of solvent of crystallization.

Anal. Calcd. for $C_{14}H_{17}N_5O_6$: C, 47.86; H, 4.88. Found: C, 48.05; H, 4.45.

Infrared spectra were obtained with a Perkin–Elmer model 21 spectrophotometer equipped with sodium chloride optics and a linear wave length scale. All spectra were determined on carbon tetrachloride solutions (3–6%). Since the precision required to obtain significant determinations of the shifts in the C=O and C≡N stretching frequencies is greater than that required by the instrument manufacturer's specifications, the following procedure was used to test the instrument's precision and is typical of that used for each pair of compounds to be compared.

The instrument was allowed to warm up for two hours and the scale expanded by a factor of 8 by changing gears. The spectrum of a solution of one of the cyclopropane compounds was then determined from 5.700 to 6.000 μ on blank paper ten consecutive times. A line was drawn through each of the C=O bands at that point which visually appeared to bisect the band. The positions of the peaks were then determined by measuring the distance from the 5.700 μ (by counter) line to the line bisecting the C=O band. The average value obtained from the ten C=O bands was 5.944 ± 0.0006 μ. The 5.700–6.000 μ region of the spectrum of a second cyclopropane compound to be compared with the first was then determined five times in the same way. The C=O band of the first compound was redetermined at this point and its value was within the limits of the values of the first ten determinations. The last five determinations for the second compound were then made. The average value for the C=O band of the second compound was 5.936 ± 0.0004 μ. Similar reproducibilities of better than ±1 cm.$^{-1}$ were obtained with each pair of compounds.

The instrument was calibrated periodically in the region of the C=O band against water vapor and in the region of the C≡N band against a polystyrene film. After applying these corrections the average values were converted to frequency values.

Ultraviolet spectra were determined with a Beckman model DU spectrophotometer using 95% ethanol solutions. Readings were taken at 0.5-mμ intervals in the regions of the maxima. Maxima below *ca.* 215 mμ were obtained with the selector switch set at the 0.1 position.

Amherst, Mass.

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(51) P. B. Russell, This Journal, **72**, 1853 (1950).

(52) R. Marburg, *Ann.*, **294**, 111 (1896).

(53) L. I. Smith and W. L. Kohlhase, *J. Org. Chem.*, **21**, 816 (1956). Prior to publication of this paper we had independently carried out the same reaction sequence in an attempt to prepare 1-nitro-1,2,2-trimethylcyclopropane. Attempts to cleave 1-acetyl-2-nitro-2,3,3-trimethylcyclopropane by the haloform reaction and the method of L. C. King [This Journal, **66**, 894 (1944)] failed.

[Contribution from the Department of Chemistry, University of Wisconsin]

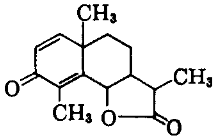
The Structure of Photosantonic Acid[1]

By Eugene E. van Tamelen, Stephen H. Levin,[2] Gerald Brenner, Joseph Wolinsky
and Paul E. Aldrich

Received October 1, 1958

Chemical and physico-chemical findings are presented which define the structure (VIII) of photosantonic acid, the well-known irradiation product of the sesquiterpene santonin. Various chemical transformations and the mechanism of formation of photosantonic acid are discussed in terms of the developed structure.

Of the major constitutional problems which substances derived from santonin (I) have posed in past years, only the structure of photosantonic acid has remained unsolved, despite the fact that this irradiation product has been known since the dawn of structural organic chemistry.[3]



I

Photosantonic acid, an optically active solid of melting point 154–155°, can be prepared by irradiating a solution of santonin with ultraviolet light, or, as was the practice of the early Italian workers, exposing the solution to sunlight for some weeks.

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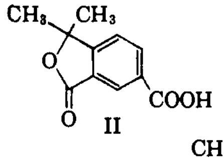
(1) First reported in a Communication to the Editor, This Journal, **80**, 501 (1958).

(2) Allied Chemical and Dye Corporation, Nitrogen Division, Fellow.

(3) For reviews and references to the early Italian work on photosantonic acid, see (a) "Elsevier's Encyclopedia of Organic Chemistry," edited by F. Radt, Elsevier, Amsterdam, 1953, Series III, Vol. 12B, p. 3733, and (b) J. Simonsen and D. H. R. Barton, "The Terpenes," University Press, Cambridge, 1952, Vol. III, 2nd Edition, p. 249.

Of the substances formed under such conditions, photosantonic acid has been the object of greatest attention in the past, having been studied during the last century by Sestini, Cannizzaro, Villavechia, Bargellini and others.[3] It was demonstrated early that photosantonic acid possesses the molecular formula $C_{15}H_{20}O_4$. The substance is, therefore, a hydration product of santonin, implying that the carbonyl containing ring of santonin has been opened, leaving two double bonds, or their equivalents, somewhere in the molecule. This interpretation received support in the study of what is perhaps the most important transformation product, "dehydrophotosantonic acid"[4,5] ($C_{15}H_{20}O_4$), formed by the action of hydrogen chloride–ethanol under vigorous conditions. On the basis of its oxidation to 3,3-dimethylphthalide-6-carboxylic acid (II),[4,6,7] and decarboxylation to 2,4-diethyl-isopropylbenzene (III), the presence of a trisubstituted benzene ring seemed likely, and structure IV was proposed for this isomerization product. In 1892, Cannizzaro[4] suggested for photosantonic acid the partially conjectural structure V, which, ten years later, was modified on trivial grounds to VI.[8] Finally, structure VII, apparently an equally arbitrary proposal, appeared in 1952.[3b]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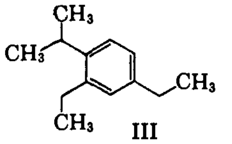
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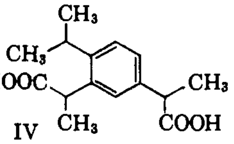
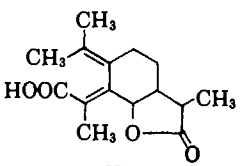

IV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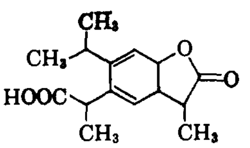
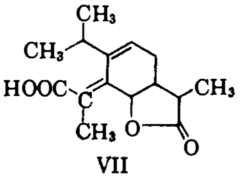

VI

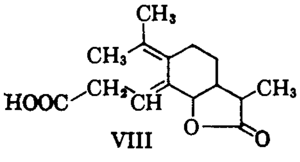

VII

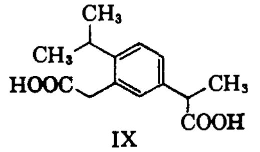
Investigations in these laboratories began with examinations of the general, physical and spectral properties of photosantonic acid. The acid appeared to be homogeneous, since the melting point range could not be improved by repeating crystallization, and no separation was detected by chromatography. Despite the use of techniques which allow reliable ultraviolet measurements down to about 200 mμ, no maximal absorption in the spectrum of photosantonic acid or its methyl ester could be detected.[9] The infrared spectrum served well in substantiating the nature of the oxygen functions in the irradiation acid. The carboxy group showed the expected absorption at 5.84 μ. A second carbonyl band, at 5.65 μ, of the same general shape and falling at the same position as the lactone band in santonin, suggested that during the conversion to photosantonic acid this function had remained intact, and subsequent findings did not require revision of this view.

Although photosantonic acid, as will be demonstrated later, possesses an unusual structure and arises from santonin by an intricate reaction sequence, the degradation results which minimally define the constitutional nature of this acid are simple. For a rigorous development of the structure, we must refer to subtle physical methods as well as additional definitive chemical evidence, which will be presented in turn.

Ozonization of photosantonic acid in acetic anhydride at −78° resulted in the formation of acetone in high yield—thereby indicating the presence of an isopropylidene group— and also a crystalline lactonic diacid with the formula $C_9H_{12}O_6$. By using a reductive work-up of the ozonide, there was formed in modest amount, acetaldehyde; if, on the other hand, hydrogen peroxide was allowed to act on the ozonization products, a fair yield of malonic acid could be isolated. This set of results can be interpreted readily if we assume that photosantonic acid bears a *vinylacetic acid side chain*. This unit is cleaved initially to formylacetic acid, or its equivalent; normally this unstable acid will suffer decarboxylation, giving acetaldehyde, but under oxidizing conditions, it can be converted instead to the observed diacid. A close parallel of this set of results can be found in the case of γ,γ-dimethylvinylacetic acid.[10] Bearing in mind the evidence which reflects the presence of a 1,2,4-trisubstituted cyclohexane ring, we see that structure VIII for photosantonic acid represents the most direct utilization of the ozonization data.[11] This expression

$$\begin{tikzcd}
>C{=}CHCH_2COOH \arrow[d] & & CO_2 + CH_3CHO \\
\text{ozonide} \arrow[r] & C_9H_{12}O_6 + (CH_3)_2CO + & CHOCH_2COOH \arrow[u] \arrow[d, "(O)"] \\
 & & CH_2(COOH)_2
\end{tikzcd}$$


VIII


IX

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(4) S. Cannizzaro and P. Gucci, *Atti R. accad. Lincei*, **5**, 1, II, 149 (1892); *Gazz. chim. ital.*, **23**, I, 286 (1893).

(5) This misnomer was coined at a time when photosantonic acid was believed to have the formula $C_{15}H_{22}O_5$.

(6) (a) G. Bargellini, *Gazz. chim. ital.*, **40**, II, 27 (1910); (b) G. Bargellini and G. Forli-Forti, *ibid.*, **40**, II, 74 (1910).

(7) Confirmed in this Laboratory.

(8) L. Francesconi and L. Venditti, *Gazz. chim. ital.*, **32**, I, 281 (1902).

(9) D. H. R. Barton, P. de Mayo and M. Shafiq, *J. Chem. Soc.*, 929 (1957), report for photosantonic acid λ_{max} 210 mμ (ε 6700).

(10) A. A. Goldberg and R. P. Linstead, *ibid.*, 2354 (1928).

(11) Structures which contain a five-membered carbocyclic ring (*e.g.*, I) were rejected because of: their remote resemblance to san-

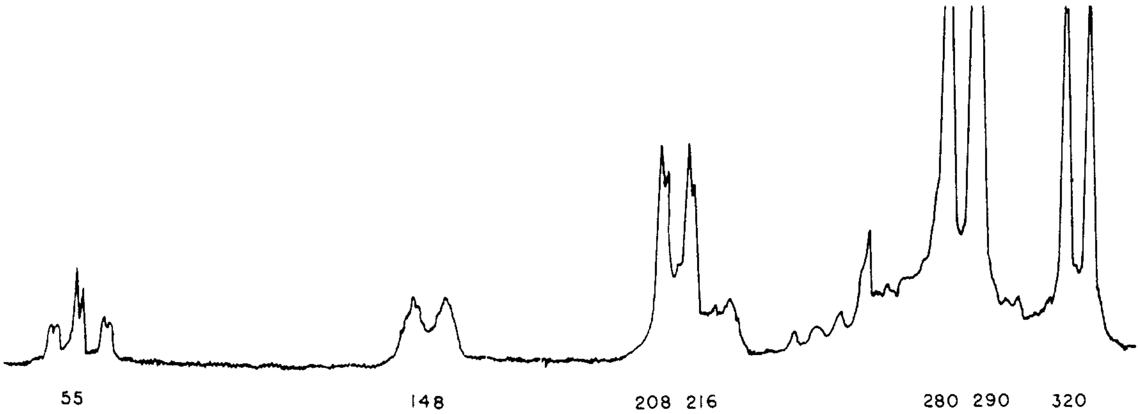
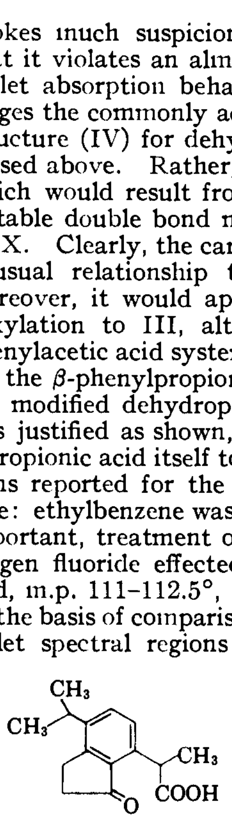
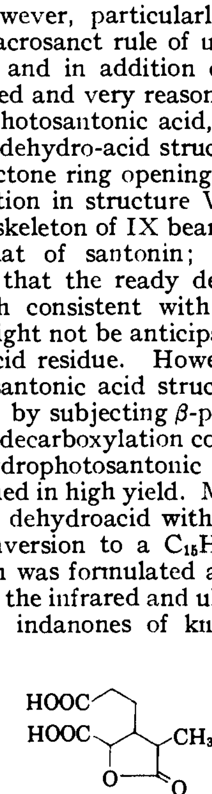


Fig. 1.—Proton magnetic resonance spectrum of photosantonin, dissolved in 50:50 CCl_4-$CDCl_3$; frequency, 60 mc.; field, 14,100 gauss. Benzene reference = 0.

evokes much suspicion, however, particularly in that it violates an almost sacrosanct rule of ultraviolet absorption behavior, and in addition challenges the commonly accepted and very reasonable structure (IV) for dehydrophotosantonic acid, discussed above. Rather, the dehydro-acid structure which would result from lactone ring opening and suitable double bond migration in structure VIII, is IX. Clearly, the carbon skeleton of IX bears an unusual relationship to that of santonin; and moreover, it would appear that the ready decarboxylation to III, although consistent with the phenylacetic acid system, might not be anticipated for the β-phenylpropionic acid residue. However, the modified dehydrophotosantonic acid structure was justified as shown, first, by subjecting β-phenylpropionic acid itself to the decarboxylation conditions reported for the dehydrophotosantonic acid case: ethylbenzene was formed in high yield. More important, treatment of the dehydroacid with hydrogen fluoride effected conversion to a $C_{15}H_{16}O_3$ acid, m.p. 111–112.5°, which was formulated as X on the basis of comparison in the infrared and ultraviolet spectral regions with indanones of known structure.[12] The observed cyclodehydration excludes the historical structure for the dehydro-acid and places the newer structure, and also the presently proposed structure for photosantonic acid, on more secure grounds. The constitution XI for the $C_9H_{12}O_6$ ozonization product follows, and its formation can be considered to support the assignment made.

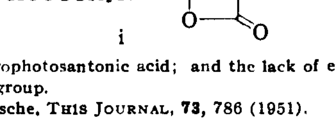

X


XI

While the work described above was in progress, there was acquired physico-chemical evidence which excludes certain other photosantonic acid structures, subtle modifications of VIII capable of readily accommodating much of the known chemistry. Through the coöperation of Varian Associates, 60 mc. proton magnetic resonance spectra of photosantonic acid (and derivatives) were obtained, and one of these is reproduced in Fig. 1.[13] The doublet falling at 320 c.p.s. is associated with the lactone methyl group, the peak being split by the single hydrogen on the α-position of the ring. Appearing at a slightly lower field (280 and 290 c.p.s.) are the two remaining methyl groups, their positions relative to the lactone methyl being due to the shielding of the double bond to which they are attached. The separation of the bands indicates that the two methyl groups are non-equivalent, a deduction in keeping with the different steric environments of the two groups as required by structure VIII. The absorption between approximately 200 and 280 c.p.s. reflect the presence of the various methylene groups and also the β-methine hydrogen of the lactone ring. Attention should be drawn particularly to the doublet (208 and 216 c.p.s.), which, because of its low position in the spectrum, indicates the presence of a methylene group attached to certainly one, and probably two unsaturated carbon atoms, which are, in fact, the carboxyl carbon and the β-carbon in the vinylacetic acid side chain. The doublet at 148 c.p.s. arises from the γ-hydrogen on the lactone ring, interacting with the single neighboring β-hydrogen; thus the presence of the lactone system, substituted as shown in formula VIII, is independently confirmed by its n.m.r. behavior. Finally, the presence of a vinylic hydrogen, as featured in structure VIII for photosantonic acid, is completely confirmed by the presence of a triplet at 55 c.p.s., the position being normal for a hydrogen on an olefinic bond, and the area enclosed by the peaks indicating the presence of *one* such atom.

Dehydrophotosantonic acid was also subjected to n.m.r. analysis. After confirming by its ultraviolet

tonin, and the great difficulty in rationalizing the genesis of such structures; the complications involved in arriving at the benzenoid system



present in dehydrophotosantonic acid; and the lack of evidence for a fourth C-methyl group.

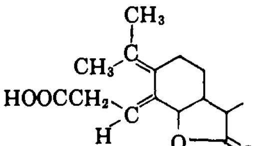
(12) C. D. Gutsche, This Journal, 73, 786 (1951).

(13) The chemical shifts reproduced herein should be regarded as replacing the values listed in ref. 1, footnote 11, some of which were in error.

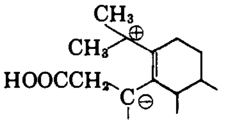
spectrum the presence of an aromatic ring, the problem was treated as a differentiation of isomeric side chain possibilities, in particular those represented by structures IV and IX. In the C-methyl hydrogen region of the n.m.r. spectrum the isopropyl group manifests itself as a region of two equivalent methyl groups, the peak being split by the benzylic hydrogen. Falling at somewhat lower fields, because of its proximity to the carboxyl group, the peak of the methyl group in the α-propionic acid side chain—split, as expected, by the benzylic hydrogen—possesses an area indicating the presence of *one* such unit. The absorption area, falling at still lower fields, which was ascribed to the methylene groups, bears to the C-methyl hydrogen area a ratio very close to that (4:9) required by structure IX. Thus, in several respects, the favored expression for dehydrophotosantonic acid is supported by interpretation of its n.m.r. pattern.

The derived structure IX for the dehydro-acid, possessing only one asymmetric center, does not allow for the two racemates alleged to have been isolated by Cannizzaro and Gucci.[4] Although an attempt was not made in this Laboratory to confirm this report, no racemic, diastereoisomeric forms of the dehydrophotosantonic acid used were encountered, and we are inclined to the view that, if Cannizzaro and Gucci had in hand an optically inactive substance with different physical properties, it was a crystalline modification.[14]

By making full use of the physical data available, it becomes possible to develop a more detailed structural picture of photosantonic acid. As pointed out above, the acid, despite the presence of a conjugated diene system, has no discernible absorption peak in the usual ultraviolet region, a property which is, in terms of structure VIII, sufficiently unusual to justify some comment. It can be demonstrated (*vide infra*) that the geometry around the trisubstituted double bond in photosantonic acid is represented correctly by formula XII. In this geometrical isomer, the steric interference between the acetic acid radical and one of the methyl groups of the isopropylidene residue is severe, and a molecular model demonstrates that the two olefinic systems cannot begin to approach planarity; rather, a carbocyclic, chair-like conformation with olefinic bonds extending radially, with normal bond angles, seems to be preferable, at least sterically. As a consequence of this geometry, resonance interaction between the two double bonds appears to be hampered to such an extent that ultraviolet-induced excited states such as XIII are of such high energy that above 200 mμ they do not make any detectable contribution. Although this case is a striking one, it should be mentioned that (1) the parent system 1,2-dimethylenecyclohexane has itself an abnormally low (λ_{max} 220 mμ) absorption band,[15] and (2) the spectral effects of restricted rotation in the biphenyl series are also dramatic[16] and serve to illustrate how important a role steric factors can play. This effect has not been as widely recognized in the aliphatic series, but the present case shows that the ultraviolet region cannot be used indiscriminately as a diagnostic test for the conjugated diene system.[17]

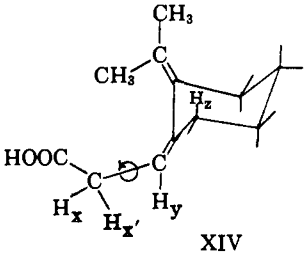


XII



XIII

Returning to the nuclear magnetic resonance spectrum, we find that the fine structure reflects otherwise obscure characteristics and interactions of atoms in the area of the diene system. The fact that the vinyl hydrogen resonance appears as a *symmetrical* triplet indicates that the attached methylene group is free to rotate (as indicated by the circular arrow in formula XIV) and that, therefore, equal coupling of the two methylene hydrogens (H_x and $H_{x'}$) with the olefinic hydrogen can occur ($H_xH_y = H_{x'}H_y$). Further, additional splitting of each of the lines in the 55 c.p.s. region and also of the methylene hydrogen (H_x and $H_{x'}$) bands at 208 and 216 c.p.s. indicates[18] that coupling to a *fourth* hydrogen atom must be involved. The only hydrogen close enough for such interaction is the one (H_z) on the carbon bearing the ethereal oxygen of the lactone ring, and the complex, although only partially resolved, group of spin-spin components in the 148 c.p.s. region supports this interpretation. Thus, in the structural makeup of photosantonic acid, we must include the nuclear magnetic interactions H_yH_z, and also (H_xH_z, $H_{x'}H_z$), despite the fact that the latter coupling involves *five* bonds. It would be anticipated normally that coupling through this many bonds would not occur: thus, for example, the isopropylidene methyl group hydrogens and the closest hydrogen neighbor (again a hypothetical five-bond interaction) do not coöperate to give peak splitting in the 280–290 c.p.s. region.[19]



XIV

At about the same time that our preliminary Communication[1] describing the above results appeared, Barton, de Mayo and Shafiq[20] published

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[14] The "second racemate was obtained from the first by heating, and possessed a melting point (133.5–134.5°) virtually identical with that (134.5–135.5°) of the original substance.

[15] A. T. Blomquist and D. T. Longone, THIS JOURNAL, **79**, 3916 (1957).

[16] B. Williamson and W. H. Rodebush, *ibid.*, **63**, 3018 (1941).

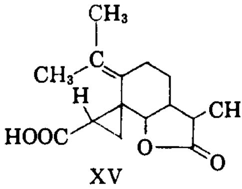
[17] A. T. Blomquist and A. Goldstein, *ibid.*, **77**, 998 (1955), report that *cis-cis*-cyclodecadiene does not display maximal absorption in the 215–230 mμ region.

[18] These splittings are unchanged at 25 mc., indicating that they are independent of applied magnetic field and are true spin–spin couplings.

[19] Because of peak heights, this is not evident from Fig. 1 but is observable in different, unpublished spectra.

[20] D. H. R. Barton, P. de Mayo and M. Shafiq, *Proc. Chem. Soc.*, 345 (1957).

their proposal (XV) for the structure of photosantonic acid. Some of the results used to deduce this structure will be treated in subsequent parts of this discussion, although we believe that the findings already presented herein are sufficient to eliminate this structure from consideration. Rationalization of the ozonization results in their entirety is awkward on the basis of the cyclopropane structure. In addition, the structure fails to account for certain of the n.m.r. data, especially that which demands a trisubstituted olefinic system. Corresponding to the vinylic hydrogen in structure VIII is the hydrogen in the α-position of the cyclopropanecarboxylic acid system, and one might question whether, because of its unique environment in structure XV, its chemical shift in the n.m.r. might be of such magnitude that it would be mistaken for an olefinic hydrogen. Fortunately, the n.m.r. spectrum of an excellent model, dihydro Feist's acid (XVI),[21] provides an unequivocal answer. The olefinic hydrogen region is, as expected, free of absorption, and the signals due to carbon-bound hydrogen appear at much higher fields, 125–150 c.p.s. relative to water (obtained at 40 mc., 9400 gauss), normal for hydrogens of this type.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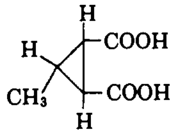
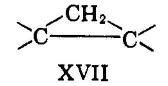
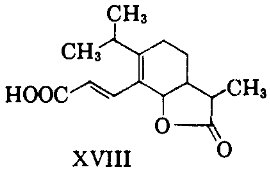
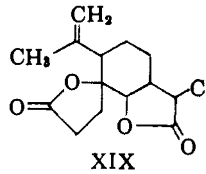

XVI

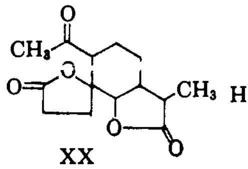
Recently Washburn and Mahoney[22] demonstrated that in the near infrared region of the spectrum, a varied series of model compounds with the partial structure XVII, including a cyclopropanecarboxylic acid derivative, consistently show absorption within the narrow limits 1.63–1.65 μ. Photosantonic acid is completely transparent in this region, indicating again the unsuitability of structure XV.[23]

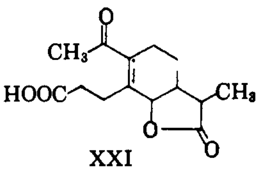

$$>C\overset{CH_2}{\text{——}}C<$$
XVII

With the structure of photosantonic acid well established, it becomes appropriate to consider certain others of the chemical transformations which the substance undergoes. It has been noted already that hydrogen chloride–ethanol can, under severe conditions, cause conversion of photosantonic acid to dehydrophotosantonic acid (IX). We have found that, whereas the irradiation acid is largely recovered after treatment with hydrogen chloride–chloroform at room temperature or 70% sulfuric acid at 0°, a complex mixture results on shaking the acid for several hours at room temperature with concentrated hydrochloric acid. Chromatography of the acidic portion of this mixture resolved it into the starting material; dehydrophotosantonic acid; and two oily acids, one absorbing in the ultraviolet at 242 mμ, and the other at 268 mμ, possibly indicating the presence of an α,β–γ,δ-doubly-unsaturated carboxylic acid (XVIII). From the neutral material obtained by the hydrochloric acid treatment, there crystallized in small yield a substance, $C_{15}H_{20}O_4$, for which we propose the structure XIX. The product displayed in the infrared, olefinic absorption at 6.10 μ and a single broad carbonyl band at 5.65 μ, with an intensity indicative of two γ-lactone systems. Ozonization of the dilactone yielded formaldehyde and the norketone XX, m.p. 215.5–217.5°, the structure of which was confirmed by: the presence of a new carbonyl band at 5.86 μ; a positive iodoform test; and development, on treatment with dilute aqueous base, of an ultraviolet maximum at 244 mμ, due to the unsaturated ketone XXI formed by β-elimination of the ethereal lactone oxygen.


XVIII


XIX


XX


XXI

Treatment of photosantonic acid with molecular bromine resulted in the formation of a bromination product[24] ($C_{15}H_{19}BrO_4$), m.p. 171–171.5°, in high yield. Examination of its infrared spectrum revealed that the original γ-lactone band had been retained, but that the carboxyl band had been replaced by a new one, appearing at 5.80 μ, consistent with the presence of a δ-lactone grouping. Although the bromodilactone was resistant to further bromination, the magnitude of the end absorption in the ultraviolet (Fig. 2) indicated that a double bond, di- or trisubstituted, was still included in the molecular makeup. The observation that treatment with metallic zinc smoothly regenerated photosantonic acid suggests that the bromination is not complicated by any unusual chemical change, and the structure XXII is therefore proposed for the bromodilactone.

It is of interest that attempted catalytic reduction of the bromolactone over platinum gave, in

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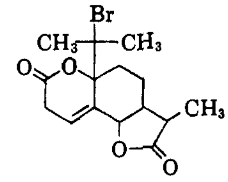
[21] (a) M. Ettlinger, *Chemistry & Industry*, 166 (1956); (b) A. S. Kende, *ibid.*, 437 (1956); (c) A. T. Bottini and J. Roberts, *J. Org. Chem.*, **21**, 1169 (1956).

[22] W. H. Washburn and M. J. Mahoney, This Journal, **80**, 504 (1958).

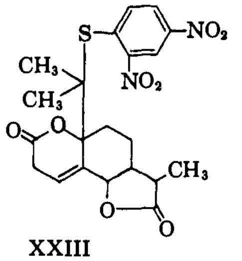
[23] Prof. Barton has acknowledged the correctness of our photosantonic acid structure (VIII): D. H. R. Barton, P. de Mayo and M. Shafig, *J. Chem. Soc.*, 3314, (1958).

[24] This transformation product, or a similiar one, was prepared independently by Barton, de Mayo and Shafiq (ref. 20).



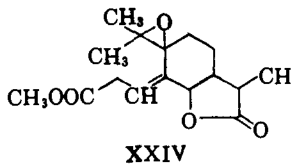
XXII

addition to starting material, some photosantonic acid. The latter arose, in all probability, by a reaction in which platinum, like zinc, serves to abstract halogen and thereby generate a double bond. In a similar vein, the derived 2,4-dinitrobenzenemercaptodilactone (XXIII) was found to give, on treatment with Raney nickel in ethanol, the ethyl ester of photosantonic acid.

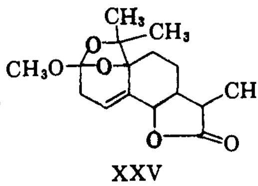


XXIII

Photosantonic acid or its methyl ester consumes only one mole of peracid. Thus, methyl photosantonate, when subjected to the action of excess monoperphthalic acid in ether, was transformed into an oxide,[24] m.p. 76–77°. The presence of the lactone and ester functions was confirmed by infrared analysis, and the persistence of a double bond was suggested again by the ultraviolet data (Fig. 2). Even more revealing in the way of physical data was the n.m.r. behavior: the close similarity to the spectrum of photosantonic acid and its methyl ester indicated that the vinylacetic acid side chain had remained intact, and that no oxygenation of a double bond with hydrogen attached had taken place, *i.e.*, epoxidation of a tetrasubstituted double bond had occurred. Structure XXIV for the oxido derivative thus becomes mandatory. Now, if perbenzoic acid or sodium pertrifluoroacetate was used instead for the oxidation, no epoxide was obtained, but rather, an isomer (m.p. 187–188°) was formed[24]; this higher-melting substance could be obtained from the epoxide under the influence of mineral acid. The new material bore a methoxyl group, but exhibited in the infrared only one carbonyl group, that due to the γ-lactone moiety. The trisubstituted double bond remained, as revealed by the ultraviolet end absorption (Fig. 2). These observations are consistent with an ortho ester formulation (XXV), which was confirmed by hydrolysis to a hydroxydilactone (XXVI), m.p. 179–180°,[24] secured independently by oxidation with osmium tetroxide,[25] or better, warm peracetic acid. The spectral characteristics of the hydroxydilactone confirmed the assigned structure in that they paralleled in every major respect those of the bromodilactone: γ- and δ-lactone bands appeared in the infrared region; end absorption indicative of a substituted double bond was present in the ul-



XXIV



XXV

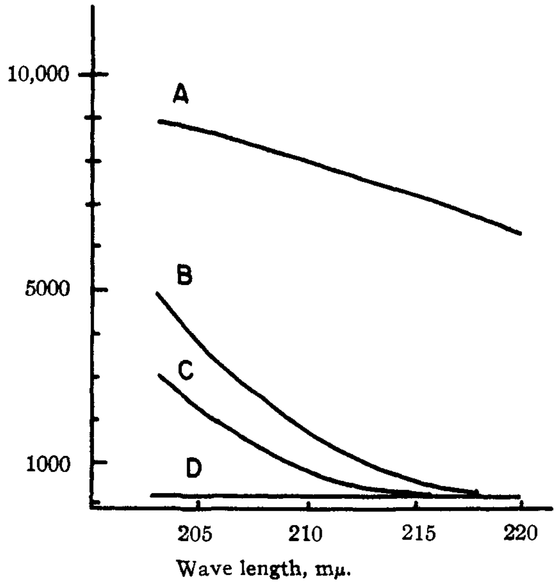
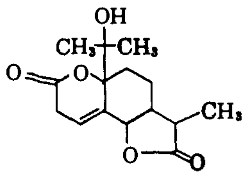


Fig. 2.—Far ultraviolet absorption spectra[a]: A, photosantonic acid, ethyl photosantonate, methyl photosantonate; B, dehydrodilactone; C, bromodilactone, methyl photosantonate oxide, *o*-methyl ester, hydroxydilactone, acetoxydilactone; D, dihydroacetoxydilactone, oxidoacetoxydilactone, dihydrohydroxydilactone.

[a] P. Bladon, H. B. Henbest and G. W. Wood, *J. Chem. Soc.*, 2737 (1952). Spectra were taken on a Cary recording spectrophotometer model 11MS using 1-mm. cells and purified 95% ethanol.



XXVI

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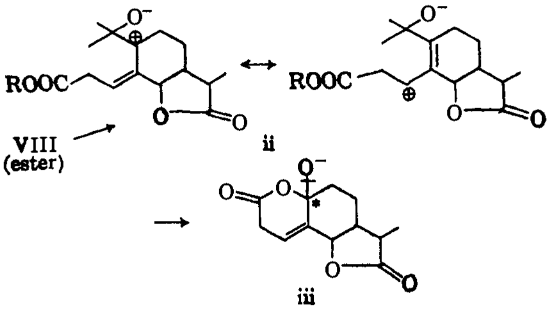
(25) The fact that the same hydroxydilactone is secured by osmium tetroxide or peracid oxidation is interesting in the stereochemical sense. Steric and mechanistic considerations lead one to expect diastereoisomers, epimeric at the newly-created asymmetric center (*)(iii). It is

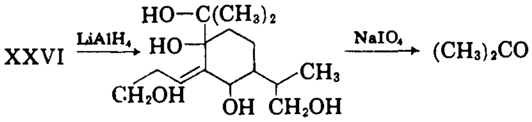


possible, however, that in one (or both) of the oxidation processes, an allylic carbonium ion (ii) may intervene, with the effect that a common intermediate, and final product, will result from the oxidation processes.

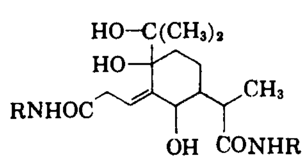
traviolet;[26] and, in addition, manifestations of one vinylic hydrogen were located in the low field region of the n.m.r.

Since the hydroxydilactone seemed amenable to further degradation, its chemistry was investigated in some detail. The observations that the substance did not form a p-toluenesulfonate or an acetate on treatment with acetic anhydride-pyridine indicated that the hydroxyl group was tertiary; and this conclusion was reinforced by recovery of starting material after attempted Oppenauer or chromic acid oxidation. However, the alcoholic group is exposed by the infrared spectrum and, under forcing conditions, the dilactone was convertible to the O-acetate. Hot mineral acid had no effect on the substance, and alkali brought about only lactone ring opening. Although the ethylenic linkage evidenced by the spectral data was unreactive in many respects, its presence was confirmed chemically in several instances. Catalytic hydrogenation of both the lactone and its acetate led to well-defined dihydro products; these reduction products showed no end absorption in the ultraviolet (Fig. 2), thereby indicating that a carbon–carbon double bond had been saturated. Under relatively drastic conditions, pertrifluoracetic acid converted the acetoxydilactone to the corresponding oxide XXVII, m.p. 235–237.5°, which was also virtually transparent in the region above 200 mμ.

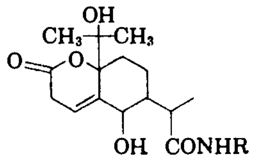
Because the ozonization process is prone to rearrangement, it was deemed desirable to confirm in an independent manner the presence of the isopropylidine group in photosantonic acid. Accordingly, the hydroxydilactone was reduced by means of lithium aluminum hydride, and the resulting crude product, presumably the polyol XXVIII, was cleaved with periodic acid. Again, acetone resulted from the oxidation, although in mediocre yield. The separate, and very different, techniques which led to acetone formation thus leave little doubt that the isopropylidene group constitutes part of the photosantonic acid molecule. In another approach designed to set the stage for diol cleavage, the hydroxy dilactone was converted to the triol-N,N'-dibenzylamide (XXIX) (characterized as the monoacetate, m.p. 148°), along with an amorphous, difficultly purifiable product, which infrared analysis indicated to be the diol monoamide XXX. In keeping with the structures assigned, the triol consumed one mole of periodate, whereas the diol was unattacked by this reagent. Methanolic ammonia acted upon methyl photosantonate to give, as indicated by their infrared characteristics, the hydroxy amide methyl ester, m.p. 107–108° (XXXI) and, in poor yield, photosantonamide, m.p. 116–117°.



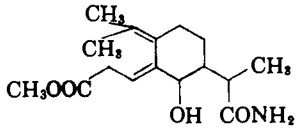
XXVIII



XXIX, R = $-CH_2C_6H_5$

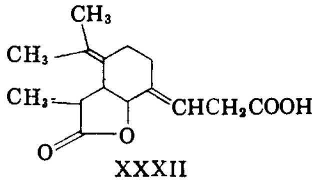


XXX

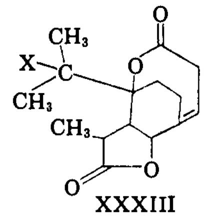


XXXI

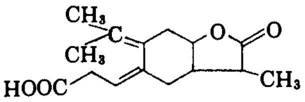
It is worth noting that the alternative, but less likely, photosantonic acid structures which are permitted by the ozonization, n.m.r. and other results, can be disqualified by the dilactone chemistry. One of these possible structures is XXXII, a case requiring consideration if only because it accounts more simply for the ultraviolet behavior than does the photosantonic acid structure already promulgated. However, on the basis of this proposal, the structure XXXIII must be written for the bromo- or hydroxydilactone, a structure patently impossible because of Bredt's rule. A more remote possibility, XXXIV, is inconsistent with the incidental observation in this Laboratory that the lactone ethereal oxygen of photosantonic acid can be hydrogenolyzed, thereby revealing its allylic nature.



XXXII



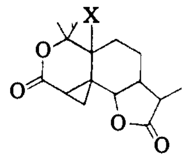
XXXIII



XXXIV

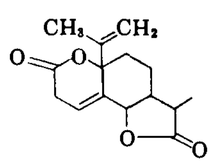
Dehydrohalogenation of the bromodilactone, or dehydration[20] of the hydroxydilactone, gave rise to an anhydrohydroxydilactone (m.p. 139–140°), $C_{15}H_{18}O_4$. The simplest view on the structure of this substance, based on the diene formulation for photosantonic acid, is embodied in the formula XXXV, certain features of which, namely, the γ- and α-lactone systems and the olefinic unsaturation, were confirmed readily by spectral means. In the ultraviolet, no peak absorption could be detected, but there was end absorption of such dimensions that the presence of two olefinic bonds was considered likely. Barton, de Mayo and Shafiq[20]

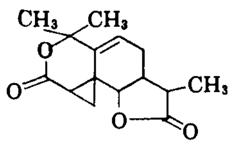
[26] The simple ultraviolet spectral data (Fig. 2) of the bromo- and hydroxydilactones[14] are sufficient to prevent serious consideration of structures (IV) and (V),[20] respectively, for these substances and, therefore, structure XV[20] for photosantonic acid itself.



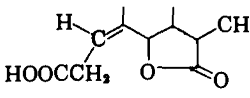
(iv), X = Br
(v), X = OH

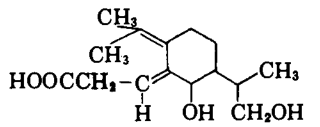
reported that the anhydrodilactone "did *not* give formaldehyde on ozonolysis," thereby pointing to (presumably) structure XXXVI for the anhydro compound. This ozonolysis result, which was cited in support of the cyclopropane structure for photosantonic acid, cannot be accommodated in any reasonable fashion by the diene formulation VIII and places the latter, therefore, in jeopardy. On carrying out the ozonolysis of the anhydrodilactone in our own laboratory, we obtained repeatedly about a 50% yield of formaldehyde. In addition, all of the absorption bands characteristic of a terminal, disubstituted methylene group were discernible in the infrared spectrum. Consequently, we regard structure XXXV for the anhydrodilactone as above suspicion.


XXXV


XXXVI

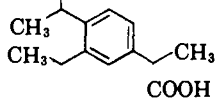
Several pieces of information constitute the basis for the assignment of geometry referred to and used in earlier discussion. Because of the easy formation of the bromo- and hydroxydilactones, one may presume that the carboxyl group in photosantonic-acid is suitably oriented, *i.e.*, *cis* to the isopropylidene group, for such reactions. There is the possibility that photosantonic acid possesses the alternative stereochemistry (XXXVII) and that the reagent not only brings about formation of the dilactone but also prior isomerization to the geometry required for ring closure. This explanation is rendered unlikely by the observation that photosantonic acid, and not an isomer, is produced by the action of zinc on the bromolactone, wherein the geometry is fixed. Further, we have found that the diol XXXVIII, m.p. 77–78°, obtained by lithium borohydride reduction of photosantonic acid, exhibits no tendency to lactonize, a characteristic in keeping with the assigned stereochemistry. That the trisubstituted double bond in photosantonic acid possesses the less stable spatial position is interesting but not altogether surprising in view of its probable mode of genesis (see below), and the fact that under irradiation conditions, the more stable geometrical isomer can often be converted into the less stable. With regard to susceptibility to electrophilic agents, the trisubstituted double bond is, as a net effect, less coöperative than the tetrasubstituted link. Moreover, in the derived dilactones, the resistance of the remaining double bond to attack is so great that it easily could remain undetected, or mistaken for a cyclopropane ring[20] (especially in view of the fact that the dilactones give no color with tetranitromethane). For example, the hydroxydilactone was recovered from attempted oxidation with selenium dioxide in ethanol, sodium dichromate in acetic acid, excess perbenzoic or pertrifluoroacetic acid at or near room temperature, or ozone at −78°.

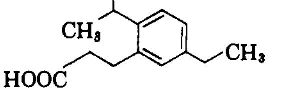

XXXVII


XXXVIII

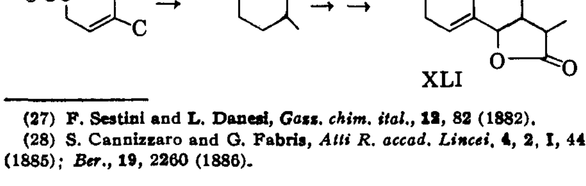
Although photosantonic acid or its methyl ester could be made to consume catalytically about two moles of hydrogen, homogeneous products were not obtained, despite assiduous application of crystallization and chromatographic techniques. Similarly, catalytic dehydrogenation experiments led to no useful result.

When photosantonic acid is pyrolyzed[27] or heated with hydriodic acid,[28] decarboxylation occurs, and from the reaction products there can be obtained the so-called "pyrophotosantonic acid," $C_{14}H_{20}O_2$. Despite claims to the contrary,[3b] there have been recorded no chemical reactions or other data for this acid; however, repetition of the described decarboxylation procedure did provide a small amount of product having the same melting point as that previously recorded. The ultraviolet spectrum revealed the presence of a benzenoid ring; this structural restriction leaves only two expressions (XXXIX and XL) for consideration. Although it might be predicted that the pyrolysis process would be initiated by decarboxylation at the site of the β,γ-unsaturated carboxylic acid system and therefore lead to structure XXXIX, the evidence bearing on the question favors structure XL. Analysis of the proton magnetic resonance pattern reveals a ratio for aromatic:methylene–methine:methyl hydrogens which is more in keeping with the values anticipated for structure XL. This tentative assignment was confirmed by pyrolyzing dehydrophotosantonic acid; pyrophotosantonic acid was formed although again in small yield. In this selective decarboxylation, the phenylacetic acid system is the labile one, and therefore XL doubtless represents the structure of the resulting monoacid.


XXXIX


XL

Successive treatment of photosantonic acid with trifluoroacetic anhydride and sodium bicarbonate involves over-all dehydration with the formation of a ketone A (m.p. 129–130°), characterized as an orange dinitrophenylhydrazone. The ultraviolet absorption of this new substance (λ_{max} 232.5 mμ) and the appearance of *two* vinylic hydrogens in the n.m.r. can be accommodated by either of two structures, XLI and XLII, the first arising normally by attack of the acylonium ion on the isopropyli-


XLI

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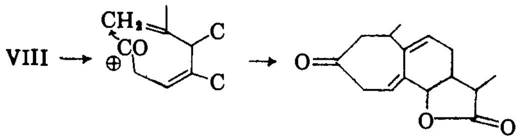
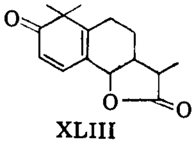
[27] F. Sestini and L. Danesi, *Gazz. chim. ital.*, **12**, 82 (1882).

[28] S. Cannizzaro and G. Fabris, *Atti R. accad. Lincei*, **4**, 2, I, 448 (1885); *Ber.*, **19**, 2260 (1886).

dene group, and the second being formed through intervention of the isopropenyl isomer or a related intermediate (*cf.* the conversion of photosantonic acid to the dilactone XIX).

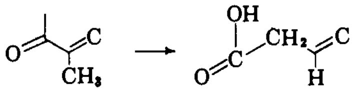

XLII

Ozonization was selected as a reliable means for distinguishing the two possibilities: the normal action of the reagent, followed by decarboxylation and/or β-dicarbonyl cleavage of intermediate oxidation products, might be expected to yield methyl isopropyl ketone and 2-methyllevulinic acid, respectively, from XLI and XLII. The former ketone in fact was obtained in fair yield. Acetic hydrochloric acid-promoted isomerization of ketone A to an α,β-γ,δ-doubly unsaturated ketone B(XLIII) (λ_{max} 308 mμ) further confirms the proposed structure.

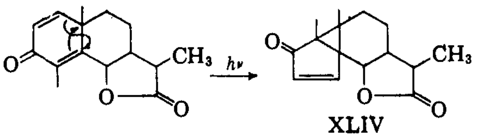

XLIII

The second ketone remained an oil, but was convertible to a crystalline, crimson dinitrophenylhydrazone.

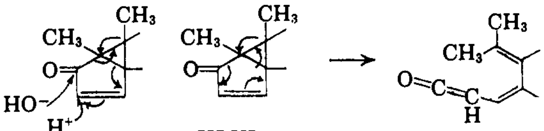
In the transformation of santonin to photosantonic acid, rearrangement of the α-methyl-α,β-unsaturated carbonyl system to a normal, β,γ-unsaturated carboxylic acid side chain is an unusual over-all change, deserving of comment.



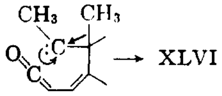
Considerable assistance in rationalizing this and associated changes can be gained by referring to lumiphotosantonin, an intermediary santonin irradiation product to which structure XLIV has been assigned.[29]


XLIV

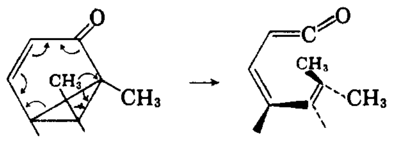
Several distinctly different routes, proceeding from lumiphotosantonin, present themselves. In the first, hydroxyl ion (or its equivalent) attack at the ketone carbonyl group, and hydrogen ion attack at the α-position, accompany the methyl migration and concerted shift of electron pairs (XLV) required to yield the observed product. A second possible route, which involves formation of a ketene function, is depicted in XLVI as a completely concerted process.


XLV XLVI

Alternatively, initiation of the change XLVI may bring the molecule to the intermediary point XLVII, a carbene, which subsequently may rearrange[30] to the same product resulting from the concerted pathway.


XLVII

All of these changes also may be formulated as free radical processes. The carbene route has a certain advantage in that it avoids the transition state of the concerted mechanism, which would probably be of high energy. Organic photochemical reactions of unsaturated systems characteristically involve electron shifts with minimal movement of atoms, according to which view the stereochemical relationships depicted in formulas XLVIII and XLIX would obtain in the completely concerted case.


XLVIII XLIX

The olefinic bonds in XLIX are considerably distorted from planarity, an unfavorable development from which the stepwise route is more nearly free.

Acknowledgment.—The authors are grateful to Merck and Co. and The Santonin Corporation of America for generous quantities of santonin; to W. H. Washburn of the Abbott Laboratories for supplying the near infrared spectrum; and to James N. Shoolery and Robert C. Jones for detailed n.m.r. spectral interpretations, many of which are reproduced or referred to above.

Experimental

Decarboxylation of Hydrocinnamic Acid.—An intimate mixture of 7 g. of hydrocinnamic acid, 40 g. of barium hydroxide octahydrate and 10 g. of barium oxide was heated with a micro burner until distillation ceased. Extraction with ether and distillation afforded 3.1 g. of crude ethyl benzene, b.p. 127–136°. A redistilled sample, b.p. 132–135°, $n^{25}D$ 1.4952, displayed an infrared spectrum identical with that of authentic ethylbenzene.

Pyrophotosantonic Acid.—On distillation of photosantonic acid under a pressure of *ca.* 50 mm., a viscous dark oil came over, which solidified after standing for one month. Chromatography on silica gel and recrystallization from ethanol–water gave white needles, m.p. 90.5–92.5°. A resublimed sample, m.p. 92.5–94.5°, exhibited λ_{max} 275 and 266 mμ (ε 1,010 and 1,000). The infrared spectrum showed a sharp band at 6.7 μ indicative of a proton bound to an aromatic ring. Treatment of dehydrophotosantonic under similar conditions gave, after chromatography, a small yield of pyrophotosantonic, the identity of which was demonstrated by mixed melting point and infrared spectral comparison.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.74; H, 9.16.

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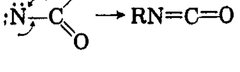
[29] (29)(a) D. H. R. Barton, P. de Mayo and M. Shafiq, *Proc. Chem. Soc.*, 205 (1957); (b) Arigoni, Bosshard, Bruderer, Büchi, Jeger and Krebaum, *Helv. chim. Acta*, **40**, 1732 (1957).

[30] (30) *Cf.* the well-known rearrangement encountered in the Hofmann and related reactions:



Ozonolysis of Photosantonic Acid. A. Reductive Work-up.—A solution of 274.8 mg. of anhydrous photosantonic acid in 30 ml. of acetic anhydride, cooled in a Dry Ice–trichloroethylene-bath, was ozonized until blue (*ca.* 10–15 minutes). The resulting solution was poured into a stirred slurry of 5 g. of zinc dust and 300 ml. of water. After 30 minutes the mixture was distilled directly into solution (ethanol, water and sulfuric acid) containing 500 mg. of 2,4-dinitrophenylhydrazine. The precipitate which formed immediately was collected and dried, 303 mg., m.p. 100–110°.

Chromatography, using silicic acid–Celite and eluting with 4% ether–petroleum ether gave, after recrystallization of suitably combined fractions, 70.0 mg. of acetone 2,4-dinitrophenylhydrazone, yellow needles, m.p. 124–126°, undepressed when mixed with an authentic sample and 33 mg. of acetaldehyde 2,4-dinitrophenylhydrazone, m.p. (shrinks 145°) 156–159°. These identities were confirmed by infrared spectroscopy.

In separate experiments, ozonolysis of 419.1 and 216.8 mg. of photosantonic acid afforded 458.4 and 271.8 mg. of crude 2,4-DNP, respectively.

B. Oxidative Work-up.—A solution of 536.9 mg. of anhydrous photosantonic acid in methylene chloride was ozonized at −78° until blue. The solution was kept at room temperature for 30 minutes; water containing 0.6 ml. of 30% hydrogen peroxide was added; and, after stirring overnight, the two layers were separated. Removal of the methylene chloride gave a small amount of oil which was discarded. The aqueous phase was concentrated *in vacuo* and the viscous colorless residue dissolved in ether. Standing overnight at room temperature afforded 51.0 mg. of crystals, m.p. 127–130°. Additional crops were obtained by concentrating the mother liquors and adding petroleum ether. Recrystallization of the first three crops gave colorless needles of lactone diacid XI, m.p. 128–130°.

Anal. Calcd. for $C_9H_{12}O_6$: C, 50.01; H, 5.58. Found: C, 50.23; H, 5.59.

Careful processing, including sublimation of the later crops gave 5.5 mg. of oily solid and 16 mg. of crystals, m.p. 130–134°, undepressed when mixed with an authentic sample of malonic acid. The infrared spectrum and R_f of this sample were identical with those of malonic acid.

Cyclization of Dehydrophotosantonic Acid.—Dehydrophotosantonic acid (261 mg.) was placed in a 125-ml. polyethylene bottle equipped with a polyethylene screw-cap. An estimated 80 ml. of anhydrous liquid hydrogen fluoride was run into the bottle, which was capped and allowed to stand eight days at room temperature. The bottle was cooled in an ice-bath and cautiously opened. After the hydrogen fluoride was blown off with a stream of dry nitrogen, there remained a brown, tarry residue. The residue was distributed between water and ether. The red ether layer was washed with aqueous saturated sodium chloride, dried over magnesium sulfate, and evaporated to furnish 205 mg. of brown, tarry material.

The product was partially purified by chromatography on silicic acid (Mallinckrodt AR, 100 mesh) with chloroform elution to give 177 mg. of yellow-brown material, which was fractionally crystallized in small amounts of carbon tetrachloride. Nine such crystallizations furnished 59.8 mg. of colorless crystals, m.p. 111–112.5°.

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 73.26; H, 7.29.

Further fractional crystallization of the mother liquors yielded an additional 32.3 mg. of indanone, m.p. 109–113°, for a total yield of 92.1 mg. (38%).

Other crystalline fractions were obtained whose infrared spectra suggested that they were intermolecular condensation products. These were not further characterized.

The infrared spectrum of the cyclized dehydrophotosantonic acid showed broad absorption in 3–4 μ region characteristic of an acid but less intense than that absorption in the dehydrophotosantonic acid spectrum. A single carbonyl absorption band appeared at 5.86 μ. However, when the cyclized dehydrophotosantonic acid was esterified with diazomethane, the characteristic 3–4 μ carboxylic acid bands disappeared and the carbonyl region was resolved into two bands at 5.81 (ester) and 5.90 μ (ketone). An authentic sample of hydrindanone absorbed at 5.86 μ.

The indanone in methanol solution showed absorption maxima at 214 (30,200), 254 (10,600) and 302 (3,220) mμ.

Ethyl (Photosantonate Photosantonin).—A solution of 1.13 g. of photosantonic acid hydrate in a mixture of ethanol and ether was treated with excess ethereal diazoethane. The excess was destroyed by the addition of acetic acid and the solution evaporated on the steam-bath in a stream of nitrogen to a pale yellow oil. An ether solution of this oil was washed with 10% potassium carbonate and saturated salt solution and then dried over sodium sulfate. The white solid obtained on evaporation of the ether was recrystallized from hexane containing 10% (vol.) ether at 0° to yield 0.83 g. of large white plates, m.p. 70.3–71.0°. Concentration and cooling of the mother liquors afforded about 0.3 g. of crystals having m.p. 69.0–70.3° (reported m.p. 68–69°).

Methyl Photosantonate.—A solution of 2.80 g. of photosantonic acid hydrate in a mixture of methanol and ether was treated with excess diazomethane. Processing as described above for VI afforded 2.44 g. of material having m.p. 57–58° after crystallization from ice-cold 10% ether–hexane.

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.05; H, 7.97. Found: C, 69.02; H, 8.06.

Bromodilactone XXII.—A solution of 2.40 g. (8.50 mmoles) of photosantonic acid hydrate in chloroform was treated with excess bromine (persistent color). The solution was washed twice with 5% potassium carbonate solution and once with saturated salt solution and dried over sodium sulfate. Evaporation left 2.86 g. of solid which was purified by solution in chloroform and precipitation with hexane; yield 2.47 g. (7.20 mmoles, 84.6%), darkening at 160° and melting at 173–174°, with evolution of hydrogen bromide. The melting point was variable and dependent on the rate of heating; infrared spectrum: bands at 5.65 μ (γ-lactone) and 5.80 μ (δ-lactone); ultraviolet spectrum: end absorption indicative of one di- or tri-substituted ethylenic linkage (see Fig. 2). A sample having m.p. 170.7–171.8° (dec.) was submitted for analysis.

Anal. Calcd. for $C_{15}H_{19}O_4Br$: C, 52.49; H, 5.58. Found: C, 52.21; H, 5.58.

Regeneration of Photosantonic Acid.—A mixture of 187.1 mg. (0.545 mmole) of the above bromodilactone XXII and 104 mg. of zinc dust was refluxed overnight in 10 ml. of acetic acid. The hot solution was filtered and evaporated almost to dryness. The residue was partitioned between ether and 5% potassium carbonate solution. Acidification of the carbonate solution and isolation with ether afforded 103.2 mg. (0.39 mmole, 71.5%) of impure photosantonic acid, m.p. 144.5–148°, m.m.p. 146.5–150.5°. Recrystallization from aqueous alcohol produced 76 mg. (0.27 mmole, 49.5%) of photosantonic acid hydrate, m.p. 152–154° (with loss of water near 100°), no depression on admixture with an authentic sample. The infrared spectrum of either the crude or the recrystallized material was indistinguishable from that of authentic material.

Dehydrodilactone XXXV.—A mixture of 100 mg. of the bromodilactone XXII and 200 mg. of Mallinckrodt "anhydrous" sodium acetate was heated in 25 ml. of acetic acid at 100° for 51 hours. The residue on evaporation was partitioned between water and benzene and the water layer back-extracted with fresh benzene. The combined benzene extracts were dried and evaporated, leaving 49 mg. of material which slowly crystallized, m.p. 134–138°. Several recrystallizations from ether afforded an analytical sample, m.p. 139.0–140.2°.

Alternately, the hydroxydilactone (147 mg.) was dissolved in dry pyridine (5 ml.) and cooled to 0°. Thionyl chloride (1 ml.) was added and the solution allowed to stand for 20 minutes after which time it was added to chipped ice and extracted with benzene. The benzene extract was washed with both dilute acid and base, concentrated to 20 ml. and the dehydrodilactone precipitated on addition of petroleum ether followed by refrigeration overnight. Filtration gave white needles (97 mg., m.p. 138–139°). The melting point was not depressed by admixture with dehydrodilactone prepared by dehydrobromination of the bromodilactone and indistinguishable from the latter by its absorption spectrum in the infrared; infrared spectrum: bands at 5.64 (γ-lactone), 5.81 (δ-lactone) and 6.13 μ (C═C); ultraviolet spectrum: end absorption indicative of two isolated ethylenic linkages (see Fig. 2).

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.57; H, 6.89.

Ozonolysis of the Dehydrodilactone.—The dehydrodilactone (156 mg.) dissolved in anhydrous acetic anhydride (6 ml.) was cooled in Dry Ice–acetone and treated with ozone for 25 minutes. Addition of the solution to a stirred suspension of zinc dust in water (stirring for 2 hours) followed by steam distillation into an aqueous dimedon (238 mg.) solution buffered at pH 4.7 afforded dimedon derivatives (146 mg.), m.p. 129–186°, which were treated as described by Vorlander[31] for separation of the dimedon derivatives of formaldehyde and acetaldehyde. Acetic acid (1 ml.) was added to the derivatives (139 mg.) and the solution heated on a steam-bath for 7 hours. Addition of water and filtration gave 125 mg. of material which was extracted with dilute sodium carbonate (density 1.095) leaving the anhydrodimedon derivative of acetaldehyde (39 mg., 23%) identified by m.p. and mixed m.p. with an authentic specimen. Acidification of the sodium carbonate extract and filtration afforded the dimedon derivative of formaldehyde (82 mg., 47%) identified by m.p., mixed m.p. and infrared absorption spectrum.

Reaction of Photosantonic Acid with 2,4-Dinitrobenzenesulfenyl Chloride.—A solution of 0.60 g. of photosantonic acid and 0.45 g. of 2,4-dinitrobenzenesulfenyl chloride in 50 ml. of chloroform was refluxed for 1 week, protected from light. Washing with 10% sodium carbonate removed the excess and unreacted photosantonic acid (hydrate), 0.26 g. The neutral portion was slurried in hot ethanol and allowed to stand several days. The filtered solution was refluxed for 1 hour with about 7 g. of (W-1) Raney nickel. After removal of the metal the solution was evaporated to dryness, and the residue was taken up in ether and washed with 5% hydrochloric acid solution. Evaporation left 0.37 g. of an oil whose infrared spectrum was almost identical to that of ethyl photosantonate. This oil was taken up in benzene and passed over a column of Florex. The benzene and ether eluates, 0.30 g., were combined and evaporatively distilled two times at 100–150° and 0.5 mm. pressure to produce 0.16 g. of material, m.p. 57–67°. Several recrystallizations from cold ligroin gave material having m.p. 70.3–70.8°, undepressed on admixture with ethyl photosantonate (VI). The infrared spectra of the two samples were identical.

Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.92; H, 8.18.

Ketone A (XLI).—A solution of 1.586 g. of photosantonic acid in 6.0 ml. of trifluoroacetic anhydride was allowed to stand at room temperature for 4 hours and then added dropwise to a well-stirred ice-cold solution of 160 ml. of 1*M* sodium bicarbonate. The viscous gum which first separated soon solidified to a pale yellow solid. The dried material, 1.442 g., was recrystallized from ether in two crops of yellow needles, (a) 0.711 g., m.p. 126–128°, and (b) 0.374 g., m.p. 119.5–125°, for a total yield of 73%. The remainder of the material had $\lambda_{max.}$ 308 mμ and was undoubtedly mainly ketone XLIII. The analytical sample had m.p. 128.8–129.8°. It gave a yellow color with tetranitromethane; infrared spectrum: bands at 5.65 (γ-lactone) and 5.85 μ (C=O); ultraviolet spectrum: $\lambda_{max.}$ 232.4 (ϵ 11,700) and 287.5 mμ (250).

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 73.45; H, 7.27.

The 2,4-dinitrophenylhydrazone, prepared in acetic acid, separated from ethyl acetate as orange needles, m.p. 211–212° dec. It exhibited maximal absorption in the ultraviolet spectrum at 229 and 359.5 mμ.

Anal. Calcd. for $C_{21}H_{22}O_6N_4$: C, 59.15; H, 5.20. Found: C, 59.26; H, 5.27.

Ozonolysis of Ketone A.—Ozone was passed for 30 min. through a solution of ketone A (161 mg.) in acetic anhydride (6 ml.) at Dry Ice–methylene chloride temperature. After stirring with 50 ml. of water and 2 ml. of 30% hydrogen peroxide for 2 hours, the excess peroxide was decomposed with thiosulfate and the solution steam distilled directly into a solution of 2,4-dinitrophenylhydrazine (990 mg.) in 80 ml. of water and 20 ml. of concentrated sulfuric acid. After standing overnight, the precipitated 2,4-dinitrophenylhydrazone (53 mg., 30%) was filtered and chromatographed on Davidson 100–200 mesh silica gel. Elution with 1:1 petroleum ether–benzene, followed by recrystallization from ethanol gave yellow-orange crystals, m.p. 123–124°, undepressed upon admixture of authentic methyl isopropyl ketone 2,4-dinitrophenylhydrazone. The infrared spectra of the two were identical.

Isomerization of Ketone A to Ketone B (XLIII).—When 233 mg. of ketone A was allowed to stand in a solution of 4 ml. of acetic acid and 1 ml. of concentrated hydrochloric acid for 2 hours at room temperature the neutral (potassium carbonate solution) material isolated, 190 mg. of yellow oil, exhibited a single intense absorption band in the ultraviolet spectrum at 308 mμ. The 2,4-dinitrophenylhydrazone separated from ethyl acetate as crimson plates. m.p. 228° dec., λ_{max} 396 mμ.

Anal. Calcd. for $C_{21}H_{22}O_6N_4$: C, 59.15; H, 5.20. Found: C, 58.71; H, 5.35.

Ketone B (as its 2,4-dinitrophenylhydrazone) was obtained in minute yield from the neutral portion of a reaction of 70% sulfuric acid with photosantonic acid hydrate for 6 hours at room temperature.

Methyl Ester Oxide XXIV.—A solution of 508 mg. of methyl photosantonate in 10 ml. of ether was treated with 10 ml. of 0.353 *M* monoperphthalic acid (an excess) and allowed to stand at 10° for 36 hours. The precipitated phthalic acid was washed with ether and the combined ether solutions were washed with 10% potassium carbonate solution and then with saturated salt solution. Drying and evaporation of the ether left 518 mg. of oil which was crystallized from cold hexane to afford 355 mg. of plates, m.p. 71–73°; infrared spectrum: bands at 5.64 (γ-lactone) and 5.79 μ (ester); ultraviolet spectrum: end absorption indicative of one di- or trisubstituted ethylenic linkage (see Fig. 2). The analytical sample was crystallized from aqueous methanol, m.p. 76–77°. It gave no color with tetranitromethane.

Anal. Calcd. for $C_{16}H_{22}O_5$: C, 65.18; H, 7.53. Found: C, 65.35; H, 7.23.

Ortho Ester (XXV).—When methyl photosantonate in benzene was treated with excess perbenzoic acid (only one mole consumed) and the product worked up in the usual manner there was obtained a 57% yield of material, m.p. 186–188° (from methanol), which showed no band in the infrared spectrum for ester carbonyl and which gave no color with tetranitromethane; infrared spectrum: bands at 5.65 (γ lactone) and 5.99 μ (weak) (C=C?); ultraviolet spectrum: end absorption indicative of one di- or trisubstituted ethylenic linkage (see Fig. 1). The analytical sample had m.p. 187–188°.

Anal. Calcd. for $C_{16}H_{22}O_5$: C, 65.18; H, 7.53; 1 OCH_3, 10.55. Found: C, 65.17; H, 7.63; OCH_3, 10.92.

The same compound resulted (60% yield) when methyl photosantonate was treated with peroxytrifluoroacetic acid in the presence of sodium carbonate.

Isomerization of the Methyl Ester Oxide.—A few drops of carbon tetrachloride which had been equilibrated with concentrated hydrochloric acid was added to a solution of 25 mg. of the methyl ester oxide XXIV in 2 ml. of carbon tetrachloride. Evaporation left 26 mg. of material, m.p. 174–182°, the infrared spectrum of which indicated the presence of, at most, a trace of the starting ester. Crystallization of 20 mg. of this material from methanol afforded 12 mg., m.p. 187.5–188.3°, undepressed on admixture with the *ortho* ester XXV.

Hydroxydilactone (XXVI). (a) From Photosantonic Acid.—Hydrogen peroxide (30% solution, 5.0 ml.) was added in one-tenth portions over a 20-minute period to a solution of 1.41 g. of photosantonic acid hydrate in 50 ml. of acetic acid at 50–55°. The solution was maintained at this temperature for 15 minutes longer and then heated to 75 ± 2° for 30 minutes. It was then evaporated to dryness. A chloroform solution of the residue was washed twice with saturated sodium bicarbonate solution and then with saturated salt solution. The residue on evaporation of the dried chloroform solution crystallized on trituration with ether to afford 1.37 g. of material having an infrared spectrum identical to that of the analytical sample; infrared spectrum: bands at 2.9 (OH), 5.65 (γ-lactone) and 5.81 μ (δ-lactone); ultraviolet spectrum: end absorption indicative of one di- or trisubstituted ethylenic linkage (see Fig. 2). Crystallization from ethyl acetate gave 1.10 g. of large irregular prisms, m.p. 178.8–180°. It gave no color with tetranitromethane.

Anal. Calcd. for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.01; H, 7.15.

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[31] D. Vorlander, *Z. Anal. Chem.*, **77**, 321 (1929).

(b) **By Hydrolysis of the Ortho Ester XXV.**—A solution of 34 mg. of XXV in 3 ml. of acetic acid and 1.5 ml. of water containing one drop of concentrated hydrochloric acid was heated at 100° for about 1 hour. Evaporation left 34 mg. of material, m.p. 171.5–173°, with an infrared spectrum identical to that of the hydroxydilactone. Recrystallization of this material gave a sample, m.p. 175.5–177.5°, undepressed on admixture with the hydroxydilactone.

(c) **By the Action of Osmium Tetroxide on Methyl Photosantonate.**—A solution of 556.6 mg. of methyl photosantonate in 10 ml. of ether was added to a cold solution of 525 mg. of osmium tetroxide in 50 ml. of ether. Only a trace of material separated after 14 hours at room temperature. When 5 ml. of pyridine was added a dark precipitate formed slowly. After 2 weeks standing the ether was evaporated and a chloroform slurry of the residue was saturated with hydrogen sulfide. Evaporation of the filtered chloroform solution left a residue of 610 mg. of (solvated) dark colored oil which was chromatographed over a column of Mallinckrodt silicic acid packed in chloroform and eluted with chloroform and 2% methanol–chloroform. The first four fractions, 518 mg., had an infrared spectrum almost identical to that of the hydroxydilactone. Crystallization of a 367-mg. portion of this material from ethyl acetate afforded 109 mg. of hydroxydilactone, m.p. 177.0–178.8°, undepressed on admixture with an authentic sample. Fraction 5, 10 mg., was discarded.

Lithium Aluminum Hydride Reduction and Periodate Cleavage of the Hydroxy-dilactone.—The hydroxy-dilactone, 98 mg., was reduced using 137 mg. of lithium aluminum hydride in 50 ml. of tetrahydrofuran. Water was added, the inorganic salts removed and the solvent evaporated leaving a colorless, viscous oil. The oil was dissolved in water, 150 mg. of sodium periodate in water added, and the solution kept at room temperature overnight. A vigorous stream of nitrogen was passed into the solution and then into a solution of Brady reagent. The precipitate (54 mg.) was filtered after 2 hours, dissolved in hot petroleum ether and unaltered 2,4-dinitrophenylhydrazine removed. Cooling gave 39 mg. of yellow needles, m.p. 126–127°. This melting point was not depressed when the sample was admixed with authentic acetone 2,4-dinitrophenylhydrazone.

Dihydrohydroxydilactone.—When the hydroxydilactone XXVI in acetic acid was hydrogenated using platinum oxide as the catalyst one mole of hydrogen was absorbed and there was obtained a quantitative yield of material, m.p. 164.5–166.5°. Several crystallizations from ethyl acetate afforded an analytical sample, m.p. 171.5–172.0°.

Anal. Calcd. for $C_{16}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.84; H, 7.62.

Acetoxydilactone.—A solution of 3.012 g. of the hydroxydilactone XXVI and 0.15 g. of *p*-toluenesulfonic acid monohydrate in 30 ml. of acetic acid and 15 ml. of acetic anhydride was allowed to stand overnight at room temperature. The solution was poured onto 175 g. of ice and stirred occasionally until the odor of acetic anhydride had disappeared. The air-dried solid weighed 2.943 g. and had m.p. 215–218°; infrared spectrum: bands at 5.63 (γ-lactone) and 5.78 (acetate and δ-lactone) and 6.10 μ (weak) (C=C?); ultraviolet spectrum: end absorption indicative of one di- or trisubstituted ethylenic linkage (Fig. 2). On crystallization from methanol there was obtained 2.838 g. of material, m.p. 219.5–221.3°. Further crystallization raised the m.p. to 221.0–221.8°. The acetate gave no color with tetranitromethane.

Anal. Calcd. for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 63.22; H, 7.01.

Dihydroacetoxydilactone.—The above acetoxydilactone, 161 mg., was hydrogenated in acetic acid using platinum oxide as the catalyst. One mole of hydrogen was absorbed. Crystallization of the product from benzene—cyclohexane gave 142 mg., m.p. 161–164°; infrared spectrum: bands at 5.63 (γ-lactone) and 5.79 μ (acetate and δ-lactone); infrared spectrum: bands at 5.63 (γ-lactone) and 5.79 μ (acetate and δ-lactone); ultraviolet spectrum: trivial end absorption (see Fig. 2). Further crystallization from methanol-ether afforded an analytical sample, m.p. 173.0–173.5°.

Anal. Calcd. for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46. Found: C, 63.20; H, 7.46.

Oxidoacetoxydilactone XXVII.—A solution of peroxytrifluoroacetic acid prepared from 0.135 ml. (4.8 mmoles) of 90% hydrogen peroxide and 0.85 ml. (6.0 mmoles) of trifluoroacetic anhydride in 2 ml. of methylene chloride was added to a well stirred solution of 322.4 mg. (1.0 mmole) of the acetoxydilactone XXXVII in 5 ml. of methylene chloride in which 565 mg. (4.0 mmoles) of anhydrous disodium hydrogen phosphate was suspended. The mixture was refluxed with stirring for at least 0.5 hour and then cooled and sufficient water to dissolve the salts was added. The methylene chloride layer was washed with 1 *M* sodium bicarbonate solution and then with saturated salt solution. Drying and evaporation left 347 mg. of white foam which was crystallized from methanol to afford 243 mg. (70%) of white crystals, m.p. 231–234°; infrared spectrum: bands at 5.64 (γ-lactone) and 5.78 μ (acetate and δ-lactone). The analytical sample had m.p. 235.2–237.5°.

Anal. Calcd. for $C_{17}H_{22}O_7$: C, 60.34; H, 6.55. Found: C, 60.65; H, 6.74.

The Action of Benzylamine on the Hydroxydilactone (XXVI).—A mixture of 500 mg. of the hydroxydilactone and 10 ml. of benzylamine was heated on the steam-bath for 2 days and then poured into an excess of cold 2 *N* hydrochloric acid. The gum which separated was extracted into chloroform and the chloroform solution washed successively with 2 *N* hydrochloric acid, 5% potassium carbonate and saturated salt solutions. A concentrated chloroform solution of the residue obtained on evaporation of the dried chloroform extracts was chromatographed over 15 times its weight of acetone-washed silicic acid and eluted with chloroform and chloroform containing 1, 2 and 5% methanol. Fractions were assayed by infrared spectroscopy. In this way there was usually obtained about 520 mg. (60% yield) of material which consisted largely of the desired triol-N,N'-dibenzyldiamide (XXIX) with only a trace of an impurity giving rise to a weak peak or shoulder at 5.8 μ (δ-lactone) in the infrared spectrum. This substance was characterized as its crystalline monoacetate (pyridine–acetic anhydride, 8 minutes at 100°), m.p. 148.5–148.7° (from ethyl acetate–cyclohexane); infrared spectrum: bands at 2.92 and 3.06 (OH and NH), 5.83 (acetate) and 6.08 and 6.63 μ (secondary amide). The triol consumed only one mole of periodic acid from a solution 0.05 molar in triol and 0.10 molar in periodic acid in 90% methanol.

Anal. Calcd. for $C_{31}H_{40}O_6N_2$: C, 69.38; H, 7.51. Found: C, 69.57; H, 7.32.

The Action of Ammonia on Methyl Photosantonate.—A solution of 557 mg. of methyl photosantonate in 4 ml. of methanol was added to 40 ml. of ammonia-saturated methanol. After 8 hours at room temperature the solution was evaporated to dryness. The residue was slurried in 25 ml. of ethyl acetate and a trace of material removed by filtration Evaporation of the filtrate left 606 mg. of a foam which was chromatographed over 5.6 g. of silicic acid (chloroform and chloroform containing small amounts of methanol). Fractions were assayed by infrared spectroscopy. In this manner there was obtained 400 mg. of material which was mainly the hydroxy methyl ester amide XXXI. This material was crystallized several times from ethyl acetate–ether and afforded a sample having m.p. 107.2–107.8°; infrared spectrum: bands at 2.90 and 3.03 (OH and NH), 5.83 (methyl ester) and 6.04 and 6.15 μ (primary amide).

Anal. Calcd. for $C_{16}H_{25}O_4N$: C, 65.06; H, 8.53. Found: C, 65.21; H, 8.36.

There was also obtained about 20 mg. of material, the infrared spectrum of which indicated it to be photosantonamide; infrared spectrum: bands at 2.85 and 2.95 (NH), 5.68 (γ-lactone) and 6.01 and 6.31 μ (primary amide). Crystallization from ether gave a sample having m.p. 116–117°.

Anal. Calcd. for $C_{15}H_{21}O_3N$: C, 68.41; H, 8.04. Found: C, 68.31; H, 7.85.

Lithium Borohydride Reduction of Photosantonic Acid.—A solution of 528.6 mg. of photosantonic acid in 5 ml. of sodium-dried tetrahydrofuran was added to a slurry of 114 mg. (an excess) of lithium borohydride in 10 ml. of sodium-dried tetrahydrofuran. The mixture was refluxed with stirring for 7 hours and then cooled and the excess reagent destroyed by the addition of 2 *N* hydrochloric acid solution. Most of the tetrahydrofuran was evaporated at reduced pressure and the product isolated by extraction into ethyl acetate (2 × 25 ml.). The ethyl acetate extracts were washed with 2% sodium hydroxide solution. The alkaline extracts were acidified and extracted with ethyl acetate. There was obtained 426 mg. of light brown oily acid which was crystallized from ether to product 236 mg. of material, m.p. 73–74°, with prior softening; infrared spectrum: 3.04 (broad) (OH) and broad ascending band 3.6–4.3 (OH of –COOH) and 5.86 μ (COOH) (mull). Two further crystallizations from ether gave an analytical sample of the diol acid XXXVIII, m.p. 77.0–77.8°.

Anal. Calcd. for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02. Found: C, 67.43; H, 8.74.

The Action of Concentrated Hydrochloric Acid on Photosantonic Acid. (a) Acidic Portion.—A suspension of 280 mg. of photosantonic acid hydrate in 14 ml. of concentrated hydrochloric acid was stirred at room temperature for 20 hours and then diluted with 42 ml. of ice-water and extracted with ethyl acetate. The ethyl acetate was washed with two portions of 5% potassium carbonate solution. Acidification and isolation with ether gave 206 mg. of yellow oil. A concentrated chloroform solution of 188 mg. of this oil was placed on a column of acetone-washed silicic acid. Elution with chloroform gave 27 mg. of a yellow oil, intense λ_{max} 268 mμ, followed by 100 mg. of solid with an ultraviolet spectrum characteristic of "dehydrophotosantonic acid" (weak peaks at 265–266 and 274 mμ). Recrystallization of this material from benzene-hexane gave 37 mg. of material, m.p. 128.0–129.5°, mixture melting point with pure material, 132.2–134.2°. Elution of the column with 1–2% methanol–chloroform gave 50 mg. of yellow oil, intense λ_{max} 242 mμ.

After 12 hours stirring with concentrated hydrochloric acid the approximate proportions of acids were 40 (λ_{max} 268 mμ):68 (dehydrophotosantonic acid):32 λ($_{max}$ 242 mμ).

(b) Neutral Portion.—The neutral material from four runs at 1, 2, 4.5 and 8 hours (using 1.129 g. of photosantonic acid hydrate), 321 mg., was recrystallized from ethyl acetate–cyclohexane yielding 85 mg. of the dilactone XX as white needles, m.p. 218.5–220°; infrared spectrum: bands at 5.65 (broad) (2 γ-lactones) and 6.17 μ (C=C). Further crystallization gave an analytical sample, m.p. 224.7–225.3°.

Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.51; H, 7.76.

Ozonization of the Dilactone XX.—Ozone (from a Welsbach Laboratory Ozonator) was passed through a cooled solution of 50 mg. of the dilactone in 5 ml. of acetic acid for 30 minutes. The solution was steam distilled into an aqueous solution of methone (1 hour). The *p*H of the distillate was adjusted to about 4.5 by the addition of 5% sodium hydroxide solution. After standing overnight at 10° the precipitate was removed by filtration and dried to constant weight. There was obtained 26.1 mg. (47%) of the methone derivative of formaldehyde, m.p. 186.5–190°, mixture m.p. 189–191.5°. The pot residue was extracted several times with chloroform. Evaporation left 45 mg. of nearly white crystals, m.p. 198–203°; infrared spectrum: bands at 5.65 μ (broad) (2 γ-lactones) and 5.86 μ (–C=O). The analytical sample was prepared by several recrystallizations from ethyl acetate–cyclohexane, m.p. 215.5–217.5° dec.

Anal. Calcd. for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 63.10; H, 6.73.

The norketone (10 mg.) was dissolved in water (0.1 ml.) and dioxane (0.2 ml.) and the solution made basic on addition of 3 *N* NaOH (0.2 ml.). Potassium iodide–iodine reagent was added until color persisted, followed by warming to 60° and the further addition of the reagent until the brown color lasted a full minute. Addition of 3 *N* NaOH to remove any persisting brown color and warming for 2 minutes followed by dilution with water (1 ml.) gave after standing, iodoform (7 mg., m.p. 120°, 45%), confirmed by m.p. and mixed m.p.

MADISON, WISC.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, SMITH COLLEGE]

The Structure of the Crystalline Cadinol from Citronella Oil

BY MILTON D. SOFFER, MARLENE BREY AND JANE FOURNIER

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The action of methylmagnesium iodide on the epoxide of the crystalline cadinol from citronella oil, followed by treatment with palladium–carbon under conditions inducing the elimination of the isopropyl group gives 1,2,5-trimethylnaphthalene, indicating in the light of previous evidence that the structure of the cadinol from citronella oil is represented by formula I.

In a recent communication[1] we have reported the conversion of the crystalline cadinol isolated by Plattner and Markus[2] from citronella oil to the reference compound agathalene, 1,2,5-trimethylnaphthalene. These reactions (I–IV) when taken together with the conversion[2] of the sequiterpene alcohol to cadinene dihydrochloride (V)[3] provide evidence that the structure of the natural product is represented by formula I.

More recently Motl, Sykora, Herout and Šorm[4] have reported the conversion of the same cadinol through a useful extension of the epoxide–Grignard–dehydrogenation method[3,5–7] to 5-methylcadalene (VI), indicating the same gross structure, I.

In the present work, treatment of the crystalline cadinol with perbenzoic acid gave a product melting over a wide range (65–90°) which was assumed to be a mixture of stereoisomeric epoxides (IIa,b), but since it was thought that both isomers might serve as precursors to the same final degradation product no separation was attempted. The action of methylmagnesium iodide produced a new mixture of products, m.p. 196–204° from which in separate experiments one well defined dihydroxytetrahydromethylcadinene, $C_{16}H_{28}(OH)_2$, m.p. 211–212.5°, could be isolated in about 30% yield. In previous applications of the method the isomers were usually not separated and it was assumed[3,5–8] that in analogy with the Grignard addition to the oxides of acyclic olefins[9] the reaction would produce pre-

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