279. Some Photochemical Rearrangements[1])

by **D. H. R. Barton**

(8. X. 59)

The absorption of a quantum of radiant energy by an organic molecule causes the excitation of the molecule to a higher energy state. If ultraviolet or visible light be employed, the excitation is electronic in nature and may vary from tens to hundreds of kilocals in magnitude in accordance with the EINSTEIN equation. The energy absorbed by the molecule may be dissipated by thermal degradation or by phosphorescence and fluorescence, in which cases, of course, no chemical change results. Alternatively the extra energy may lead to bond fission or to bond formation concerted with bond fission. Bond fission produces pairs of radicals whose subsequent fate is, in general, the same as that of the same radicals generated by ordinary thermal means. When, however, the light energy is employed in forming new bonds in concert with the breaking of old ones, there must be an absorption of energy. In principle, therefore, highly strained and unusual structures may result. Some of the compounds described in the sequel illustrate this point. In some cases one can make in a single photochemical step a highly strained structure that would only be obtainable otherwise (if at all) by a long series of conventional thermal processes.

This lecture will be concerned with a number of new photochemical reactions that have been discovered during the last few years. We commence with a discussion of the photochemistry of the sesquiterpenoid lactone santonin (I)[2]). The earlier workers had shown that irradiation of santonin gave two major compounds, photosantonic acid, $C_{15}H_{20}O_4$, and isophotosantonic acid lactone, $C_{15}H_{20}O_4$. In our first paper on photochemistry[3]) we showed that this latter compound, obtained by irradiation in aqueous acetic acid, has the constitution (II). The change from (I) to (II) represents a new type of rearrangement which is of potential interest for the synthesis of perhydro-azulene derivatives. Such compounds occur frequently in Nature and so far none has been synthesised by ordinary thermal methods. As a preliminary to the synthesis of sesquiterpenoid lactones found in Nature we have examined the generality of the rearrangement. The Table shows seven examples of the reaction[3])[4]) and we conclude that it is, indeed, of a general character (see also below). The stereochemistry assigned to isophotosantonic lactone (II) is not, as yet, rigidly established

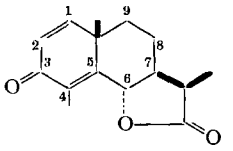
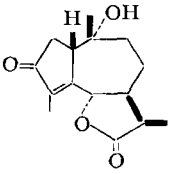
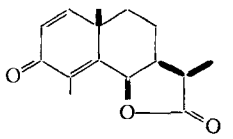
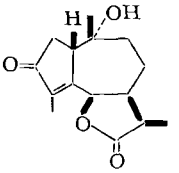
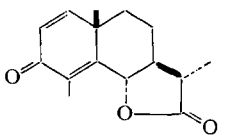
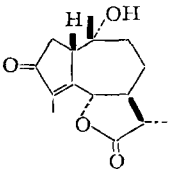
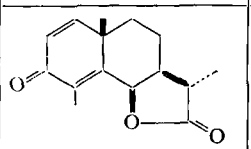
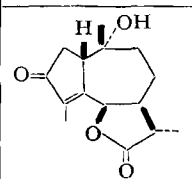
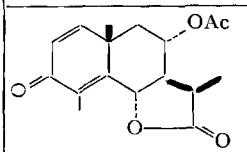
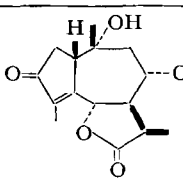
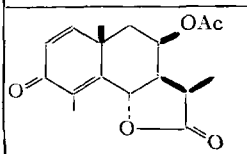
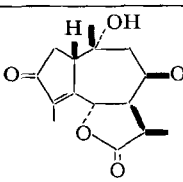
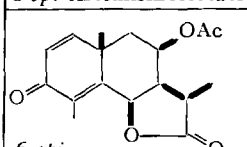
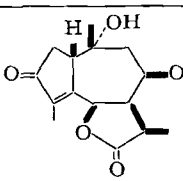
[1]) A lecture delivered before the Swiss Chemical Society on February 28th, 1959, at the Winter Meeting of the Society. The material presented at this lecture was also incorporated into an acceptance address before the American Chemical Society on June 16th (1959) in Seattle, Washington, on the occasion of the award of the first Roger Adams Medal. – Published by special decision of the Editorial Board.

[2]) For earlier literature see J. L. SIMONSEN & D. H. R. BARTON, 'The Terpenes', Cambridge University Press 1952, Vol. III, p. 292 *et seq.*

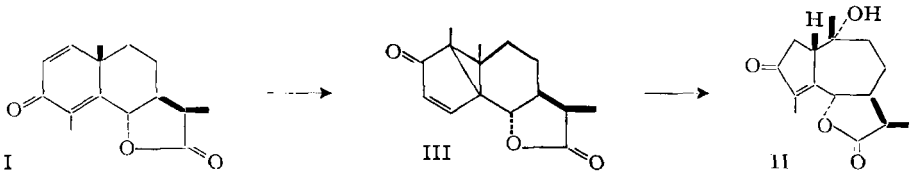
[3]) D. H. R. BARTON, P. DE MAYO & M. SHAFIQ, J. chem. Soc. **1957**, 929.

[4]) D. H. R. BARTON, J. E. D. LEVISALLES & J. T. PINHEY, J. chem. Soc., in preparation.

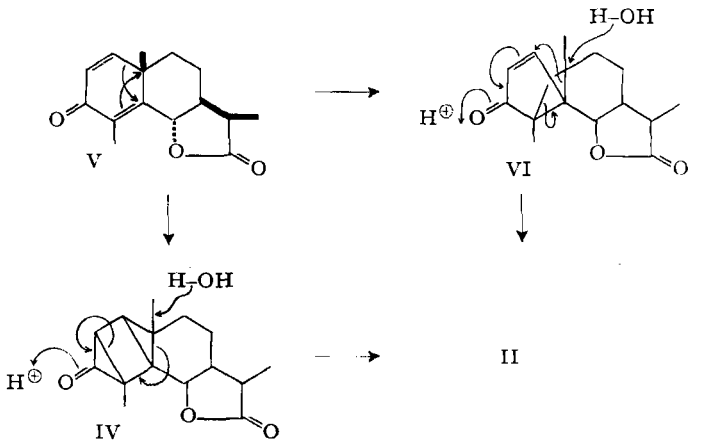
Photochemical Rearrangements

Compounds		Properties of photo-product			
Starting lactone	Photo-product	M. p.	$[\alpha]_D$ in $CHCl_3$	λ_{max} with ϵ (in parentheses) in EtOH	Yield (%): approx. data only
 (α)-Santonin		165–167°	+129°	239 mμ (13,000)	30
 6-*epi*-(α)Santonin		180–181°	−105°	239 mμ (11,600)	24
 β-Santonin		154–157°	+207°	240 mμ (12,900)	19
 6-*epi*-β-Santonin		200–201°	−101°	241 mμ (11,700)	23
 Artemisin acetate		230–233°	+120°	239 mμ (13,900)	5
 8-*epi*-Artemisin Acetate		174–175°	+72°	239 mμ (13,400)	25
 6-*epi*- 8-*epi*-Artemisin acetate		171–174°	−70.5°	242 mμ (11,600)	31

but it is probably correct[5]). It is not possible to discuss the evidence in detail in the time available.



The irradiation of santonin in neutral solution affords an isomeric substance containing an umbellulone ring. By general agreement[6])[7])[8]) this compound has been designated lumisantonin. Extensive structural work[7])[8]) has shown that lumisantonin has the constitution (III). The rearrangement of (I) to give (III) is indeed unusual and the novelty is further enhanced by the fact[7]) that the action of hot aqueous acetic acid on (III) gives (II). However, irradiation of santonin in cold aqueous acetic acid also furnished the lactone (II) under conditions where lumisantonin (III) gives no (II). This suggests[7]) that there are two routes to (II) in hot aqueous acetic acid: a direct transformation possibly through the collapse of a photochemically reversible intermediate such as (IV), and an indirect route through lumisantonin. We represent the conversion of santonin to lumisantonin as a bond-crossing process (V) (without any additional intermediates) which is almost certainly reversible photochemically. The further acid-catalysed rearrangement of lumisantonin to give (II) becomes more intelligible if this is written as in (VI). This formula indicates a series of conventional 1:2-shifts but, of course, a more complicated path[8]) to the end product (II) is not excluded.



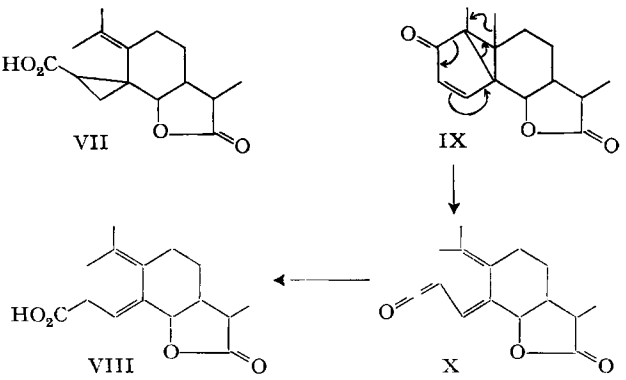
[5]) See D. H. R. BARTON, Proc. chem. Soc. **1958**, 61.

[6]) W. COCKER, K. CROWLEY, J. T. EDWARD, T. B. H. MCMURRY & E. R. STUART, J. chem. Soc. **1957**, 3416.

[7]) D. H. R. BARTON, P. DE MAYO & M. SHAFIQ, Proc. chem. Soc. **1957**, 205; J. chem. Soc. **1958**, 140.

[8]) D. ARIGONI, H. BOSSHARD, H. BRUDERER, G. BÜCHI, O. JEGER & L. T. KREBAUM, Helv. **40**, 1732 (1957).

Photosantonic acid has already been referred to above. It is the sole product[7]) of the irradiation of lumisantonin in aqueous acetic acid. The ethyl ester of photosantonic acid, the so-called photosantonin, is formed when irradiations are carried out in ethanol. At first[5][9]) we favoured the formula (VII) for photosantonic acid, but later work[10]) showed conclusively that the compound was correctly formulated as (VIII), this structure being first proposed by VAN TAMELEN *et al.*[11]) on the basis of independent evidence. The formation of photosantonic acid from irradiation of lumisantonin can be rationalised easily through a rearrangement reaction (IX) leading to the keten (X) and thus, in the presence of water, to photosantonic acid or, in the presence of ethanol, to photosantonin. Whilst isophotosantonic lactone (II) can be formed without the intervention of lumisantonin (see above), it is probable that all the photosantonic acid arises *via* lumisantonin.



The interesting results secured from the irradiation of santonin naturally stimulated interest in the photochemistry of other cyclohexadienones. The obvious compound to study was prednisone acetate[12]) (XI). This substance is of importance in medicine and, indeed, it was conceivable that the useful activity of the compound might stem from photochemical transformation products formed in the skin.

Irradiation of prednisone acetate in aqueous acetic acid[13][14]) gave a product formulated on the basis of further degradation and by analogy (see above) as (XII). Irradiation in neutral solution[14][15]) afforded firstly an isomeric compound, lumiprednisone acetate. This was assigned the constitution (XIII) on the basis of its physical properties, its further degradation, and especially upon the fact that mild treatment with acid or with activated alumina gave an isomer (XIV) which on

[9]) D. H. R. BARTON, P. DE MAYO & M. SHAFIQ, Proc. chem. Soc. **1957**, 345.

[10]) D. H. R. BARTON, P. DE MAYO & M. SHAFIQ, J. chem. Soc. **1958**, 3314.

[11]) E. E. VAN TAMELEN, S. H. LEVIN, G. BRENNER, J. WOLINSKY & P. E. ALDRICH, J. Amer. chem. Soc. **80**, 501 (1958); **81**, 1666 (1959).

[12]) H. L. HERZOG, C. C. PAYNE, M. A. JEVNIK, D. GOULD, E. L. SHAPIRO, E. P. OLIVETO & E. B. HERSHBERG, J. Amer. chem. Soc. **77**, 4781 (1955); A. NOBILE, W. CHARNEY, P. L. PERLMAN, H. L. HERZOG, C. C. PAYNE, M. E. TULLY, M. A. JEVNIK & E. B. HERSHBERG, *ibid.* **77**, 4184 (1955).

[13]) D. H. R. BARTON & W. C. TAYLOR, Proc. chem. Soc. **1957**, 96, 147.

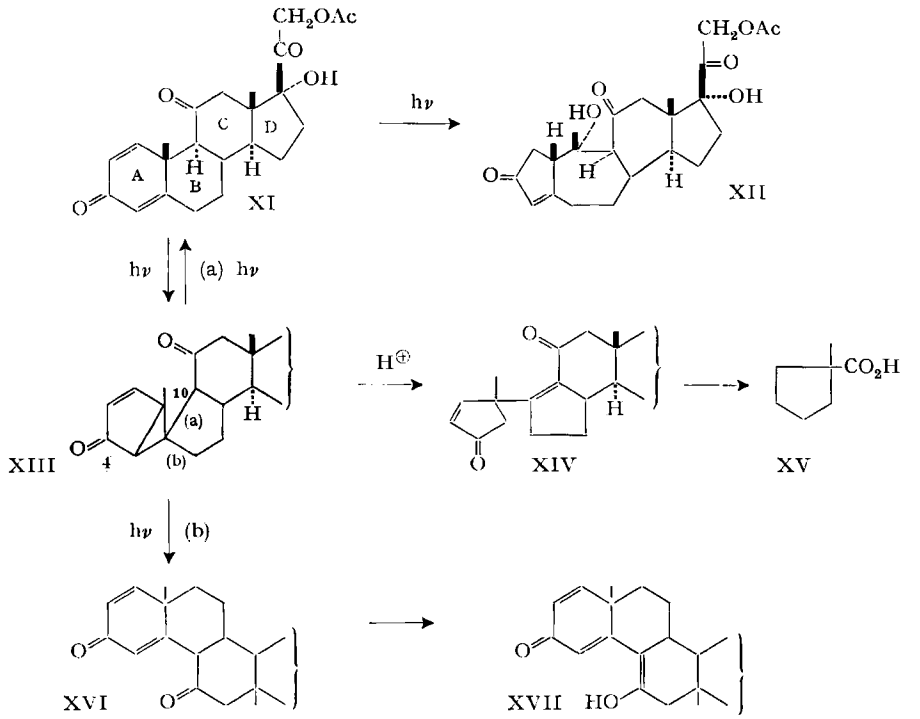
[14]) D. H. R. BARTON & W. C. TAYLOR J. chem. Soc. **1958**, 2500.

[15]) D. H. R. BARTON & W. C. TAYLOR, J. Amer. chem. Soc. **80**, 244 (1958).

hydrogenation, WOLFF-KISHNER reduction and then chromic acid oxidation gave 1-methylcyclopentane-1-carboxylic acid (XV).

Inspection of the formula (XIII) of lumiprednisone acetate shows that the original A and B rings of the precursor (XI) are now related in a spiranic manner. Thus, neglecting any stereochemical complications, the bonds marked (a) and (b) are symmetrically placed with respect to C-10. If we envisage the migration of bond (a) back to C-10 with collapse of the umbellulone ring we return to the formula of the starting material (XI). Although there is no proof of this, we believe that such a process very probably occurs under the influence of light. If we consider now the comparable migration of bond (b) to C-10 we attain a new structure (XVI). Interestingly enough more prolonged irradiation of (XI), or irradiation of (XIII), does afford a neoprednisone acetate[14]) which has formula (XVI). The physical properties are identical with those of prednisone acetate and, in addition, treatment with base under extremely mild conditions affords an enolic system whose spectroscopic properties show that it must be formulated as in (XVII).

Prolonged irradiation also affords a phenolic isomer of lumiprednisone acetate[14]). This is easily understood in terms of the migration of either bond (a) or bond (b) to C-4 giving, after collapse of the umbellulone ring, a homoannular dienone no longer blocked from attaining aromaticity. There is, of course, a prior literature on the photochemically induced rearrangement of dienones to give phenols[16]).

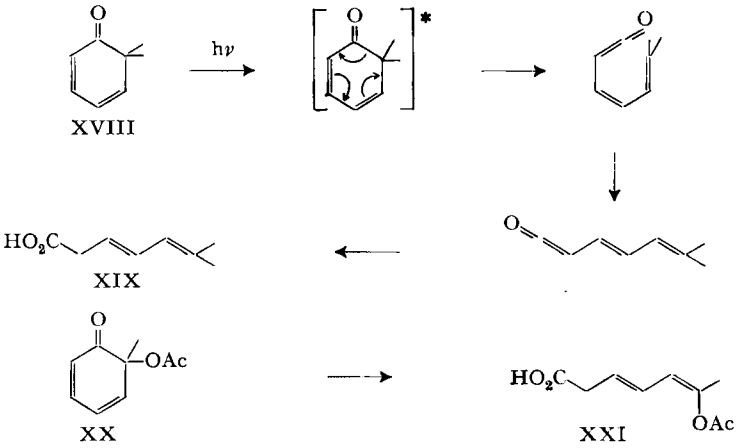


[16]) H. DUTLER, H. BOSSHARD & O. JEGER, Helv. **40**, 494 (1957); H. STAUDINGER & S. BEREZA, Liebigs Ann. Chem. **380**, 243 (1911).

The photochemistry of cyclohexadienones discussed so far has been based on compounds of the *para*-type. Irradiation of *ortho*-type cyclohexadienones produces quite different results[17]). The *ortho*-type cyclohexadienones are readily available from the acetoxylation[18]) or alkylation[19]) of suitable *ortho*-substituted phenols. We have found[17]) that such cyclohexadienones are smoothly converted on irradiation with ultraviolet light in the presence of an appropriate nucleophilic reagent into acids or acid derivatives in high yield. The reaction sequence represents a new procedure for the fission of the phenolic nucleus and, because of the high yields obtainable, may have synthetic applications.

Our first experiments[17]) were conducted using water as the nucleophilic reagent. Irradiation of 6:6-dimethylcyclohexa-2:4-dien-1-one[20]) (XVIII) in ether saturated with water afforded 5-methylhexa-2:4-diene-1-carboxylic acid (XIX). The *trans*-configuration for this compound is based on its spectroscopic properties. Similar irradiation of 6-acetoxy-6-methyl-cyclohexa-2:4-dien-1-one[18]) (XX) furnished the diene (XXI) in high yield[21]). Reactions of this kind are best formulated as proceeding through an excited state, which by redistribution of electrons would give *cis*- and then *trans*-ketens furnishing on hydration the *trans*-diene (as XIX) actually isolated. Hydration of the *cis*-keten to a *cis*-diene followed by photochemical rearrangement is not, however, excluded.

In support of the postulated keten intermediate, irradiation of (XX) in dry ether containing some aniline or cyclohexylamine gave respectively the anilide and cyclohexylamide of the acid (XXI).



An interesting diene (XXII) resulted from the irradiation of 6:6-diacetoxy-4-methyl-cyclohexa-2:4-dien-1-one (XXIII). As would be expected, this compound was

[17]) D. H. R. Barton & G. Quinkert, Proc. chem. Soc. **1958**, 197; J. chem. Soc. **1959**, in press.

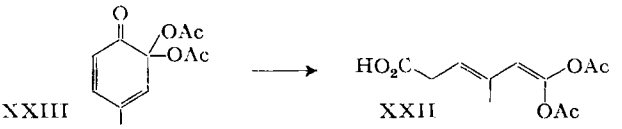
[18]) F. Wessely & F. Sinwel, Mh. Chem. **81**, 1055 (1950).

[19]) D. Y. Curtin, R. J. Crawford & M. Wilhelm, J. Amer. chem. Soc. **80**, 1391 (1958).

[20]) K. Alder, F. H. Flock & H. Lessenich, Chem. Ber. **90**, 1709 (1957).

[21]) The formula XXI is not intended to denote a definite configuration for the acetoxyl group relative to the methyl group attached to the same vinylic carbon. The same reservation holds for analogous compounds described hereinafter.

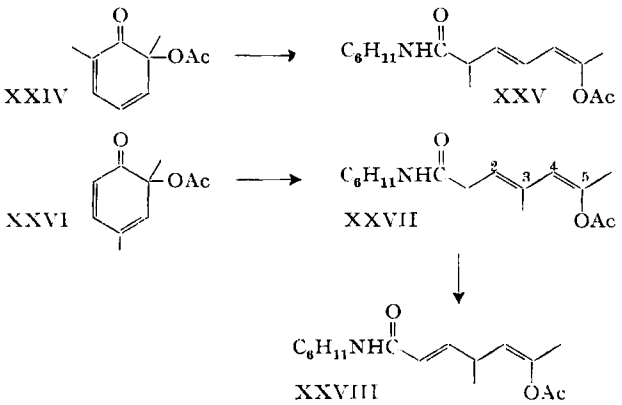
labile to heat and to polar solvents. The simplicity of the photochemical method makes it readily available.



Irradiation of 6-acetoxy-6-methyl-cyclohexa-2:4-dien-1-one in dry ether in the absence of any nucleophile gave, as main product, *ortho*-cresol. This reaction was, however, about ten times slower than the ring cleavage processes described above. Clearly the rate of conversion of (XX) to the keten cannot be altered by the absence of a nucleophile, and we consider that there must not only be a ring cleavage reaction of this kind but also a photochemically induced reclosure process. Eventually a less probable photochemical reaction occurs in the homolytic cleavage of the dienone (XX) into *ortho*-cresyloxy-radicals, which abstract hydrogen from solvent ether to give *ortho*-cresol, and acetoxyl radicals. The latter decompose in a well known way[22]) to methyl radicals and carbon dioxide.

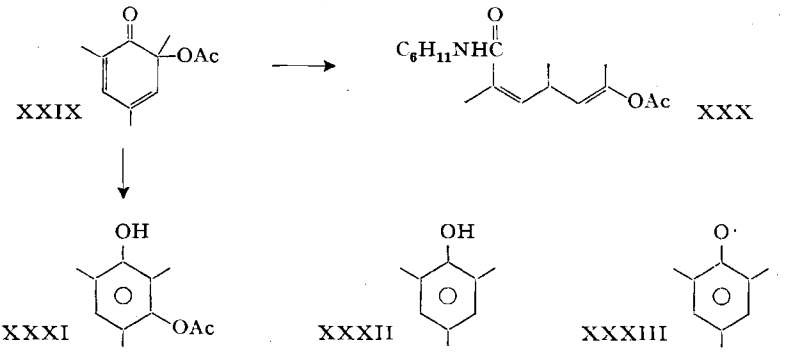
Irradiation of 2:6-dimethyl-6-acetoxy-cyclohexa-2:4-dien-1-one (XXIV) in ether containing cyclohexylamine afforded the expected cyclohexylamide (XXV) in high yield, but analogous irradiation of the isomeric dienone (XXVI) afforded not the expected amide (XXVII) but the isomer (XXVIII). We do not construe this result as contrary to the general theories advanced above. The expected diene (XXVII) is, no doubt, formed initially but, owing to the unfavourable 1:3-interaction of the methyl at C-3 in (XXVII) with the acetoxyl (or methyl)[21]) attached to C-5, it is destabilised and so rearranges through the appropriate anion (produced by the action of the excess of cyclohexylamine) to give the observed product (XXVIII).

A similar result was obtained from the irradiation of the mesitol derivative (XXIX) in the presence of cyclohexylamine. The product, formed in high yield, was the α,β-unsaturated amide (XXX), and no doubt a similar explanation for this result holds good also.

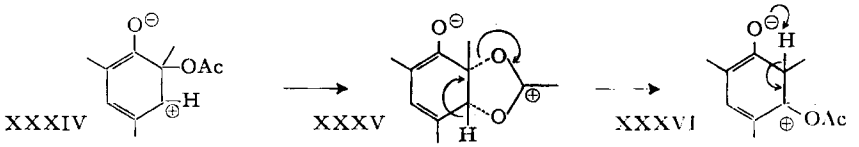


[22]) A. Rembaum & M. Szwarc, J. Amer. chem. Soc. **77**, 3486 (1955); C. Walling, Free Radicals in Solution, John Wiley and Sons Inc., New York 1957, pp. 491–493.

Irradiation of (XXIX) in the presence of water or aniline gave especially interesting results. The photochemical reaction was slow compared with amide formation in the presence of cyclohexylamine (see above). There resulted mainly the 2:4:6-trimethylresorcinol derivative (XXXI) together with some mesitol (XXXII). The latter no doubt is produced in the say way as is *ortho*-cresol from the comparable irradiation of (XX). The formation of (XXXI) cannot be explained on a similar radical basis. First the acetoxyl radical is not stable enough[22]) to explain recombination. Secondly, if it did recombine it would do so at the *ortho* and *para* positions in the simultaneously formed radical (XXXIII), not at the *meta* position. Thirdly, the addition of a large excess of *para*-cresol, known to be an efficient trap for acetoxyl radicals[23]), did not effect the formation of (XXXI) in any way. The rearrangement to give (XXXI) also proceeds in a polystyrene film as well as in thoroughly dry ether. Accepting that the excited state of the dienone (XXIX) would show charge separation (XXXIV), then the reaction can be represented by the sequence (XXXIV)



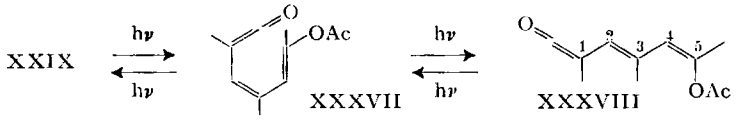
→ (XXXV) → (XXXVI) → (XXXI). This scheme assigns to the acetate residue its well known capacity to bear positive charge during neighbouring group participation and this explains the failure of the analogous allyl derivative of mesitol (see below) to undergo any rearrangement.



The rate of light induced cleavage of (XXIX) can hardly be dependent upon the nucleophile present, and therefore the failure of water or aniline to give cleavage products requires a special explanation. We consider[17]) that the relative stabilities of the *cis* (XXXVII) and *trans* (XXXVIII) ketens must be the critically important factor. Both ketens, being fully substituted, might react relatively slowly with nucleophiles. One has, therefore, a competition between the rate of reaction of these ketens with nucleophiles and the rate of ring closure of the *cis*-keten (XXXVII) to give back (XXIX). Now (XXXVIII) has two destabilising 1:3 interactions between

[23]) C. WALLING & R. B. HODGDON, J. Amer. chem. Soc. **80**, 228 (1958).

the methyl groups at C-1 and C-3 and the acetoxyl (or methyl)[21]) at C-5. The *trans*-keten (XXXVIII) must, therefore, be destabilised relative to other *trans*-ketens and



relative to (XXXVII). This means that the rate of the back reaction from (XXXVIII) to (XXXVII) will be greater and that therefore the rate of reclosure of (XXXVII) to give (XXIX) will be greater. It will certainly be of interest to attempt to prepare ketens of the types (XXXVII) and (XXXVIII) by normal chemical methods and confirm that their photochemical closure to give (XXIX) is indeed rapid.

Irradiation of the cyclohexadienones[19]) (XXXIX) and (XL) in the presence of cyclohexylamine caused smooth cleavage to the β,γ- and α,β-unsaturated amides that would be respectively anticipated from results already discussed above. More interesting was the stability of (XL) to light in the presence of water. Prolonged irradiation for very long periods caused no change. We explain this by the theory outlined above in the case of the mesitol derivative (XXIX).

We have also considered another scheme whereby the nucleophile adds to the carbonyl group of the *ortho*-type cyclohexadienone prior to cleavage. There are excellent reasons both theoretical and experimental which preclude this and the matter is discussed fully elsewhere[17]).

The conversion of ergosterol (XLI) through precalciferol[24]) (XLII) into calciferol (XLIII) illustrates a common behaviour of steroidal dienes which has received a great deal of attention[25]). The first step is photochemically induced, the second is wholly thermal[26]). Until recently the steroid 5:7-diene system was the only cyclohexadiene in which photochemical cleavage had been demonstrated. We have now been able to show[27]) that irradiation of methyl dehydro-ursolate acetate[28]) (XLIV) followed by appropriate thermal treatment affords an analogue (XLV) of calciferol. Since this breaks down on ozonolysis to give the dicarboxylic acid (XLVI) and a methyl ester ketone (XLVII), characterised as the crystalline keto-acid (XLVIII),

[24]) L. Velluz, A. Petit, G. Michel & G. Rousseau, C. r. hebd. Séances Acad. Sci. **226**, 1287 (1948); L. Velluz, A. Petit & G. Amiard, Bull. Soc. chim. France, **1948**, 1115.

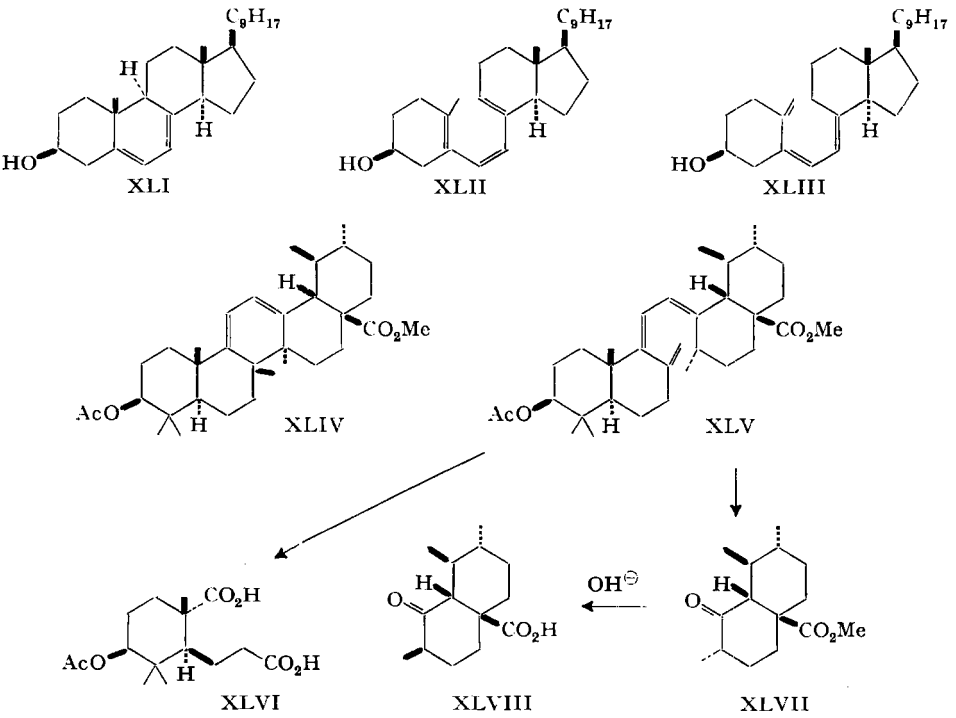
[25]) L. F. Fieser & M. Fieser, «Steroids», Reinhold Publishing Corporation, New York 1959, p. 90 *et seq.*; for other references see I. T. Harrison & B. Lythgoe, Proc. chem. Soc. **1957**, 261; H. H. Inhoffen, G. Quinkert, H.-J. Hess & H.-M. Erdmann, Chem. Ber. **89**, 2273 (1956).

[26]) See M. P. Rappoldt, J. A. Keverling Buisman & E. Havinga, Rec. Trav. chim. Pays-Bas **77**, 327 (1958), and earlier papers.

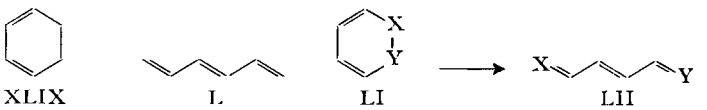
[27]) R. L. Autrey, D. H. R. Barton & W. H. Reusch, Proc. chem. Soc., **1959**, 55.

[28]) L. Ruzicka, O. Jeger & J. Redel, Helv. **26**, 1235 (1943); E. J. Corey & E. W. Cantrall, J. Amer. chem. Soc. **81**, 1745 (1959).

the reaction provides a procedure of potential value for the breakdown and synthesis of pentacyclic triterpenoids.



In preliminary experiments[29]) it has been shown that cyclohexa-1:3-diene (XLIX) affords on irradiation hexa-1:3:5-triene (L). These observations on 1:3-cyclohexadienes, coupled with our work[17]) on the *ortho*-cyclohexadienones referred to above, suggests to us[27]) that ring cleavage of the type (LI) → (LII) should be a general reaction. It is not, of course, required that methine groups (CH) be present; they could well be replaceable by the appropriate hetero-atoms or other groupings.

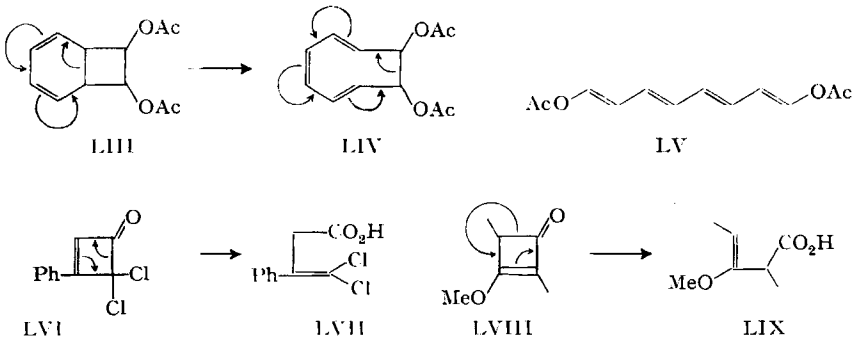


This generalisation, which should be of value in predicting further photochemical reactions, can be extended as follows. If one considers any ring of 2n members containing (n – 1) conjugated double bonds then, in principle, irradiation with ultraviolet light of the appropriate wave length should furnish an open chain compound containing (n – 1 + 1) = n conjugated double bonds. In support of this idea we have been able to show that irradiation of (LIII)[30]) in ether produces, *via* (LIV), the

[29]) D. H. R. Barton & J. Courtney, unpublished observations.

[30]) A. C. Cope, N. A. Nelson & D. S. Smith, J. Amer. chem. Soc. **76**, 1100 (1954).

tetraene (LV). Although we have not yet obtained[31]) the latter in a state of purity it shows the correct[32]) ultraviolet maxima at 273, 283, 298, 310 and 325 mμ. Similarly, irradiation[33]) of the cyclobutenone (LVI)[34]) in ether saturated with water gave the same acid (LVII) as has been obtained earlier by more conventional methods[34]). Irradiation[33]) of the cyclobutenone (LVIII)[35]) in ether containing water afforded spectroscopic evidence for the formation of the expected acid (LIX). However, these cleavage reactions of the cyclobutenone ring proceed with much less facility than the analogous reaction of *ortho*-cyclohexadienones[17]).



LIII LIV LV

LVI LVII LVIII LIX

Of course, the generalisation propounded above predicting the existence of new photochemical cleavage reactions is only permissive in character, and alternative reactions involving bridging are not excluded. An example of the need for this qualification is provided by the photochemistry of the pyro- and isopyro-calciferols[36]). Both compounds contain 1:3-cyclohexadiene rings but furnish derivatives of (LX) on irradiation. If the bridging reaction is reversible, then the final product of the reaction should still be in accordance with the above enunciated cleavage principle.

Quite different considerations apply to rings that contain (2n + 1) members and n conjugated double bonds. Here it can be predicted that cleavage reactions should not be observed, only bridging reactions. This is certainly true for the seven-membered tropolone ring[37]), but so far there are no examples for five- or nine-membered rings. Irradiation of cyclopentadiene does not furnish[33]) the expected isomer (LXI) because the rate of dimerisation to dicyclopentadiene is so fast. It will certainly be

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[31]) D. H. R. BARTON & J. COURTNEY, unpublished observations; further experiments are planned.

[32]) P. NAYLER & M. C. WHITING, J. chem. Soc., **1954**, 4006.

[33]) D. H. R. BARTON & O. A. STAMM, unpublished observations.

[34]) E. F. SILVERSMITH, Y. KITAHARA, M. C. CASERIO & J. D. ROBERTS, J. Amer. chem. Soc. **80**, 5840 (1958), and references there cited. A specimen of (LVI) was very kindly provided by Professor JOHN D. ROBERTS (Cal. Tech., Pasadena).

[35]) G. SCHROETER, Ber. deutsch. chem. Ges. **49**, 2715 (1916); R. B. WOODWARD & G. SMALL, J. Amer. chem. Soc. **72**, 1297 (1950); E. B. REID, *ibid.* **72**, 2853 (1950).

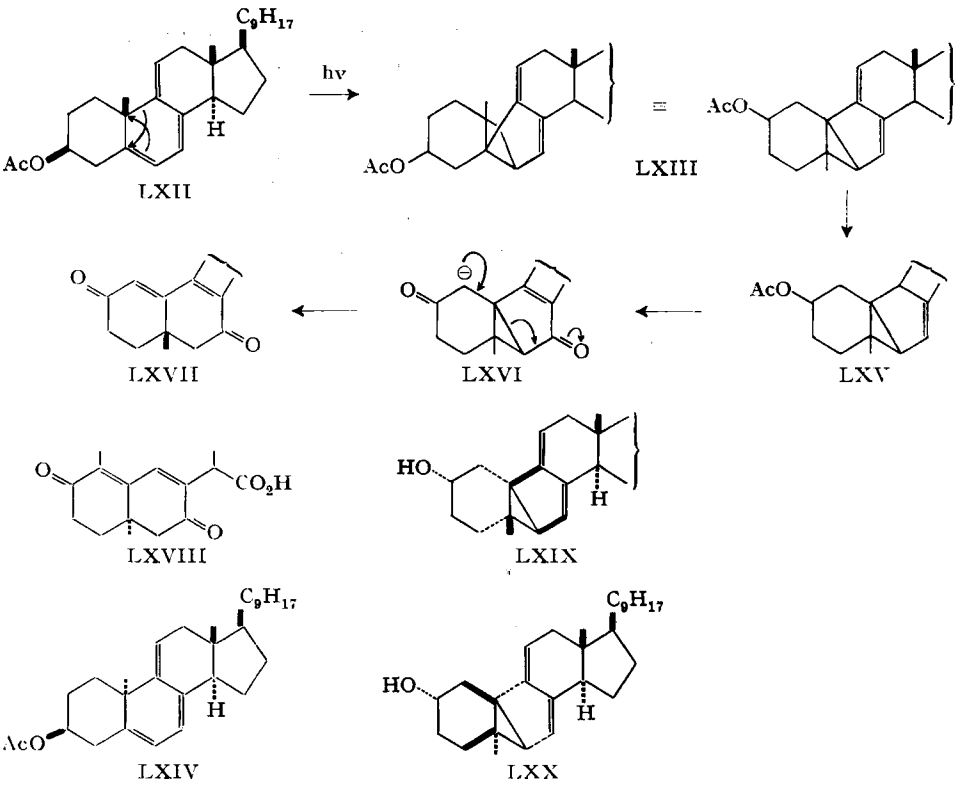
[36]) See W. G. DAUBEN & G. J. FONKEN, J. Amer. chem. Soc., **79**, 2971 (1957).

[37]) E. J. FORBES, J. chem. Soc., **1955**, 3864; P. D. GARDNER, R. L. BRANDON & G. R. HAYNES, J. Amer. chem. Soc. **79**, 6334 (1957); O. L. CHAPMAN & D. J. PASTO, *ibid.* **80**, 6685 (1958).

of interest to attempt the preparation of derivatives of (LXI) from cyclopentadienes so substituted as to reduce the rate of dimerisation.

LX LXI

Another interesting bond-crossing process is provided by the photochemical conversion of dehydro-ergosterol acetate (LXII) into photo-dehydro-ergosterol acetate (LXIII)[38]. Since dehydro-lumisterol acetate (LXIV) is also available, we are able to examine for the first time the stereospecificity of these bond-crossing rearrangements. We have shown[39] that (LXIV) affords a stereoisomer of (LXIII) and thus the process is indeed sterospecific. The question of whether the methyl group of (LXIII) is of inverted or retained configuration has been answered in the following way. Hydrogenation of (LXIII) gives a tetrahydro-derivative (LXV) which, on hydrolysis



and chromic acid oxidation, affords (LXVI). Treatment of the latter with mild base (see LXVI) affords the diene-dione (LXVII). The rotation of this compound is strongly negative in contrast to that of the model diene-dione (LXVIII)[39] which is strongly positive. We conclude then[39] that the compounds are enantiomeric in

[38]) D. H. R. Barton & A. S. Kende, J. chem. Soc., **1958**, 688.

[39]) D. H. R. Barton, R. Bernasconi & J. Klein, J. chem. Soc., **1959**, in press.

type[40]) as already indicated in (LXVII). If we accept that a cyclopropane ring must with a high degree of probability be *cis*-fused to a six- or five-membered ring, then the stereochemistry given in (LXIX) must be assigned to photo-dehydro-ergosterol. Photo-dehydro-lumisterol acetate (LXIV) has been degraded[39]) in the same way as outlined above to give a stereoisomer of (LXVII) with a marked positive rotation, as would be expected if the two stereoisomers differed in the configuration of the angular methyl group. We assign, therefore, the stereochemistry indicated in (LXX) to photo-dehydro-lumisterol.

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[40]) W. KLYNE, J. chem. Soc. **1952**, 2916; **1953**, 3072.

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280. Synthese von Ubichinon(45) und Ubichinon(50)

von **R. Rüegg, U. Gloor, R. N. Goel, G. Ryser, O. Wiss** und **O. Isler**

(13. X. 59)

Nachdem MORTON und seine Schule die Grundlagen für die Erforschung der Ubichinone IV gelegt hatten[1]), beschrieben wir vor einem Jahr die exakte Strukturaufklärung des Ubichinons(50) (IV, x = 10) aus Schweineherzen[2]) und die Totalsynthese des Ubichinons(30) (IV, x = 6) aus Hefe[3]). In unserer letzten Arbeit zeigten wir[4]), dass dem aus Tabak leicht isolierbaren Solanesol die Struktur I (x = 9) zukommt. Dabei erwähnten wir als zusätzlichen Beweis für diesen Befund die Synthese von Ubichinon(45) und Ubichinon(50) aus Solanesol, worüber wir nun ausführlich berichten[4a]).

Die Kondensation von Solanesol (I, x = 9) mit 5-Methyl-2,3-dimethoxy-hydrochinon (II) mittels Zinkchlorid und nachfolgende Oxydation des Kondensationsproduktes III (x = 9) mit Silberoxyd ergab Ubichinon(45) (IV, x = 9), das nach Smp. und Mischprobe, UV.- und IR.-Absorptionsspektren sowie Vergleich im Papierchromatogramm und RÖNTGEN-Pulverdiagramm mit einem natürlichen Präparat von Ubichinon(45) aus Lebern von Vitamin-A-Mangelratten identisch ist.

Solanesol wurde nun um einen Isoprenrest verlängert. Dies wurde erreicht durch Überführung in das Bromid V, Kondensation mit Acetessigester und Verseifung zum C_{48}-Keton VI, Acetylenanlagerung zu VII, Partialhydrierung zum tertiären Carbinol

[1]) G. N. FESTENSTEIN, F. W. HEATON, J. S. LOWE & R. A. MORTON, Biochem. J. **59**, 558 (1955); N. I. FAHMY, F. W. HEMMING, R. A. MORTON, J. Y. F. PATERSON & J. F. PENNOCK, *ibid.* **70**, 1P (1958); R. A. MORTON, Nature **182**, 1764 (1958).

[2]) R. A. MORTON, U. GLOOR, O. SCHINDLER, W. M. WILSON, L. H. CHOPARD-DIT-JEAN, F. W. HEMMING, O. ISLER, W. M. F. LEAT, J. F. PENNOCK, R. RÜEGG, U. SCHWIETER & O. WISS, Helv. **41**, 2343 (1958).

[3]) U. GLOOR, O. ISLER, R. A. MORTON, R. RÜEGG & O. WISS, Helv. **41**, 2357 (1958).

[4]) M. KOFLER, A. LANGEMANN, R. RÜEGG, U. GLOOR, U. SCHWIETER, J. WÜRSCH, O. WISS & O. ISLER, Helv. **42**, 2252 (1959).

[4a]) Anmerkung bei der Korrektur: C. H. SHUNK, R. E. ERICKSON, E. L. WONG & K. FOLKERS, J. Amer. chem. Soc. **81**, 5000 (1959), berichteten in einer kurzen Mitteilung ebenfalls über die Synthese von Ubichinon(45).