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Photodimeric Cage Compounds. I. The Structure of the Photodimer of 2,6-Dimethyl-4-pyrone¹BY PETER YATES^{2a} AND MARGARET JEFRAIM JORGENSEN^{2b}

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Irradiation of 2,6-dimethyl-4-pyrone in either the solid state or in solution with ultraviolet light gives a single photodimer which has been shown to be 2,4,8,10-tetramethyl-3,9-dioxapentacyclo[6.4.0.0.0²⁷.0⁴¹¹.0⁵¹⁹]dodecane-6,12-dione (IX) by degradation of the two dilactones, 2,4,9,11-tetramethyl-3,6,10,14-tetraoxapentacyclo[7.5.0.-(0²⁸.0⁴¹².0⁵¹¹)]tetradecane-7,13-dione (XII) and 2,4,9,11-tetramethyl-3,6,10,13-tetraoxapentacyclo[7.5.0.0²⁸.-(0⁴¹².0⁵¹¹)]tetradecane-7,14-dione (XIII), obtained by the action of perbenzoic acid on the dimer. The dimer has been found to revert to monomer on treatment with acid and to give the "open" isomer, 2,4,8,10-tetramethyl-3,9-dioxatriacyclo[6.4.0.0²⁷]dodeca-4,10-diene-6,12-dione (XLV), on pyrolysis. Reduction of the photodimer with hydrogen over platinum gives a mixture of four products which have been shown to arise by both hydrogenation and hydrogenolysis of the carbonyl groups. The spectra of the dimer are discussed briefly in terms of interaction between the p-electrons of the ether oxygen atoms and the carbonyl groups; the unusually facile hydrogenolysis reaction is discussed in related terms. The exclusive formation of the "head-to-tail" cage dimer in the solid state is interpreted in terms of the spatial disposition of the monomer molecules in the crystal lattice. The factors which may govern its exclusive formation in solution are also considered.

α,β -Ethylenic carbonyl compounds have been found to be exceptionally reactive under the influence of light. Irradiation may lead to geometrical isomerization, to rearrangement, often followed by reaction with the solvent, or to intermolecular reactions, which include dimerization, polymerization, and other addition reactions.³ Of these processes, dimerization is the most widely observed but, in many respects, the least fully investigated. The number of types of α,β -ethylenic carbonyl compounds which undergo photodimerization is large and includes ketones, *p*-quinones, acids, esters, anhydrides, and coumarins.^{3a-d} In those cases which have been fully investigated, it has usually been found that photodimerization leads to the formation of a cyclobutane derivative by bond formation between the ethylenic carbon atoms of two molecules of the α,β -ethylenic carbonyl compound; in the many cases where no rigorous proof of structure has been obtained, it has generally been assumed that photodimerization also occurs in this manner. However, it has recently been demonstrated that photodimerization of several α -pyridones does not give cyclobutane derivatives but proceeds instead by 1,4-addition.⁴ Attention may also be called to the case of α -lumicolchicine, a photodimer of colchicine, which, although a cyclobutane derivative, is structurally related to β -lumicolchicine, a rearrangement product of colchicine.⁵

The present investigation had its origin in our interest in the photodimer of 2,6-dimethyl-4-pyrone (I), the only recorded example of the photodimer of a γ -pyrone. This was first prepared by Paternò⁶ and subsequently assigned structure II by Guia and Civera.⁷

(1) A preliminary communication on part of this work has appeared previously: P. Yates and M. J. Jorgenson, *J. Am. Chem. Soc.*, **80**, 6150 (1958).

(2) (a) Department of Chemistry, University of Toronto, Toronto, Canada; Alfred P. Sloan Foundation Fellow, 1957-1960; (b) N. I. H. Fellow, 1957-1958.

(3) (a) A. Mustafa, *Chem. Rev.*, **51**, 1 (1952); A. Schönberg, "Präparative Organische Photochemie," Springer Verlag, Berlin, 1958; P. de Mayo in "Advances in Organic Chemistry: Methods and Results," ed. by R. A. Raphael, E. C. Taylor, and H. Wynberg, Vol. II, Interscience Publishers, Inc., New York, N. Y., 1960, p. 367; (b) G. W. Griffin, A. F. Velturo, and K. Furukawa, *J. Am. Chem. Soc.*, **83**, 2725 (1961); G. W. Griffin, R. B. Hager, and D. F. Veber, *ibid.*, **84**, 1008 (1962); G. W. Griffin, J. E. Basinski, and L. I. Peterson, *ibid.*, **84**, 1012 (1962); (c) P. E. Eaton, *ibid.*, **84**, 2344, 2454 (1962); (d) R. Anet, *Can. J. Chem.*, **40**, 1249 (1962); (e) I. H. R. Barton, *Helv. Chim. Acta*, **42**, 2604 (1959); P. de Mayo and S. T. Reid, *Quart. Rev. (London)*, **15**, 393 (1961); (f) H. E. Zimmerman and D. I. Schuster, *J. Am. Chem. Soc.*, **84**, 4527 (1962).

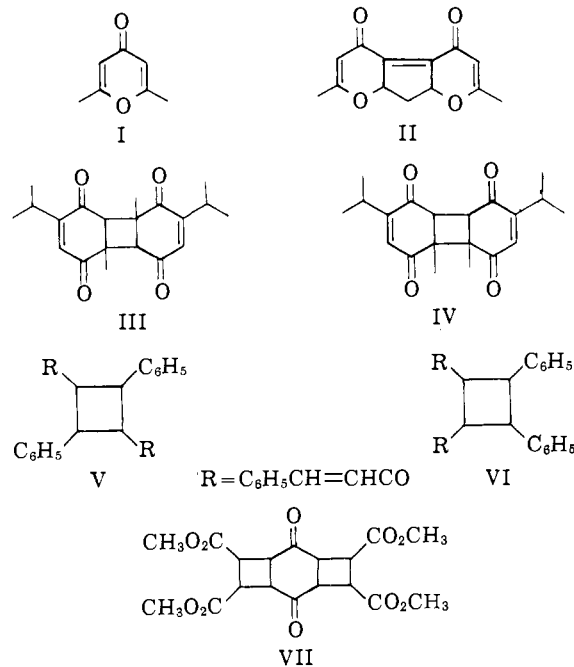
(4) W. A. Ayer, R. Hayatsu, P. de Mayo, S. T. Reid, and J. B. Stothers, *Tetrahedron Letters*, 648 (1961); G. Slomp, F. A. MacKellar, and L. A. Paquette, *J. Am. Chem. Soc.*, **83**, 4472 (1961).

(5) O. L. Chapman and H. G. Smith, *ibid.*, **83**, 3014 (1961).

(6) E. Paternò, *Gazz. chim. ital.*, **44**, I, 151 (1914).

(7) M. Guia and M. Civera, *ibid.*, **81**, 875 (1951).

Related carbocyclic compounds containing an $\alpha,\beta,\alpha',\beta'$ -dienone system have been found to undergo facile rearrangement on irradiation^{8c} and we considered that a detailed investigation of the structure of the photodimer of I was desirable. At the time of our investigation the only other photodimers derived from compounds containing an $\alpha,\beta,\alpha',\beta'$ -dienone system whose structure had been investigated were: (i) a dimer of thymoquinone, which was shown⁸ to have structure III or IV; (ii) two dimers of dibenzalacetone with structures V⁹ and VI¹⁰; and (iii) a dimer of dimethyl 3-oxo-1,4-pentadiene-1,5-dicarboxylate, considered to have structure VII.¹¹ In none of these cases was the stereochemistry of the dimer fully established. Subsequently, Cookson, Cox, and Hudec¹² have reported on an extensive investigation of the photodimerization



(8) E. Zavarin, *J. Org. Chem.*, **23**, 47 (1958).

(9) P. Praetorius and F. Korn, *Ber.*, **43**, 2744 (1910).

(10) G. W. Recktenwald, J. N. Pitts, Jr., and R. L. Letsinger, *J. Am. Chem. Soc.*, **75**, 3028 (1953).

(11) H. Stobbe and E. Färber, *Ber.*, **58**, 1548 (1925); F. Straus, *ibid.*, **37**, 3293 (1904). Further evidence in support of this structure has been reported recently: J. Corse, B. J. Finkle, and R. E. Lundin, *Tetrahedron Letters*, 1 (1961).

(12) R. C. Cookson and J. Hudec, *Proc. Chem. Soc.*, 11 (1959); R. C. Cookson, D. A. Cox, and J. Hudec, *J. Chem. Soc.*, 4199 (1961); cf. W. Flaig, J.-C. Salfeld, and A. Llanos, *Angew. Chem.*, **72**, 110 (1960).

of methylated *p*-benzoquinones, which in some cases resembles that of I (*vide infra*).

The photodimer of 2,6-dimethyl-4-pyrone was conveniently prepared by irradiation of the solid monomer with a sunlamp; this procedure afforded yields of *ca.* 30% after 3 weeks. The same product was also obtained by similar irradiation of solutions of the pyrone in acetic acid, ethanol, or benzene; however, the yield of dimer was considerably lower in these cases.¹³ The dimer is sparingly soluble in most organic solvents, but can be crystallized conveniently from dimethylformamide. It melts with decomposition at 281–284° in a sealed capillary tube.

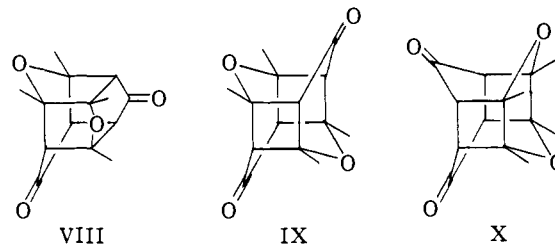
Elemental analysis confirmed the previously assigned empirical formula. Earlier molecular weight determinations⁶ by the cryoscopic method with phenol as solvent had indicated the dimeric nature of the product, and the molecular formula C₁₄H₁₆O₄; this formula was confirmed in the present work by elemental analysis of certain transformation products of the photoproduct (*vide infra*). The infrared spectrum of the dimer has a strong band at 5.88 μ and lacks other significant absorption in the 5–6.6 μ region. Its ultraviolet spectrum in acetonitrile has a maximum at 233 mμ (log ε 3.82), whose position is unchanged in ethanol.

The presence of two carbonyl groups in the photodimer was established by the preparation of a bis-2,4-dinitrophenylhydrazone and a dioxime. The ultraviolet spectrum of the former, λ_{max}^{dioxime} 367 mμ (log ε 4.72), is in better accord with an unconjugated than with a conjugated carbonyl derivative.¹⁴ The infrared spectra of both derivatives show no bands in the 5–6.5 μ region other than those associated with simple 2,4-dinitrophenylhydrazones and oximes, establishing that no carbonyl groups remain and that, in the absence of hydroxyl absorption, the other two oxygen atoms in the dimer molecule are present as ether linkages.

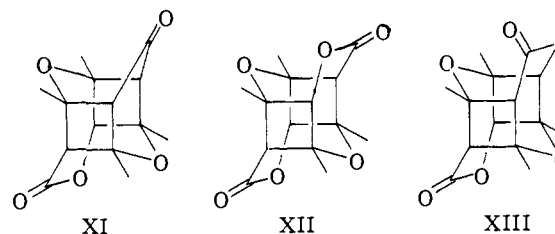
Several pieces of evidence pointed to the absence of ethylenic double bonds in the photodimer: (i) its infrared spectrum has no band in the ethylenic double bond-stretching region, (ii) it is unaffected by hydrogen in the presence of palladium-charcoal, (iii) it fails to undergo reaction with potassium permanganate in refluxing acetone, (iv) it gives no color with tetranitromethane. Although none of these pieces of evidence was individually compelling, taken together they suggested strongly the absence of ethylenic double bonds. A single observation suggested that the contrary might be true, *i.e.*, the ultraviolet spectrum of the dimer; however, the maximum at 233 mμ, although falling in a region associated with an α,β-unsaturated ketone function, has an extinction coefficient of 6600, which is exceedingly low for two such functions. It seemed probable, therefore, that this spectrum is anomalous.

Having established the nature of the functional groups, we next sought to determine whether the monomer units had retained their skeletal integrity in the process of dimerization or whether they had undergone skeletal rearrangement. It was observed that the photodimer reverted to monomer on treatment with ethanolic hydrochloric acid; since slightly more than 50% of I could be isolated from the reaction mixture, it could be concluded that both monomer units had been incorporated into the dimer molecule without skeletal change. On the basis of this conclusion and the earlier conclusions regarding the functional groups, three structures, VIII–X, could be written for

the photodimer. Of these, VIII was rejected since it placed the carbonyl groups in five-membered rings, while the position of the carbonyl band in the infrared spectrum of the dimer (5.88 μ) contraindicated this possibility. Degradative experiments were therefore based on the assignment of either structure IX or X to the photodimer. These experiments showed that the photodimer must be assigned the "head-to-tail" structure IX, and will be interpreted accordingly *ab initio*.



Reaction of the photodimer with perbenzoic acid afforded after 1 week a compound, C₁₄H₁₆O₆, which is formulated as the keto lactone XI. In conformity with this assignment is the presence of strong bands at 5.76 μ (δ-lactone) and 5.87 μ (ketone) in its infrared spectrum and the fact that it forms a mono-2,4-dinitrophenylhydrazone which retains the 5.76 μ band in its infrared spectrum. The characterization of this keto lactone and its 2,4-dinitrophenylhydrazone provided confirmation of the assignment of a dimeric rather than a trimeric structure to the photoproduct, since a trimer would furnish a diketo lactone or a keto dilactone of significantly different elemental composition.



When the reaction time of the photodimer with perbenzoic acid was extended to 3 weeks, two isomers, C₁₄H₁₆O₆, m.p. 340–350° dec. and *ca.* 280° dec., were obtained which are formulated as the dilactones XII and XIII, respectively. The infrared spectrum of each has a strong, single band in the carbonyl-stretching region at 5.75 μ. The higher-melting isomer, which is much less soluble in common organic solvents than the other isomer, was treated with aqueous sodium hydroxide for 2 hr. Acidification of the reaction mixture with 10% hydrochloric acid gave a mixture of acidic products from which a crystalline compound, C₇H₁₂O₅, could be isolated in 25% yield. The infrared spectrum (KBr) of this compound has complex, strong absorption in the 2.9–4.7 μ region, a broad, weak band at 5–5.5 μ, a strong band at 6.0 μ with a shoulder at 6.10 μ and a medium intensity band at 6.25 μ. These features suggested that the compound is a hydrate: thus, the spectra of the hydrates of several benzene polycarboxylic acids have weak or medium bands in the 5–5.4 μ region which are absent from the spectra of the anhydrous acids,¹⁵ and the spectrum of oxalic acid dihydrate has a band at 5.26 μ.¹⁶ This view was strengthened by the observation that, when a sample of the hydrolysis product was heated at 100° under high vacuum, changes occurred in its infrared spectrum which included the loss of the bands at 5–5.5 and 6.25 μ, while the position of its ultraviolet maximum [λ_{max}^{EtOH} 213 mμ (log ε 3.97)]

(15) F. González-Sánchez, *Spectrochim. Acta*, **12**, 17 (1958).

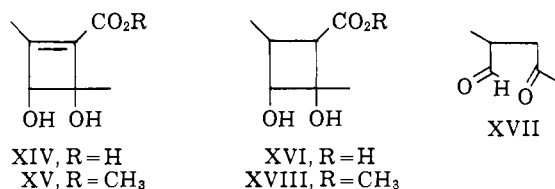
(16) R. C. Lord and R. E. Merrifield, *J. Chem. Phys.*, **21**, 166 (1953).

(13) It has recently been observed that the dimer can be prepared most expeditiously by irradiation of aqueous solutions of the pyrone with a Hanovia mercury arc lamp (Dr. I. W. J. Still, unpublished results).

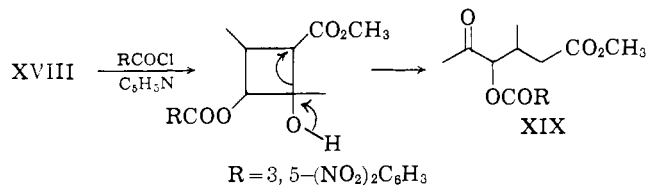
(14) A. E. Gillam and E. S. Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," 2nd Ed., Edward Arnold (Publishers) Ltd., London, 1957, p. 121.

remained unchanged. That the hydrolysis product is a monohydrate and may be formulated as $C_7H_{10}O_4 \cdot H_2O$ was shown by the formation of a methyl ester, $C_8H_{12}O_4$, on treatment with diazomethane; the ester has bands in its infrared spectrum ($CHCl_3$) at 2.7–3, 5.83, and 5.98 μ and an ultraviolet maximum at 215 $m\mu$ ($\log \epsilon$ 4.00).

The acid and ester were shown to have structures XIV and XV, respectively, in the following manner. Hydrogenation of the acid over palladium-charcoal led to the uptake of one molar equivalent of hydrogen and the formation of a dihydro acid, $C_7H_{12}O_4$ (XVI). This acid has no high intensity ultraviolet absorption above 210 $m\mu$ and its infrared spectrum (KBr) has bands at 3.02, 3.20, 3–4, and 5.86 μ . Treatment of the reduction product with sodium periodate resulted in consumption of one molar equivalent of the oxidant and the formation of 2-methyl-1,4-pentanedione (XXII). This product was identified by direct comparison of its bis-2,4-dinitrophenylhydrazone with an authentic sample prepared from the corresponding dioxime, obtained by the action of hydroxylamine on 2,4-dimethylpyrrole.¹⁷ The keto aldehyde XVII clearly arises *via* decarboxylation of a β -keto or β -aldehyde acid



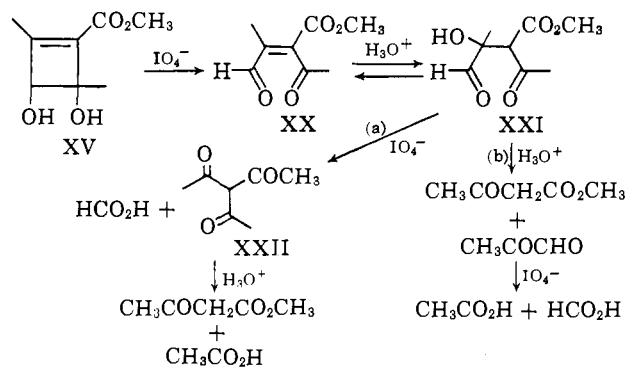
formed by oxidative cleavage of the dihydro acid. Since the spectral data establish that the unsaturated precursor of the dihydro acid is conjugated, it must have structure XIV, and the dihydro acid structure XVI. The dihydro acid was converted by diazomethane to a methyl ester, XVIII, which gave a mono-3,5-dinitrobenzoyl derivative whose molecular weight was determined to be in accord with the formulation deduced for the dihydro acid. However, this derivative possesses no hydroxyl group, as shown by an active hydrogen determination and by its infrared spectrum. It is therefore assigned structure XIX, derived by cleavage of the cyclobutane ring under the basic reaction conditions



The fact that the dihydro acid XVI gives iodoform on treatment with iodine and base can be interpreted in terms of a similar base-induced cleavage reaction.

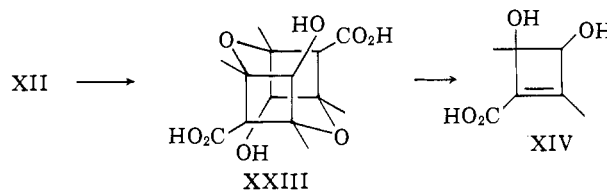
Periodate oxidation of the unsaturated acid XIV and ester XV was found to be more complex in that two molar equivalents of oxidant were consumed in each case. The product in the latter instance was shown to be methyl acetoacetate, identified as its 2,4-dinitrophenylhydrazone. These observations can readily be rationalized in terms of the assigned structures in the following ways.

Hydration of XX, the initial cleavage product, to give XXI is expected to be facile because of the accumulation of electron-withdrawing substituents on the ethylenic bond. Two pathways can then be envisaged: (a) oxidative cleavage of XXI by the second equivalent of

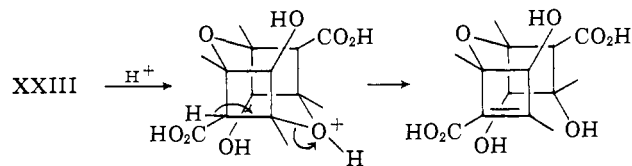


periodate to give formic acid and XXII, which then undergoes hydrolytic cleavage to acetic acid and methyl acetoacetate; or (b) cleavage of XXI by a reverse aldol reaction to give methyl acetoacetate and pyruvaldehyde, the latter then consuming the second equivalent of periodate.

The formation of the acid XIV on hydrolysis of the dilactone, m.p. 340–350° dec., establishes the structure of the latter as XII, which would be expected to give rise to XXIII on hydrolysis, which in turn could give XIV. The cleavage of the two ether linkages in the latter transformation is considered most likely to

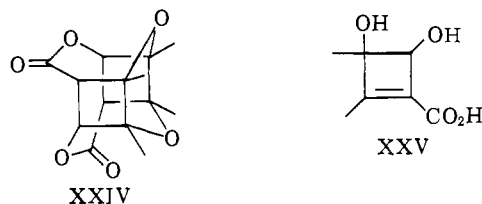


occur during the acid work-up of the hydrolysis mixture and to involve two eliminative steps as shown below.



On this view, the two hydroxyl groups of XIV should have the *cis* relationship; this is in accord with the facile cleavage of XIV, XV, and XVI by periodate.¹⁸

A dilactone of structure XXIV, derived from the "head-to-head" dimer X, could undergo a series of reactions analogous to those discussed above. The product would be XXV, an isomer of XIV, which would give 3-methyl-1,4-pentanedione, not XVII, on hydrogenation and periodate cleavage. Thus only the "head-to-tail" structure IX is admissible for the dimer. The assignment of the centrosymmetric structure XII to the higher-melting dilactone is in accord with the expectation that the more symmetrical of the two dilactones would have the higher melting point and lower solubility.

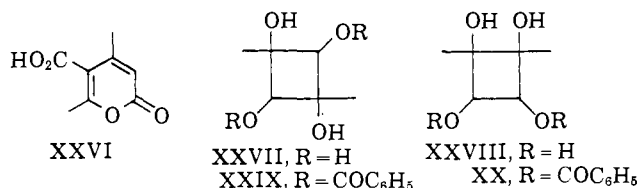


Hydrolysis of the lower-melting dilactone with aqueous base followed by acidification led to a mixture of products from which three crystalline compounds were isolated: an acid, $C_8H_8O_4$, an acid, $C_{14}H_{20}O_8$, and

(17) Cf. V. C. Bulgrin and G. Dahlgren, Jr., *J. Am. Chem. Soc.*, **80**, 3883 (1958).

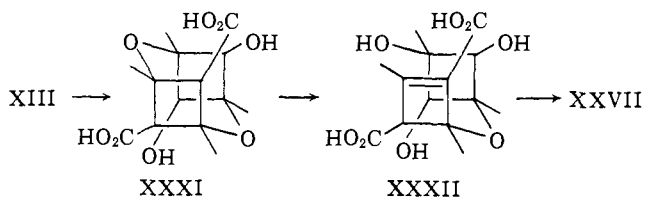
(18) G. Ciamician and C. U. Zanetti, *Ber.*, **23**, 1787 (1890).

a neutral compound, $C_6H_{12}O_4$. The C_8 -acid was identified as isodehydroacetic acid (XXVI) by comparison with an authentic sample. The C_6 -compound was assigned structure XXVII on the basis of the following evidence. Its infrared spectrum has intense bands in the 3μ region but no absorption in the $5-6 \mu$ region;



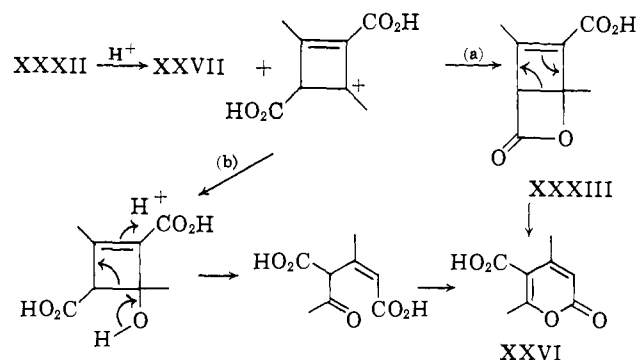
it has no appreciable ultraviolet absorption above $210 m\mu$. A Kuhn-Roth determination indicated the presence of two C-methyl groups. It consumed four molar equivalents of sodium periodate with the formation of four equivalents of acidic products, of which approximately half were shown to consist of a reducing acid. It formed a dibenzoate, $C_{20}H_{20}O_6$, with bands in its infrared spectrum (KBr) at $2.89(sh)$, 3.01 , and 5.81μ ; the results of a molecular weight determination on the dibenzoate were in accord with the formulations given. These data established that the C_6 -compound is a dimethylcyclobutanetetrol, which would give rise to two equivalents of acetic acid and two equivalents of formic acid on the consumption of four molar equivalents of periodate. There are only two structural isomers of such a compound, XXVII and XXVIII, although each of these can exist in several diastereoisomeric forms. A choice between XXVII and XXVIII was made on the basis of the observation that the dibenzoate failed to react with sodium periodate. This is explicable in terms of structure XXIX for the dibenzoate, derived from a tetrol of structure XXVII, for such a compound does not possess a vicinal glycol grouping. If XXVIII were the structure of the tetrol and thus XXX that of the dibenzoate, the resistance to periodate oxidation would have to be rationalized in terms of a *trans* disposition of the vicinal hydroxyl groups¹⁸; however, the origin of the tetrol from a cage dimer makes it likely that these hydroxyl groups would have a *cis* relationship. Structure XXIX is therefore assigned to the dibenzoate and XXVII to the tetrol. This choice is corroborated by the formation of isodehydroacetic acid together with the tetrol in the hydrolysis of the lower-melting dilactone (*vide infra*).

The formation of C_6 - and C_8 -fragments on hydrolysis of this dilactone can readily be interpreted in terms of structure XIII since this consists of six- and eight-carbon moieties joined by oxygen atoms alone. Application of considerations analogous to those invoked in the interpretation of the hydrolysis of dilactone XII leads to the reaction sequences

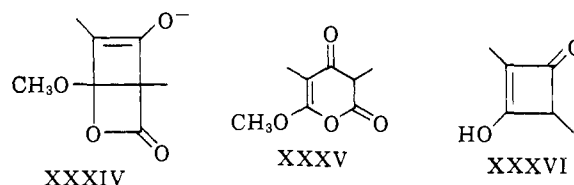


This scheme accounts for the formation of the tetrol XXVII and suggests the general nature of the C_8 -intermediate which leads to isodehydroacetic acid (XXVI). Although no definitive reaction path can be proposed at this time for the formation of XXVI, routes of the following types seem reasonable.¹⁹

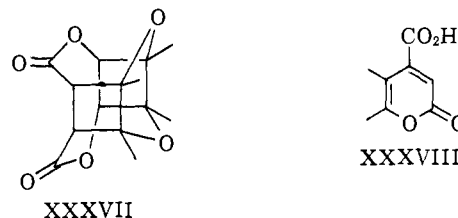
(19) An interesting, but less probable, alternative route might involve eliminative cleavage of the ether function of XXXII to give XXVII and a



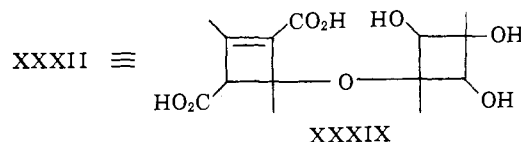
The intermediate XXXIII in route (a) is analogous to XXXIV, an intermediate suggested by Woodward and Small²⁰ to be involved in the conversion of the pyrone XXXV to the methylketene dimer XXXVI.



Irrespective of the detailed course of its formation, the isolation of isodehydroacetic acid provides further evidence in support of the assignment of the "head-to-tail" structure for the photodimer. For, although the dilactone XXXVII, derived from the "head-to-head" dimer X, could undergo hydrolytic cleavage in a manner analogous to that proposed above for the dilactone XIII, the C_8 -product would be XXXVIII rather than XXVI. It may also be noted that the C_6 -product would then be XXVIII.



The third crystalline product obtained on hydrolysis of the dilactone XIII, the acid $C_{14}H_{20}O_8$, gave on acid hydrolysis isodehydroacetic acid (XXVI) and the tetrol XXVII. This indicated that the C_{14} -acid is an intermediate in the hydrolytic cleavage of XIII to these products and that the earlier supposition that ether cleavage occurs during the acid work-up is well founded. The spectra of the C_{14} -acid are in accord with the assignment to it of structure XXXIX (\equiv XXXII), previously postulated as an intermediate in the formation of XXVI and XXVII. Its infrared spectrum (KBr) has bands at 2.94 , $3-4.5$, 5.79 , 5.85 , and 6.05μ ; its ultraviolet spectrum has a maximum at $213 m\mu$ ($\log \epsilon$ 4.12) with a shoulder at $225 m\mu$ ($\log \epsilon$ 4.03). It formed a dimethyl ester on treatment with diazomethane, whose infrared spectrum has bands at 2.95 , 5.80 , 5.84 , and 6.10μ and whose ultraviolet spectrum is similar to that of the acid. Acid treatment

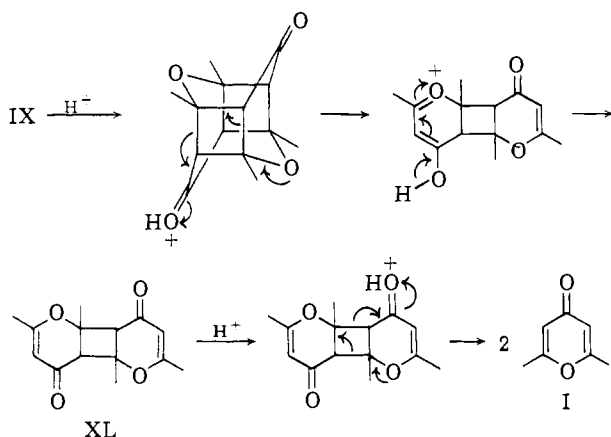


cyclobutadiene derivative, which could serve as the source of the lactone XXXIII.

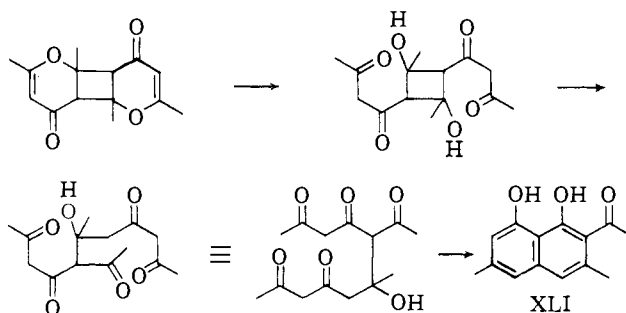
(20) R. B. Woodward and G. Small, Jr., *J. Am. Chem. Soc.*, **72**, 1297 (1950).

of the ester led to the isolation of methyl isodehydroacetate. Unexpectedly, both the acid and its dimethyl ester consumed only one molar equivalent of periodate. We suggest that this can be attributed to one of two causes: (i) steric hindrance to further cleavage of the α -ketol formed after consumption of one molar equivalent of periodate, due to the heavily substituted quaternary center adjacent to the carbon atom bearing the hydroxyl group²¹; (ii) addition of the hydroxyl group of this α -ketol to the β -carbon of the α,β -unsaturated carboxylic acid system.

With the structure of the photodimer established as IX on the basis of these cleavage reactions of the derived dilactones, we discuss now two reactions involving cleavage of the cyclobutane rings of the dimer itself. Reference has already been made to one of these—the acid-catalyzed reversion to monomer. This can be interpreted as occurring as shown below.



Although the intermediate XL has not been isolated in the case of the acid-catalyzed fission of IX, the corresponding product has been isolated²² in the case of the related reaction of the photodimer of 2,6-diethyl-4-pyrone.²³ When the acid treatment of IX was conducted heterogeneously in purely aqueous medium the dimer became coated with a yellow product which prevented further reaction. This product was found to be identical with the naphthalenic compound XLI first obtained by Collie.²⁴ This compound was not formed from the pyrone I under the conditions of the reaction. It seems likely that it arises *via* acid-catalyzed cleavage of the enol ether systems of XL in the following or related fashion



A second cleavage reaction of the dimer cage was uncovered when the decomposition reaction at its melting

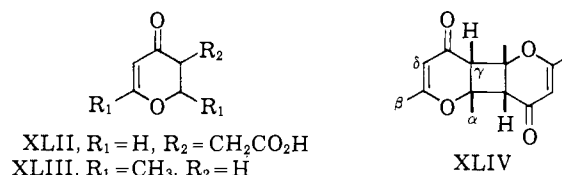
(21) Steric factors are known to influence the periodate cleavage reaction; cf., for example, P. Yates and G. H. Stout, *J. Am. Chem. Soc.*, **80**, 1601 (1958); E. F. Garner, I. J. Goldstein, R. Montgomery, and F. Smith, *ibid.*, **80**, 1206 (1958).

(22) P. Yates and S. K. Roy, unpublished results.

(23) P. Yates and E. S. Hand, *Tetrahedron Letters*, 669 (1961); E. S. Hand, Ph.D. Thesis, Radcliffe College, 1961.

(24) J. N. Collie, *J. Chem. Soc.*, **63**, 329 (1893); N. Collie and W. S. Myers, *ibid.*, **63**, 122 (1893); J. N. Collie and A. A. B. Reilly, *ibid.*, **121**, 1984 (1922).

point was investigated. From the crude product it was possible to isolate in low yield an isomer of the dimer. The infrared spectrum of this compound has a split band at 6.02–6.05 μ and a band at 6.18 μ ; its ultraviolet spectrum has a maximum at 266 m μ (log ϵ 4.34). These spectra strongly indicated that the isomer is the "half-open cage" compound XL postulated above as an intermediate in the acid-catalyzed cleavage of the photodimer. Thus, Woodward and Singh²⁵ have reported the following data for the dihydropyrone XLII: $\lambda_{\text{max}}^{\text{CH}_2\text{Cl}_2}$ 5.82, 5.98, 6.15 μ ; $\lambda_{\text{max}}^{\text{EtOH}}$ 268 m μ (log ϵ 4.10). For the dihydropyrone XLIII de Vrieze²⁶ reported $\lambda_{\text{max}}^{\text{EtOH}}$ 263 m μ (log ϵ 3.84) and Hand²³ has found $\lambda_{\text{max}}^{\text{EtOH}}$ 6.01 and 6.22 μ . The nuclear magnetic resonance spectrum of the pyrolysis product is also in accord with this structural assignment; it has four singlets with τ = 8.30, 8.07, 6.90, and 4.75 p.p.m. (intensity ratio *ca.* 3:3:1:1), which are attributed to protons on the carbon atoms designated α , β , γ , and δ , respectively, in XLIV. This structural assignment was confirmed by the observations that the compound gave the monomeric pyrone I on treatment with mineral acid and was reconverted with great facility to the photodimer IX on irradiation in either the solid state or



solution. The origin of the pyrolysis product and its ready reclosure permit the assignment to it of the stereoformula XLIV. The thermal cleavage of a cyclobutane ring formed in the dimerization of α,β -unsaturated carbonyl compounds is a commonly observed reaction.^{3a} It is probable that further thermal degradation of XLIV to the monomer I occurred during the pyrolysis reaction; however, this would have been swept from the reaction vessel under the conditions of the experiment.

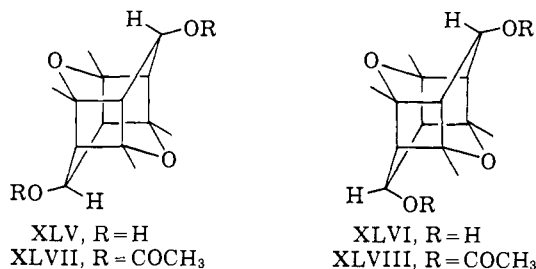
In contrast to the ready acid-catalyzed and thermal decomposition of the photodimer is its considerable stability in basic media. It was recovered unchanged to the extent of 90% after treatment for 4 hr. with boiling aqueous 10% sodium hydroxide and for 15 hr. with sodamide in boiling benzene. Even after 32-hr. treatment with sodamide in boiling xylene at least 60% of starting material was recovered. This resistance to base-catalyzed decomposition is considered to reflect the effect of two factors: first, difficulty of removal of a proton from a carbon atom α to the carbonyl groups in IX because of the unfavorable geometry for the delocalization of the resulting negative charge onto a carbonyl oxygen atom; second, inhibition of attack by negatively charged species at the carbonyl carbon atom because of unfavorable interaction in the transition state with the unshared pairs of electrons on the ether oxygen atoms. It may also be noted that in the case of acid-catalyzed decomposition, considerations related to the first of these factors make it very unlikely that reaction proceeds *via* initial enolization of IX and point to the alternative pathway proposed earlier.

Although the dimer IX was resistant to hydrogenation over a palladium catalyst, it was reduced in acetic acid over platinum, giving a mixture of products. Two components of this mixture were isolated directly: a compound, $\text{C}_{14}\text{H}_{20}\text{O}_3$, and a compound, $\text{C}_{14}\text{H}_{20}\text{O}_2$. Two further, isomeric components, $\text{C}_{14}\text{H}_{20}\text{O}_4$, were

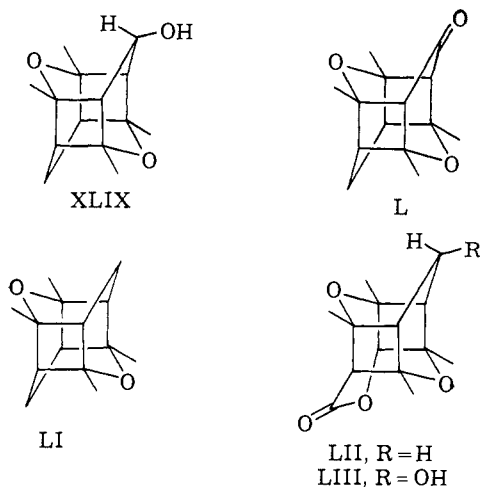
(25) G. Singh, Ph.D. Thesis, Harvard University, 1949.

(26) J. J. de Vrieze, *Rec. trav. chim.*, **78**, 91 (1959).

isolated and characterized as their diacetates. The latter pair of components are clearly the two possible stereoisomeric diols XLV and XLVI derived by reduction of the ketone groups of IX to secondary alcohol groups, since on oxidation with chromium trioxide-pyridine of a mixture containing them and the compound $C_{14}H_{20}O_3$ the photodimer IX was regenerated together with a compound $C_{14}H_{18}O_3$, which was obtained alone when a pure sample of the compound $C_{14}H_{20}O_3$ was oxidized with chromium trioxide-pyridine. There is a marked difference in the melting points and solubilities of the diacetates of the diols, and a provisional assignment of structure can be made on this basis. The centrosymmetric structure XLVII is assigned to the less soluble diacetate, m.p. 231–232°, while the less symmetrical structure XLVIII is assigned to the more soluble diacetate, m.p. 125.5–126.5°.



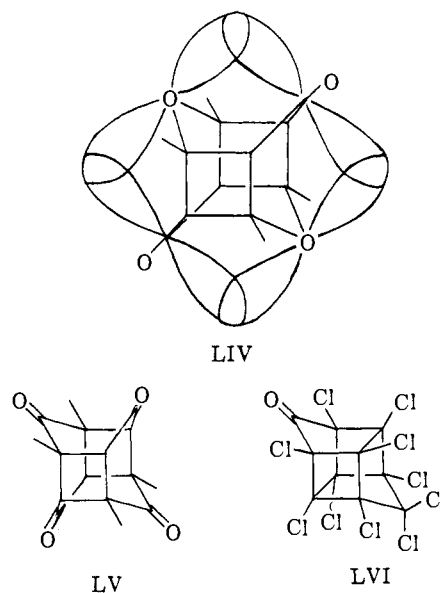
The compound $C_{14}H_{20}O_3$ formed a monoacetate, which has no hydroxyl-stretching band in its infrared spectrum. Its oxidation product, $C_{14}H_{18}O_3$, has a strong band in its infrared spectrum at 5.90μ and formed a mono-2,4-dinitrophenylhydrazone with $\lambda_{\max}^{E_{OH}}$ 367 $m\mu$ ($\log \epsilon$ 4.45) [cf. the bis-2,4-dinitrophenylhydrazone of the photodimer, $\lambda_{\max}^{dioxane}$ 367 $m\mu$ ($\log \epsilon$ 4.72)]. On the basis of these data the compound $C_{14}H_{20}O_3$ is assigned structure XLIX and its oxidation product structure L. It is thus considered to be derived by hydrogenolysis of one of the hydroxyl groups of either XLV or XLVI; a single configuration is possible for a compound of this structure. The fourth compound, $C_{14}H_{20}O_2$, has no hydroxyl- or carbonyl-stretching band in its infrared spectrum and is assigned structure LI; it results from hydrogenolysis of both of the hydroxyl groups of XLV and XLVI. The possibility that rearrangement may have occurred during the reduction in acid medium may be discounted, in that the same product was obtained when the photodimer was subjected to Wolff-Kishner reduction. When a mixture of the alcohols XLV, XLVI, and XLIX was re-exposed with fresh catalyst to the hydrogenation conditions under which they were formed, no further uptake of hydrogen took place. It is apparent, therefore, that hydrogenolysis occurs while



the compound is still absorbed on the catalyst after the hydrogenation of a carbonyl group, a mixture of products being formed because desorption and further reduction are competitive processes.

Hydrogenation of the keto lactone XI was also investigated. A product, $C_{14}H_{18}O_4$, was isolated whose infrared spectrum has a band at 5.80μ and no hydroxyl-stretching band. It is considered to be the hydrogenolysis product LII. A second compound was also obtained which is probably the hydrogenation product LIII since it has infrared bands at 2.80, 2.90, and 5.80μ , but a satisfactory elemental analysis was not obtained.

We turn next to a brief discussion of the ultraviolet and infrared spectra of the photodimer in terms of structure IX.²⁷ The strong band in its ultraviolet spectrum at 233 $m\mu$ can be associated with a charge-transfer $n_E \rightarrow \pi^*$ transition,²⁸ involving overlap of the p-orbitals of the ether oxygen atoms with the π -orbitals of the carbonyl groups.²⁹ The interesting possibility that annular orbital overlap of the type indicated in LIV gives rise to a π^* -orbital of unusually low energy is under investigation. It is instructive to compare the spectrum of the photodimer of 2,6-dimethyl-4-pyrone with the spectra of certain photodimers of the dimethyl-*p*-benzoquinones, which Cookson, *et al.*,¹² have shown to have cage structures analogous to IX, *e.g.*, LV, which is formed from 2,6-dimethyl-*p*-benzoquinone. It was found¹² that LV and the related cage compounds obtained from the other dimethyl-*p*-benzoquinones all showed only low end-absorption in the ultraviolet region. It may be concluded that although in these benzoquinone dimers the orbital disposition is similar to that in IX, the energy required for excitation of a π -electron associated with a carbonyl group is consider-



(27) It is planned to discuss in detail the spectra of the photodimer, its ethyl analog,²⁸ and their derivatives in a later paper.

(28) The symbol n_E denotes an unshared electron on an ether oxygen atom. Cf. H. Labhart and G. Wagnière, *Helv. Chim. Acta*, **42**, 2219 (1959); C. F. Wilcox, Jr., S. Winstein, and W. G. McMillan, *J. Am. Chem. Soc.*, **82**, 5450 (1960); S. Winstein, L. de Vries, and R. Orloski, *ibid.*, **83**, 2020 (1961); R. C. Cookson and N. S. Wariyar, *J. Chem. Soc.*, 2302 (1956); H. Birnbaum, R. C. Cookson, and N. Lewin, *ibid.*, 1224 (1961).

(29) Delocalization of the σ -electrons of the cyclobutane rings must also be considered as a possible cause of this phenomenon. For, although the ultraviolet spectra of methyl cyclobutyl and methyl cyclohexyl ketones have been reported to be very similar,³⁰ geometrical factors might be more favorable for such delocalization in the case of IX.³¹ However, the absence of similar bands in the ultraviolet spectra of cage compounds of type I.V (*vide infra*) makes it unlikely that such delocalization is an important factor.

(30) R. P. Mariella and R. R. Raube, *J. Am. Chem. Soc.*, **74**, 518 (1952).
(31) Cf., also, J. J. Wren, *J. Chem. Soc.*, 2208 (1956); R. N. Moore and G. S. Fisher, *J. Am. Chem. Soc.*, **78**, 4362 (1956).

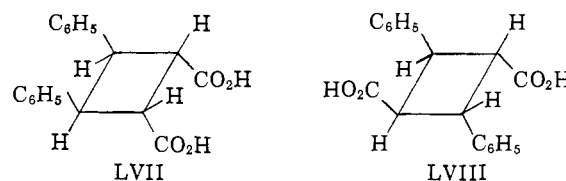
ably greater than that required for excitation of a p-electron of an ether oxygen atom in these systems.

The carbonyl-stretching band in the infrared spectrum of IX (5.88μ) occurs at only a slightly longer wave length than the corresponding bands of simple cyclohexanones. This does not necessarily imply, however, that interaction between the carbonyl groups and the unshared p-electrons on the ether oxygen atoms in the ground state is small or absent, since a shift to longer wave length due to appreciable interaction of this kind might be compensated by an effect in the opposite sense due to constriction of the C-C-C bond angles at the carbonyl groups in the cage structure. An additional factor is the possibility of coupling of the vibrations of the two carbonyl groups; however, this is contraindicated in this case by the similarity of the spectrum of IX in the carbonyl-stretching region to that of L.³² Cookson, *et al.*,¹² have found that the three cage compounds of type LV all have a strong band in their infrared spectra at 5.85 – 5.88μ . Again, vibrational coupling is possible and could be the source of the complexity of the bands, which in two cases are reported to have a shoulder at lower wave length. It is interesting to note that the dimers of type LV show a remarkable tendency to form hydrates, a property which they share with the perchloro cage ketone LVI³³ and related compounds.³⁴ The photodimer IX does not show a similar instability toward water, and it is possible that this difference may reflect ground state stabilization of IX due to ether-carbonyl interaction.

Regardless of the question of the occurrence of non-bonded interaction in the ground state of IX, the ultraviolet spectrum clearly suggests its intervention in the excited state. The unusually facile hydrogenolysis of the carbonyl groups of the dimer can be attributed similarly to interaction in the transition state of the p-electrons on the ether oxygen atoms with the reaction site, facilitating the cleavage of the carbon-oxygen bond.³⁵

It remains to discuss the formation of the photodimer. One of the most interesting features of this reaction is the exclusive formation in both the solution and solid states of the "head-to-tail" cage compound IX; neither the "head-to-head" cage isomer X nor an "open" dimer of type XL could be detected in the irradiation product. Although the detailed mechanism of the photodimerization of α,β -unsaturated carbonyl compounds is unknown, there is considerable reason to believe that, in the solid state reactions, the structure of the dimer is dependent on the mode of packing of the monomer molecules in the crystal lattice.^{36,37,38} Thus, the two different crystalline modifications of *trans*-cinnamic acid afford different dimers (LVII and LVIII) as primary products on irradiation.^{37,38} We consider it probable that a similar factor dictates the exclusive formation of the "head-to-tail" dimer in the present case. Indeed, X-ray crystallographic data show that in the crystal of 2,6-dimethyl-4-pyrone (I) the pyrone molecules occupy parallel planes and are stacked one

above the other in "head-to-tail" fashion.³⁹ It is likely that the greater variety of the irradiation products obtained by Cookson, *et al.*, in the case of the dimethyl-*p*-benzoquinones, from which "open" dimers in both the *syn* and *anti* series were formed in addition to cage dimers, reflects modes of crystal packing different from that obtaining in the case of I.



The exclusive formation of the "head-to-tail" dimer from I *in solution* stands in marked contrast to recent detailed observations on the photodimerization of simple α,β -unsaturated ketones to form a single cyclobutane ring. Büchi and Knutsen⁴⁰ have found that irradiation of 3-phenyl-2-cyclohexenone in solution gives exclusively the "head-to-head" dimer, while Eaton^{3c} has found that photodimerization of cyclopentenone as the pure liquid leads to approximately equal amounts of the "head-to-head" and "head-to-tail" products. Also, in these cases the dimers are considered to have the *cis-anti-cis* configuration, whereas formation of the cage product from I requires the intermediacy of the *cis-syn-cis* product XLIV. In the case of the α -pyrone derivative coumarin, Anet^{3d} has observed that photodimerization in solution (as in suspension) gives exclusively the "head-to-head" *syn* product.

The possibility was first considered that the mode of dimerization of I in solution is determined by its association in solution. Electrostatic forces might tend to hold the monomer molecules in a parallel "head-to-tail" relationship in the associated species, similar to that in the crystal lattice; photodimerization within such species could then lead exclusively to the "head-to-tail" product. However, this interpretation had to be discarded when it was observed that dimerization of I in aqueous solution also leads to exclusive formation of the "head-to-tail" product¹³; further, no evidence has been found for the association of I in solution in benzene.⁴¹ Two factors remain which may be invoked to account for the contrasting results. First, the process of formation of a product with a single cyclobutane ring from the γ -pyrone may differ from that in the case of simple α,β -unsaturated ketones in being reversible and thus permit ultimate formation of the "head-to-tail" cage product after initial, reversible formation of a "head-to-head" single cyclobutane ring. Second, the mechanism of formation of the cyclobutane ring may depend upon the nature of the α,β -unsaturated ketone system: in different cases the transition state for the formation of the first bond (product-determining if irreversible) may be more or less predominantly dipolar or diradical (singlet or triplet) in character^{42,43}; such

(32) Each has a very weak band at 5.72μ in addition to a strong band at 5.88 – 5.90μ with weak shoulders.

(33) E. T. McBee, C. W. Roberts, J. D. Idol, Jr., and R. H. Earle, Jr., *J. Am. Chem. Soc.*, **78**, 1511 (1956); H. E. Ungnade and E. T. McBee, *Chem. Rev.*, **58**, 249 (1958).

(34) P. E. Eaton, Ph.D. Thesis, Harvard University, 1960.

(35) The relatively ready hydrogenolysis of 1,3-diols to monohydric alcohols³⁵ may be due to a related cause.

(36) H. Adkins, "Reactions of Hydrogen with Organic Compounds over Copper-Chromium Oxide and Nickel Catalysts." University of Wisconsin Press, Madison, Wis., 1937; for a recent example, cf. T. Francis and A. S. Perlin, *Can. J. Chem.*, **37**, 1229 (1959).

(37) H. I. Bernstein and W. C. Quimby, *J. Am. Chem. Soc.*, **65**, 1845 (1943), and references therein quoted.

(38) G. M. J. Schmidt, *Acta Cryst.*, **10**, 793 (1957).

(39) G. M. Brown and H. G. Norment, *ibid.*, **8**, 363 (1955); we thank Professor G. B. Carpenter, Brown University, for an interpretation of these crystallographic data.

(40) G. Büchi and D. Knutsen, private communication; we thank Professor G. Büchi, Massachusetts Institute of Technology, for informing us of these results.

(41) V. S. Finkelstein and P. V. Kurnosova, *J. Gen. Chem. U.S.S.R.*, **3**, 121 (1933).

(42) Cf. the exposition of the effects of conjugating substituents on the course of the Diels-Alder reaction by R. B. Woodward and T. J. Katz, *Tetrahedron*, **5**, 70 (1959).

(43) It may be noted that Zimmerman^{3f} in his elegant interpretation of the mechanisms of photochemical reactions involving $n \rightarrow \pi^*$ transitions of α,β -unsaturated ketones has written the excitation step as forming a species with both ionic and radical character. Although the nature of the transition involved in the photodimerization of α,β -unsaturated

differences may clearly lead to differences in preferred modes of dimerization. Although impressive advances have been made recently in the mechanistic interpretation of several types of photochemical reactions,^{3f,44} a considerably greater corpus of experimental data must be accumulated in the case of the photodimerization of α,β -unsaturated carbonyl compounds before the influence of the factors referred to above can be elucidated in detail.

Experimental⁴⁵

Photodimer of 2,6-Dimethyl-4-pyrone (IX).—The pyrone was irradiated in the solid state in thin layers on a large surface with a General Electric 250-watt sunlamp. The layers were frequently turned to expose new surface to the radiation. After an interval of about 3 weeks the total solid was triturated twice with acetone to dissolve unconsumed starting material. The insoluble, white solid was filtered and thoroughly washed with warm acetone. In this manner pure photodimer could be isolated in yields of about 30%.

The photodimer was only sparingly soluble in all common organic solvents at elevated temperatures. It could be recovered as a fine powder by recrystallization from ethanol or acetic acid. Boiling dimethylformamide was found to be the best solvent. The dimer crystallized from this in large, flat needles which sublimed on being heated above 200°. Two recrystallizations followed by thorough washing with benzene gave an analytical sample, m.p. 281–284° dec. (sealed cap.) (lit.⁵ m.p. 270–280° dec.); $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.88, 6.92, 7.24 μ ; $\lambda_{\text{max}}^{\text{C}_6\text{H}_6}$ 233 m μ (log ϵ 3.82) [cf. 2,6-dimethyl-4-pyrone: $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.99, 6.20, 7.0, 7.17, 7.30 μ ; $\lambda_{\text{max}}^{\text{C}_6\text{H}_6}$ 210 m μ (log ϵ 3.93), 248 m μ (log ϵ 4.16)].

Anal. Calcd. for $\text{C}_{11}\text{H}_{16}\text{O}_7$: C, 67.73; H, 6.50. Found: C, 67.54; H, 6.42.

The pyrone also dimerized when a concentrated solution in ethanol, benzene, or acetic acid contained in a quartz flask was exposed to the sunlamp. The dimer was deposited on the walls of the flask and could be conveniently separated. However, the yields were inferior to those obtained from the irradiation of the solid, being less than 5% for an equivalent length of exposure.

The dimer did not revert to the monomer upon exposure to the same light source in solution or in the solid state. It gave a negative tetranitromethane test, did not react with a refluxing solution of potassium permanganate in acetone, and did not absorb hydrogen over palladium-charcoal in ethanol.

The 2,4-dinitrophenylhydrazone was prepared by the method of Fieser⁴⁶ in a heterogeneous system and was obtained as a yellow-orange solid. Three recrystallizations from pyridine followed by thorough washing with benzene yielded deep orange microcrystals, dec. ca. 300°; $\lambda_{\text{max}}^{\text{CHCl}_3}$ 3.03, 6.18, 6.29 μ ; $\lambda_{\text{max}}^{\text{C}_6\text{H}_6}$ 367 m μ (log ϵ 4.72).

Anal. Calcd. for $\text{C}_{26}\text{H}_{23}\text{O}_7\text{N}_3$: C, 51.53; H, 3.98; N, 18.42. Found: C, 51.56; H, 4.32; N, 18.80.

The dioxime was prepared by the method of Shriner and Fuson.⁴⁷ After a 3-hr. reflux period the ethanol was distilled and water was added to give the dioxime as a white precipitate (96%). Recrystallization from pyridine afforded white, sturdy needles, which sublimed ca. 300°; $\lambda_{\text{max}}^{\text{CHCl}_3}$ 3.10, 3.24, 5.98 μ ; $\lambda_{\text{max}}^{\text{C}_6\text{H}_6}$ 233 m μ (log ϵ 4.22). When the dioxime was heated at 200° its infrared spectrum was changed: $\lambda_{\text{max}}^{\text{CHCl}_3}$ 3.09, 6.08 μ .⁴⁸

Acid-Catalyzed Degradation of the Photodimer: Formation of I and XII.—The photodimer (5.0 g.) was heated under reflux with 10% hydrochloric acid (25 ml.) and ethanol (40 ml.) with stirring. After 30 min. a clear yellow solution was obtained. The ethanol was distilled *in vacuo*, when a yellow solid (*vide infra*) separated (ca. 0.1 g.). The aqueous solution was extracted with chloroform, the extracts were dried, and the chloro-

form was evaporated *in vacuo* to give a yellow semisolid residue (4.16 g.). Recrystallization of this material from benzene-petroleum ether afforded white needles (1.56 g.), m.p. 135–136°, identified as 2,6-dimethyl-4-pyrone by mixture m.p. and infrared spectral comparison. Extraction of the aqueous solution after neutralization afforded additional material (0.68 g.). This material and the material recovered from the mother liquors from the recrystallization above gave additional 2,6-dimethyl-4-pyrone (0.98 g.) upon sublimation. The total yield of pure pyrone was 51%.

When the photodimer was treated with 10% hydrochloric acid on the steam-bath in the absence of ethanol, the liquid turned yellow and a yellow material coated the photodimer, preventing further reaction. Separation of the solid, trituration with ethanol, and concentration of the ethanolic extract yielded small amounts of a yellow solid, similar to that obtained above. Recrystallization from ethanol afforded yellow needles, m.p. 178–180°, which gave a red coloration with ferric chloride in chloroform-pyridine and had $\lambda_{\text{max}}^{\text{CHCl}_3}$ 3.0, 6.10, 6.25, and 6.52 μ . This product was identified as 1,8-dihydroxy-3,6-dimethyl-2-acetonaphthone²⁴ (XLI) (m.p. 180–181°) by infrared spectral comparison and mixture m.p.

Reaction of the Photodimer with Perbenzoic Acid: Formation of XI, XII, and XIII.—The photodimer (24.0 g., 0.097 mole) was partially dissolved in chloroform (100 ml.) and a 0.885 N solution of perbenzoic acid in chloroform (1 l., 0.442 mole) added. The reaction mixture was allowed to stand at room temperature in the dark. After 2–3 days the solid had gone into solution, and after ca. 10 days solid material started to separate. After 12 days, titration of an aliquot showed the presence of only 15% of the original perbenzoic acid, owing to extensive decomposition at room temperature. The product obtained on work-up of an aliquot showed a considerable ketonic band in its infrared spectrum. Additional perbenzoic acid was added (0.14 mole in 300 ml. of chloroform) and the reaction mixture was allowed to stand for an additional 10 days. The solid was filtered and dried (10.2 g.); it was only sparingly soluble in all common solvents. Two recrystallizations from dimethylformamide followed by thorough washing with benzene afforded XII as white, sturdy prisms, m.p. 340–350° dec. (sealed cap), $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.75 μ , $\epsilon_{2.9}^{\text{C}_6\text{H}_6}$ 480.

Anal. Calcd. for $\text{C}_{11}\text{H}_{16}\text{O}_7$: C, 59.99; H, 5.75. Found: C, 60.07; H, 5.86.

The chloroform filtrate from the original reaction mixture was extracted thoroughly with aqueous 5% sodium bicarbonate; the chloroform solution was dried, concentrated, and cooled to give additional XII (4.2 g.). Concentration of the filtrate almost to dryness afforded the isomeric lactone XIII (11.2 g.) which was more soluble than XII in all common solvents. It was purified by fractional crystallization from acetone; the more soluble material was further recrystallized from acetone until its infrared spectrum showed no further change. Recrystallization of this material from benzene-petroleum ether afforded XIII as white microcrystals, m.p. ca. 280° dec. (sealed cap.), $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.75 μ , $\epsilon_{2.9}^{\text{C}_6\text{H}_6}$ 930.

Anal. Calcd. for $\text{C}_{11}\text{H}_{16}\text{O}_6$: C, 59.99; H, 5.75. Found: C, 59.96; H, 5.72.

Both isomers failed to absorb hydrogen over palladium-charcoal in ethanol and were resistant to refluxing hydrochloric and hydriodic acids. In each of several runs the product ratio XII/XIII was ca. 1.5.

When the original reaction mixture was worked up after 1 week, the keto lactone XI was obtained as a white solid (ca. 95% yield). Five recrystallizations from dimethylformamide afforded XI as sturdy prisms, m.p. ca. 280° dec. (sealed cap.); $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.76, 5.87 μ ; $\epsilon_{2.9}^{\text{C}_6\text{H}_6}$ 3,500.

Anal. Calcd. for $\text{C}_{11}\text{H}_{16}\text{O}_5$: C, 63.62; H, 6.10. Found: C, 63.82; H, 6.01.

The 2,4-dinitrophenylhydrazone of XI was prepared by the method of Fieser⁴⁶ and after five recrystallizations from ethanol was obtained as yellow-orange needles, m.p. 275–280° dec.; $\lambda_{\text{max}}^{\text{CHCl}_3}$ 3.02, 5.78, 6.18, 6.27 μ ; $\lambda_{\text{max}}^{\text{C}_6\text{H}_6}$ 245 m μ (log ϵ 4.17), 362 m μ (log ϵ 4.39).

Anal. Calcd. for $\text{C}_{26}\text{H}_{23}\text{O}_5\text{N}_3$: C, 54.05; H, 4.54; N, 12.61. Found: C, 53.72; H, 4.62; N, 12.93.

Base-Catalyzed Hydrolysis of XII: Formation of XIV.—The dilactone XII (8.0 g.) was stirred under nitrogen with aqueous 5% sodium hydroxide (200 ml.) for 2 hr., after which time almost all of the solid had dissolved. Since exposure of the basic solution to air caused immediate darkening, the solution was cooled and acidified with 10% hydrochloric acid while under nitrogen. The undissolved solid was filtered and the filtrate was saturated with ammonium sulfate and thoroughly extracted with ethyl acetate. Removal of solvent from the dried extract left a yellow sirup (8.0 g.), which upon treatment with chloroform deposited a pale yellow solid (0.98 g.), m.p. 127–128° with gas evolution. Upon standing in the cold the mother liquor deposited additional crops

ketones has rarely been defined, it seems likely to be of the $n \rightarrow \pi^*$ type in many cases since dimerization has often been observed to occur in sunlight. The possibility exists, of course, that different transitions are involved in different cases and that the variation in the modes of dimerization derives in part from this source.

(44) N. J. Turro and G. S. Hammond, *J. Am. Chem. Soc.*, **84**, 2841 (1962), and earlier papers in this series.

(45) Melting points were determined on a Fisher-Johns micro hot stage, unless otherwise specified, and are uncorrected. Analytical samples were dried at 80° *in vacuo*, unless otherwise specified. Infrared spectra were calibrated against the 2.66 and 5.88 μ bands of atmospheric water vapor.

(46) L. F. Fieser, "Experiments in Organic Chemistry," 3rd Ed. rev., D. C. Heath and Co., Boston, Mass., 1957, p. 84.

(47) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 202, Procedure 42A.

(48) Subsequent elemental analyses²⁴ have shown that the initial product is the hemihydrate of the dioxime and that the product obtained when this hemihydrate is heated at 200° is the unsolvated dioxime.

of the same compound; the combined yield was 2.27 g. (25%). One recrystallization from ethanol-chloroform afforded white prisms, m.p. ca. 75–85°. After further recrystallizations from the same solvent pair, the melting point range of the product was found to remain constant, but the melt resolidified on further heating and the compound remelted at 130–132°. After being dried *in vacuo* at room temperature it no longer showed the lower melting point, but only some softening in that temperature region, while it completely melted at 132–134° with vigorous gas evolution; $\lambda_{\text{max}}^{\text{KBr}}$ 2.93, 3.05, 3.15, 3.6–4.7, 5–5.5(w), 6.0, 6.10 (shoulder), 6.25 μ ; $\lambda_{\text{max}}^{\text{EtOH}}$ 213 $m\mu$ (log ϵ 3.97). It gave a precipitate of iodoform on treatment with iodine and aqueous sodium hydroxide.

Anal. Calcd. for $C_7H_{10}O_4 \cdot H_2O$: C, 47.72; H, 6.87. Found: C, 47.44; H, 6.74.

The acid showed distinct changes in its infrared spectrum upon being dried above room temperature while its ultraviolet spectrum was little changed. The loss of water of hydration took place only very slowly *in vacuo* at 100° and was not complete. Upon attempted sublimation at 100° and 0.01 mm. decomposition took place, but a small amount of completely dehydrated product sublimed, as shown by its infrared spectrum: $\lambda_{\text{max}}^{\text{KBr}}$ 3.02, 3–4, 5.92, 5.99 (shoulder) μ . The melting point of this product was also 132–134°. The unhydrated acid was also obtained occasionally directly from the hydrolysis mixture; upon recrystallization from a variety of solvents it always yielded the hydrated acid.

Esterification of XIV: Formation of XV.—The hydrated acid XIV (0.435 g.) was dissolved in methanol and an ethereal solution of diazomethane was added until a faint yellow color persisted. The solution was dried over sodium sulfate and the ether was removed *in vacuo*. The residue was distilled at 0.01 mm. The fraction distilling up to 70° was collected as a viscous, colorless sirup (0.30 g.) which crystallized slowly on being scratched to give a solid, m.p. 47–52°. This was recrystallized from benzene-petroleum ether and afforded prisms, m.p. 54.5–56.5°; $\lambda_{\text{max}}^{\text{CHCl}_3}$ 2.7–3.0, 5.83, 5.98 μ ; $\lambda_{\text{max}}^{\text{EtOH}}$ 215 $m\mu$ (log ϵ 4.00). The analytical sample was dried at room temperature *in vacuo*.

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.80; H, 7.03. Found: C, 55.66; H, 6.98.

Hydrogenation of XIV: Formation of XVI.—Compound XIV (0.50 g., 0.0028 mole) was hydrogenated in ethanol (25 ml.) over palladium-charcoal (0.050 g.). After 30 min. the total hydrogen uptake was 1.0 molar equivalent (71 ml. = 0.0029 mole at S.T.P.). The solution was filtered and the ethanol was evaporated *in vacuo*, leaving a semisolid residue (0.46 g.) which on treatment with chloroform yielded crystalline XVI, m.p. 113–117°. Cooling of the chloroform solution gave further crops of this product, m.p. 111–113° (total, 0.30 g.). Two recrystallizations from ethanol-chloroform afforded microcrystals, m.p. 113–115°; $\lambda_{\text{max}}^{\text{KBr}}$ 3.02, 3.20, 3–4, 5.86 μ ; no appreciable ultraviolet absorption >210 $m\mu$. This product gave a precipitate of iodoform on treatment with iodine and aqueous sodium hydroxide. The analytical sample was dried *in vacuo* at room temperature.

Anal. Calcd. for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.73; H, 7.43.

Concentration of the chloroform mother liquors gave an oil which was chromatographed on silicic acid (Davison, 100–200 mesh) in benzene. Elution with 50% benzene–50% ether and evaporation of the solvent afforded a second product as a colorless liquid; $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.60, 5.83 μ .⁴⁹

Reaction of XVI with Sodium Periodate.—Compound XVI (42.0 mg., 0.262 mmole) was treated with 0.802 *N* aqueous sodium periodate (10.00 ml., 0.401 mmole). After 10 min., titration of an aliquot (1.00 ml.) indicated the uptake of 0.97 mole of sodium periodate per mole of XVI (5.00 ml. of 0.8144 *N* sodium arsenite; back titer with 0.979 *N* iodine solution = 3.86 ml.). After 20 hr. the uptake was 1.06 molar equivalents.

When XVI (0.100 g.) was subjected to reaction with an excess of aqueous sodium periodate, and the reaction mixture was extracted with ethyl acetate, a colorless oil (80 mg.) was obtained upon drying the extract and stripping it of solvent. The crude product was treated with 2,4-dinitrophenylhydrazine by the method of Fieser.⁴⁶ A yellow insoluble solid (55 mg.), m.p. 210–212.5°, was obtained after one recrystallization from acetone. Its identity with the 2-methyl-1,4-pentanedione bis-2,4-dinitrophenylhydrazone was established by infrared and ultraviolet spectral comparison and by a mixture in p. with an authentic sample (*vide infra*).

Preparation of 2-Methyl-1,4-pentanedione Bis-2,4-dinitrophenylhydrazone.—2,4-Dimethylpyrrole (1.0 g., 0.0125 mole) was treated with hydroxylamine hydrochloride according to the procedure of Ciamician and Zanetti¹⁷ for 9 hr. to give a brown sirup (0.480 g.) which could not be induced to crystallize. Its infrared spectrum, $\lambda_{\text{max}}^{\text{CHCl}_3}$ 2.80, 3.05, 6.02(w), 6.18(w) μ , was consistent with the formation of 2-methyl-1,4-pentanedione

dioxime. This crude product was converted directly into the bis-2,4-dinitrophenylhydrazone by the method of Fieser,⁴⁶ giving a sparingly soluble yellow solid, m.p. 207–210°. This was recrystallized three times from acetone, giving pale yellow microcrystals, m.p. 211–213.5°; $\lambda_{\text{max}}^{\text{KBr}}$ 3.03, 6.18, 6.28 μ ; $\lambda_{\text{max}}^{\text{CHCl}_3}$ 230 $m\mu$ (log ϵ 4.38), 265 $m\mu$ (log ϵ 4.24), 359 $m\mu$ (log ϵ 4.62).

Anal. Calcd. for $C_{18}H_{18}O_8N_8$: C, 45.57; H, 3.82; N, 23.62. Found: C, 45.60; H, 3.96; N, 23.24.

Reaction of XIV with Sodium Periodate.—Compound XIV (0.183 g., 1.16 mmoles) was treated with 0.1338 *N* sodium periodate (48.00 mml., 6.422 mmoles). After 15 min., 2.1 moles of sodium periodate per mole of XIV had been consumed as shown by the titration of an aliquot (1.00 ml.); the pH of the solution was ca. 3. No additional uptake of reagent occurred on further standing.

The reaction proceeded more slowly at pH 8. The hydrated acid XIV (39.0 mg., 0.222 mmole) was treated with 0.0994 *N* sodium periodate (10.00 ml., 0.497 mmole) and the solution was adjusted to pH 8. After 15 min., titration of an aliquot (1.00 ml.) showed the uptake of 1.06 moles of sodium periodate per mole of XIV (5.00 ml. of 0.08144 *N* sodium arsenite; back titer with 0.1026 *N* iodine solution = 3.46 ml.). After 1.25 and 23 hr. the consumption of periodate was 1.16 and 2.02 moles, respectively.

Reaction of XV with Sodium Periodate.—The ester XV (10.32 mg., 0.061 mmole) was treated with a 0.03744 *N* solution of sodium periodate in 50% aqueous ethanol (10.00 ml., 0.187 mmole). After 1 hr., titration of an aliquot (1.00 ml.) indicated the uptake of 1.31 moles of sodium periodate per mole of XV (5.00 ml. of 0.01628 *N* sodium arsenite; back titer with 0.0192 *N* iodine solution = 3.12 ml.). After 24 and 48 hr. the total uptake was 1.91 and 2.10 moles, respectively; no further consumption of periodate occurred.

In another run the ester (0.140 g., 0.817 mmole) was treated with 0.1344 *N* aqueous sodium periodate (25.00 ml., 1.68 mmoles) for 12 hr., at which time the partially soluble ester had completely reacted. The solution was extracted with chloroform; the chloroform extracts were dried over anhydrous sodium sulfate, filtered and evaporated *in vacuo* at room temperature to give a fragrant liquid (0.105 g., 87%), $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.78, 5.83, 6.10(w) μ , which gave a red coloration with ferric chloride in chloroform-pyridine.

The liquid product was converted *in toto* to its 2,4-dinitrophenylhydrazone by the method of Fieser.⁴⁶ A yellow solid resulted, which after three crystallizations from methanol gave yellow needles, m.p. 121–122°. This product was shown to be the 2,4-dinitrophenylhydrazone of methyl acetoacetate by infrared spectral comparison with an authentic sample and mixture m.p. (lit.⁵⁰ m.p. 119–119.5°).

Esterification of XVI: Formation of XVIII.—Compound XVI (0.183 g.) was dissolved in ether and treated with an ethereal solution of diazomethane until a slight yellow color persisted. The ethereal solution was evaporated *in vacuo* leaving a colorless oil (0.200 g.); $\lambda_{\text{max}}^{\text{CHCl}_3}$ 2.90, 5.80 μ .

Reaction of XVIII with 3,5-Dinitrobenzoyl Chloride: Formation of XIX.—The crude XVIII (0.165 g.) from the above reaction was treated with 3,5-dinitrobenzoyl chloride according to the procedure of Shriner and Fuson.⁵¹ An oil separated upon addition of the reaction mixture to water. The oil was extracted with chloroform; the extract was washed with 5% hydrochloric acid and aqueous 10% sodium bicarbonate, dried, and stripped of solvent *in vacuo*, giving a faintly yellow sirup (0.390 g.). This was chromatographed in benzene on silicic acid (Davison, 100–200 mesh, 15 g.). Elution with 10% ether–90% benzene and evaporation of the solvent afforded a faintly yellow oil (0.260 g.). This sirup could only be crystallized with difficulty from benzene-petroleum ether, giving a small amount of pale yellow prisms, m.p. ca. 90°. No further crystalline material could be obtained, although the infrared spectrum of the sirup was identical with that of the crystalline product. Two additional crystallizations from benzene-petroleum ether gave an analytical sample, m.p. 92–94°, which was dried *in vacuo* at 60°; $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.78, 6.14, 6.27(w), 6.47 μ ; $\lambda_{\text{max}}^{\text{EtOH}}$ 214 $m\mu$ (log ϵ 4.42). This gave a precipitate of iodoform on treatment with iodine and aqueous sodium hydroxide.

Anal. Calcd. for $C_{15}H_{16}O_9N_2$: C, 48.92; H, 4.38; N, 7.61; mol. wt., 368. Found: C, 49.02; H, 4.36; N, 7.29; mol. wt. (Rast), 418; active H, 0.03.

In another similar run a compound, m.p. 146–148°, was isolated after chromatography and crystallization from benzene-petroleum ether. Its infrared spectrum was similar to that of the compound, m.p. 92–94°, except for the presence of a weak band at 2.82 μ . A mixture m.p. of the two compounds showed a pronounced depression of the m.p. of the lower-melting compound.

Base-Catalyzed Hydrolysis of XIII: Formation of XXVI, XXVII, and XXXIX.—The dilactone XIII (10.8 g.) was stirred

(49) This product is considered to be a 4-hydroxy-3-methyl-5-oxohexanoic acid lactone; its structure and the structures of other products derived from XVI and XIV will be discussed in a subsequent paper.

(50) G. D. Johnson, *J. Am. Soc.*, **73**, 5888 (1951).

(51) Reference 47, p. 165, Procedure 9.

at room temperature with aqueous 5% sodium hydroxide (200 ml.) under nitrogen. After 0.5 hr. the solution became yellow and after an additional 2 hr. the solid had gone into solution. The solution was cooled in ice and strongly acidified with cold 10% hydrochloric acid. The solution was saturated with ammonium sulfate and extracted four times with ethyl acetate. The combined extracts were dried and evaporated *in vacuo*. A yellow sirupy residue (11.2 g.) was obtained which could not be crystallized and was fractionated by chromatography on silicic acid (Davison, 100–200 mesh; 300 g.) in 50% ether–50% benzene. Early ether eluates gave a white crystalline acid (1.82 g., 16%), m.p. 148–150°. Further elution with ether gave semisolid materials from which a crystalline acid fraction (*ca.* 0.5 g.), m.p. *ca.* 200° dec., and an acid fraction (*ca.* 0.2 g.), m.p. *ca.* 160°, could be isolated by trituration with chloroform. Subsequent elution with ether, chloroform, and chloroform containing up to 10% ethanol gave yellow viscous materials which could not be crystallized. Elution with chloroform containing 25% ethanol afforded a semisolid material (0.8 g., 14%), which on sublimation yielded a neutral, white solid (0.5 g.), m.p. 118–120°. The total recovery of products from the chromatogram was 9.9 g. (88%).

The acid eluted in the early fractions was crystallized three times from chloroform–benzene to give long, glistening, white needles, m.p. 157–158°; $\lambda_{\text{max}}^{\text{CHCl}_3}$ 3–4, 5.80, 6.13, 6.48 μ ; $\lambda_{\text{max}}^{\text{EtOH}}$ 247 $\mu\mu$ (log ϵ 3.73), 295 $\mu\mu$ (log ϵ 3.77), identified as isodehydroacetic acid (XXVI) by infrared and ultraviolet spectral comparison with an authentic sample and mixture m.p. (lit.⁵² m.p. 155°).

The acid fraction, m.p. *ca.* 200°, was found to consist of a mixture of acids of similar melting points, which had similar ultraviolet and infrared spectra. Only one acid could be obtained in a pure state; several recrystallizations from ethyl acetate gave XXXIX, m.p. 193–195° with gas evolution (sealed cap.); $\lambda_{\text{max}}^{\text{EtOH}}$ 2.94, 3–4.5, 5.79, 5.85, 6.05 μ ; $\lambda_{\text{max}}^{\text{EtOH}}$ 213 $\mu\mu$ (log ϵ 4.12), 225 $\mu\mu$ (shoulder, log ϵ 4.03). The analytical sample was dried *in vacuo* at room temperature.

Anal. Calcd. for $\text{C}_{14}\text{H}_{20}\text{O}_8$: C, 53.16; H, 6.37. Found: C, 53.36; H, 6.41.

The acid fraction, m.p. *ca.* 160°, was crystallized from ethanol–benzene with no significant change in its infrared spectrum. It then had m.p. 159–164°; $\lambda_{\text{max}}^{\text{EtOH}}$ 2.84, 2.88, 3–4, 5.80 (complex) μ ; no appreciable ultraviolet absorption >210 $\mu\mu$. This product decomposed on being dried and no analytical sample was obtained.⁵³

The neutral solid, m.p. 118–120°, was very soluble in ethanol, water, and acetonitrile, but insoluble in chloroform and in less polar solvents. It was purified by five successive sublimations, giving XXVII as a white, crystalline solid, m.p. 118–120°; $\lambda_{\text{max}}^{\text{EtOH}}$ 2.94, 3.07 μ ; no appreciable ultraviolet absorption >210 $\mu\mu$. Although the melting point did not change upon successive sublimations, the infrared spectrum underwent considerable change in the O–H stretching and fingerprint regions.

Anal. Calcd. for $\text{C}_6\text{H}_{10}\text{O}_3$: C, 48.64; H, 8.16; 2C–CH₃, 20.3. Found: C, 48.74; H, 8.18; C–CH₃, 17.5.

Reaction of XXVII with Sodium Periodate.—Compound XXVII (52.60 mg., 0.3554 mmole) was treated with 0.0864 *N* aqueous sodium periodate (50.00 ml., 2.160 mmoles). After 17 hr. titration of an aliquot (5.00 ml.) showed an uptake of 4.04 moles of sodium periodate per mole of XXVII (8.00 ml. of 0.0848 *N* sodium arsenite; back titer with 0.0979 *N* iodine solution = 5.44 ml., periodate consumed = 1.431 mmoles). In a subsequent experiment titration indicated that the reaction was complete in 10 min. or less.

Titration for the increase of acid content due to formation of acidic products was conducted according to the method of Malaprade.⁵⁴ Titration of an aliquot (5.00 ml.) of the reaction mixture with aqueous sodium hydroxide to a methyl red end point showed an increase of 3.76 equivalents of acid (0.0242 *N* sodium hydroxide titer = 14.45 ml.; blank = 8.94 ml.).

Compound XXVII (42.00 mg., 0.284 mmole) was treated with very slightly more than 4 molar equivalents of aqueous sodium periodate and the solution after reaction was complete was steam distilled with continuous addition of water to carry all of the volatile acid products into the distillate. The total distillate was diluted to 50.00 ml. A sample of this solution when treated with alcoholic silver nitrate precipitated no silver iodide. Another aliquot was evaporated to dryness and the residue was heated with aqueous silver nitrate on the steam-bath; a heavy precipitate of silver resulted, indicating the presence of a reducing acid in the solution. This acid was estimated by the procedure

of Thorpe and Whiteley⁵⁵ for the estimation of formic acid in the presence of acetic acid. An aliquot (25.00 ml.) was treated with 0.1441 *N* aqueous potassium permanganate (10.00 ml.) on the steam-bath. After addition of ferrous ammonium sulfate, back-titration with potassium permanganate indicated the presence of 0.444 meq. of formic acid (0.222 mmole), corresponding to the formation of 1.56 moles of formic acid per mole of XXVII (potassium permanganate titer = 9.17 ml.; blank = 6.10 ml.).

Benzoylation of XXVII: Formation of XXIX.—Compound XXVII (45 mg.) was benzoylated by the method of Shriver and Fuson.⁵⁶ Upon addition of the reaction mixture to water, an oil separated which was extracted with chloroform; the extract was dried and evaporated, leaving a semisolid residue. This was chromatographed on silicic acid (Davison, 100–200 mesh, 15 g.). Early fractions eluted with benzene and benzene plus small amounts of ether contained benzoic acid and benzoic anhydride. The eluate with 10% ether–90% benzene afforded a white solid (94 mg.), which upon recrystallization from benzene–petroleum ether gave white needles, m.p. 151–152° (sealed cap.); $\lambda_{\text{max}}^{\text{EtOH}}$ 2.89 (shoulder), 3.01, 5.81, 6.25 μ .

Anal. Calcd. for $\text{C}_{20}\text{H}_{22}\text{O}_6$: C, 67.40; H, 5.66; mol. wt., 356. Found: C, 67.23; H, 5.76; mol. wt. (Rast), 307.

The dibenzoate XXXIX was recovered unchanged on treatment with sodium periodate in 50% aqueous ethanol solution.

Hydrolysis of XXXIX: Conversion to XXVI and XXVII.—Compound XXXIX (15 mg.) was heated with 10% hydrochloric acid (*ca.* 3 ml.) on the steam-bath for 2 min. Extraction with ethyl acetate yielded a semisolid product (7 mg.) whose infrared spectrum was similar to that of isodehydroacetic acid (XXVI). Recrystallization from benzene–petroleum ether yielded crystals, m.p. 140–146° undepressed on admixture with an authentic sample of XXVI.

The aqueous solution was allowed to evaporate to dryness at room temperature. The residue was sublimed to give a white solid, m.p. 100–110°, whose infrared spectrum was similar to that of XXVII. Admixture with a sample of XXVII did not depress its m.p.

Esterification of XXXIX.—Compound XXXIX (0.150 g.) in ethereal solution was treated with an ethereal solution of diazomethane until a faint yellow color persisted. The ether was evaporated *in vacuo*, and the residue crystallized from benzene–petroleum ether to give white rosettes (20 mg.), m.p. 92–94°; $\lambda_{\text{max}}^{\text{EtOH}}$ 2.95, 5.80, 5.84, 6.10 μ ; $\lambda_{\text{max}}^{\text{EtOH}}$ 215 $\mu\mu$ (log ϵ 3.99), 225 $\mu\mu$ (shoulder, log ϵ 3.95).

Hydrolysis of the Methyl Ester of XXXIX: Formation of Methyl Isodehydroacetate.—Acid hydrolysis of the methyl ester of XXXIX with 10% hydrochloric acid on the steam-bath for 0.5 hr. led to the formation of methyl isodehydroacetate, m.p. 68–70°, identified by infrared spectral comparison with an authentic sample and mixture m.p. (lit.⁵⁷ m.p. 67–67.5°).

Reaction of XXXIX with Sodium Periodate.—Compound XXXIX (10.5 mg., 0.0332 mmole) was treated with a 0.0365 *N* solution of sodium periodate in 50% aqueous ethanol (5.00 ml., 0.0912 mmole). After 14 hr. the solid had gone into solution and titration of an aliquot (1.00 ml.) indicated the uptake of 0.98 mole of sodium periodate per mole of XXXIX (5.00 ml. of 0.01628 *N* sodium arsenite; back titer with 0.01920 *N* iodine solution = 3.02 ml.). The periodate uptake was unchanged on further standing.

Reaction of the Methyl Ester of XXXIX with Sodium Periodate.—The methyl ester (8.22 mg., 0.0239 mmole) was treated with a 0.03744 *N* solution of sodium periodate in 50% aqueous ethanol (5.00 ml.). After 1 hr. 1.04 moles of sodium periodate per mole of ester had been consumed as indicated by titration of an aliquot (1.00 ml.) (5.00 ml. of 0.01628 *N* sodium arsenite solution; back titer with 0.01920 *N* iodine solution = 2.81 ml.). No further uptake of sodium periodate occurred during an additional 5 hr.

Pyrolysis of the Photodimer: Formation of XLIV.—The photodimer (5.0 g.) in a U-tube under a stream of nitrogen was heated in a metal-bath. When the temperature of the bath reached 240–270°, vapors condensed on the walls of the tube as cotton-like crystals. The solid remaining in the well of the tube became brown and melted at 280°, leaving a dark residue. The sublimed material was collected from the walls and triturated with benzene to remove the insoluble photodimer. Upon addition of petroleum ether to the benzene solution, a white solid precipitated (0.25 g.), whose infrared spectrum indicated the presence of some photodimer and a product whose infrared spectrum was similar but not identical with that of 2,6-dimethyl-4-pyrone. This product was purified by chromatography on silicic acid (Davison, 100–200 mesh), from which it was eluted with 10% ethanol–90% chloroform. Evaporation of the solvent

(52) R. H. Wiley and N. R. Smith, *J. Am. Chem. Soc.*, **73**, 3531 (1951).

(53) The spectra of this product suggest that it is the dicarboxylic acid XXXI.

(54) L. Malaprade, *Bull. soc. chim. France*, [5] **1**, 833 (1934); P. W. Clutterbuck and F. Reuter, *J. Chem. Soc.*, 1467 (1935); A. I. Vogel, 'Elementary Practical Organic Chemistry,' Part III, Longmans, Green and Co., London, 1958, p. 680.

(55) J. F. Thorpe and M. A. Whiteley, 'Organic Chemical Analysis,' Longmans, Green and Co., London, 1926, p. 175.

(56) Reference 47, p. 164, Procedure 7A.

(57) E. Buchner and H. Schröder, *Ber.*, **35**, 782 (1902).

gave a pale yellow solid (0.20 g.). Recrystallization from benzene afforded long, white needles, m.p. 219–220° (sealed cap.); $\lambda_{\text{max}}^{\text{CHCl}_3}$ 6.02, 6.05, 6.18, 7.17, 7.35 μ ; $\lambda_{\text{max}}^{\text{EtOH}}$ 266 m μ (log ϵ 4.34).

Anal. Calcd. for $\text{C}_{14}\text{H}_{16}\text{O}_4$: C, 67.73; H, 6.50. Found: C, 67.83; H, 6.39.

The pure compound decolorized bromine in carbon tetrachloride and was oxidized by a cold solution of potassium permanganate in acetone. When irradiated with the sunlamp in the solid state or in ethanolic solution, quantitative yields of the photodimer were obtained within a few hours. Treatment with aqueous hydrochloric acid on the steam-bath brought about reversion to 2,6-dimethyl-4-pyrone.

Action of Bases on the Photodimer.—The photodimer (0.20 g.) was refluxed with aqueous 10% sodium hydroxide for 4 hr. The reaction mixture was cooled, and the solid was filtered and dried; it was shown to be starting material (0.18 g., 90% recovery) by infrared spectral comparison and mixture m.p.

The photodimer (0.50 g., 0.002 mole) was refluxed with sodamide (0.50 g., 0.013 mole) in benzene (75 ml.) for 15 hr. After the mixture had cooled, water was added to decompose the unconsumed sodamide. The solid was filtered and dried, and shown as above to be starting material (0.45 g., 90% recovery).

When xylene (dried over sodium) was substituted for benzene and a twofold charge of materials was used, 60% of the photodimer was recovered after a 32-hr. reflux period. The xylene layer was dried and evaporated to give a yellow residue (0.15 g.) whose infrared and ultraviolet spectra indicated that it consisted of a mixture of photodimer and material showing bands at 2.9 and 6.2 μ , and 300 m μ .

Hydrogenation of the Photodimer: Formation of XLV, XLVI, XLIX, and LI.—A suspension of the photodimer (3.0 g., 0.012 mole) was hydrogenated in glacial acetic acid over pre-reduced platinum oxide (0.30 g.). During the reaction the photodimer went into solution and after 2 hr. had dissolved completely. The total uptake of hydrogen was three molar equivalents (900 ml. = 0.036 mole at S.T.P.). The solution was filtered and concentrated *in vacuo*. After most of the solvent had evaporated, the solid which had separated was filtered and dried (1.55 g.). This fraction was only partially soluble in benzene and chloroform. Repeated crystallizations from ethanol afforded no sharp-melting material. This product was shown to be a mixture of XLV and XLVI (*vide infra*).

Evaporation of the original filtrate to dryness afforded another solid fraction (1.4 g.) which was more soluble in organic solvents. This was chromatographed in benzene on Florisil (15 g.). Benzene eluates afforded a solid (0.27 g.), m.p. ca. 150° with sublimation. Later eluates (25% ether–75% benzene) afforded a solid, m.p. ca. 180° with sublimation.

The product obtained by elution with benzene was further purified by crystallization from petroleum ether to give LI as prisms. The analytical sample was dried by sublimation at water-aspirator pressure, giving a solid, m.p. 158–159° (sealed cap.), no infrared band <3.3 μ , $\epsilon_{210}^{\text{EtOH}}$ 350.

Anal. Calcd. for $\text{C}_{14}\text{H}_{18}\text{O}_3$: C, 76.32; H, 9.15. Found: C, 76.03; H, 9.06.

The product from the later eluates was crystallized from ether and dried by sublimation at 100° and water-aspirator pressure, giving XLIX as a white solid, m.p. 186–187° (sealed cap.), $\lambda_{\text{max}}^{\text{CHCl}_3}$ 2.80 μ , no appreciable ultraviolet absorption >210 m μ .

Anal. Calcd. for $\text{C}_{14}\text{H}_{20}\text{O}_3$: C, 71.16; H, 8.53. Found: C, 70.73; H, 8.73.

In repetitions of the hydrogenation the hydrogen uptake varied from 2.5 to 3.5 molar equivalents, resulting in some variation of the ratio of the yields of the products. In accord with the observed total hydrogen uptake, the main constituent of the product mixture was the monohydroxy compound XLIX; about equal amounts (ca. 10%) of the completely hydrogenolyzed material LI and the two isomeric dihydroxy compounds XLV and XLVI (*vide infra*) were obtained. Upon attempted further hydrogenation over fresh catalyst of the various alcohols obtained no hydrogen uptake was observed after several hours.

Acetylation of the Hydrogenation Products from the Photodimer: Formation of XLVII, XLVIII, and the Acetate of XLIX.—Compound XLIX was converted into its acetate by the method of Shiriner and Fuson.⁵⁸ The oil which was obtained upon addition of the reaction mixture to water was extracted with chloroform. The extracts were dried and stripped of solvent *in vacuo* to give an oil which crystallized slowly on standing. Recrystallization from petroleum ether gave the acetate of XLIX as square plates, m.p. 83–85°. The analytical sample, m.p. 84.5–85.5°, $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.78 μ , was prepared by sublimation at water-aspirator pressure.

Anal. Calcd. for $\text{C}_{16}\text{H}_{22}\text{O}_4$: C, 69.04; H, 7.97. Found: C, 69.28; H, 7.92.

When the less soluble fraction from the hydrogenation of the photodimer (*vide supra*) was acetylated by the same proce-

dure, an oil was obtained which partially solidified on standing. Recrystallization from ethanol gave XLVII as white needles, which after four recrystallizations from ethanol had m.p. 231–232° (sealed cap.), $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.78 μ .

Anal. Calcd. for $\text{C}_{18}\text{H}_{24}\text{O}_6$: C, 64.27; H, 7.19. Found: C, 63.91, 64.04; H, 7.35, 6.77.

In another experiment the total hydrogenation product was extracted with petroleum ether to remove the very soluble LI and then acetylated. The mixture of acetates was chromatographed on Woelm alumina in benzene. Benzene and early 2% ether–98% benzene eluates afforded the acetate of XLIX. Subsequent elution with 2% ether–98% benzene and 5% ether–95% benzene gave a mixture of acetates which consisted of XLVII and an isomeric acetate. The latter was isolated from the mother liquors after repeated crystallizations of XLVII from ethanol. Fractional sublimation gave XLVII, m.p. 125.5–126.5°, $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.78 μ .

Anal. Calcd. for $\text{C}_{18}\text{H}_{24}\text{O}_6$: C, 64.27; H, 7.19. Found: C, 64.13; H, 7.15.

All three acetates were extremely sensitive to traces of mineral acids, giving colorations from yellow to deep red.

Hydrolysis of XLVII with aqueous 10% sodium hydroxide on the steam-bath for 30 min. gave a solid product, m.p. ca. 295° with prior decomposition (sealed cap.), $\lambda_{\text{max}}^{\text{KBr}}$ 2.91 μ .

Oxidation of the Alcohols Derived by Hydrogenation of the Photodimer: Formation of L.—The mixture of hydrogenation products, after extraction with petroleum ether to remove LI, was treated with glacial acetic acid (40 ml.) and a solution of potassium dichromate (7.0 g.) in concentrated sulfuric acid (1.7 g.) and water (15 ml.). After 5 hr. at room temperature, water was added, and the solid which separated was filtered and dried (3.0 g.).

This solid was heated in benzene and filtered. The solid which did not dissolve was shown to be identical with the photodimer by infrared and ultraviolet spectral comparison and mixture m.p.

The benzene solution upon concentration *in vacuo* afforded a white solid (2.4 g.) which had an infrared spectrum very similar to that of the photodimer, but whose solubility in all solvents was greatly enhanced. Chromatography in benzene on Florisil with elution with 5% ether–95% benzene followed by crystallization from petroleum ether–benzene afforded L as plates, m.p. 223–225° (sealed cap.), $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.90 μ ; $\lambda_{\text{max}}^{\text{EtOH}}$ 212 m μ (log ϵ 3.56), 223 m μ (log ϵ 3.55). The analytical sample was dried by sublimation *in vacuo*.

Anal. Calcd. for $\text{C}_{14}\text{H}_{18}\text{O}_3$: C, 71.77; H, 7.74. Found: C, 72.07; H, 7.95.

The same ketone was obtained by a similar oxidation of pure XLIX. Oxidation of the mixture of alcohols with chromic anhydride–pyridine led to the same mixture of ketones.

The 2,4-dinitrophenylhydrazone of L was prepared by the method of Fieser⁵⁵ and was obtained as an orange solid. Recrystallization from ethanol afforded orange-yellow plates, m.p. 228–230°; $\lambda_{\text{max}}^{\text{KBr}}$ 3.03, 6.18, 6.29 μ ; $\lambda_{\text{max}}^{\text{EtOH}}$ 233 m μ (log ϵ 4.26), 367 m μ (log ϵ 4.45).

Anal. Calcd. for $\text{C}_{20}\text{H}_{22}\text{O}_6\text{N}_4$: C, 57.96; H, 5.35; N, 13.52. Found: C, 57.69; H, 5.42; N, 13.75.

Wolff-Kishner Reduction of the Photodimer: Formation of LI.—The photodimer (6.2 g., 0.025 mole), potassium hydroxide (10 g.), and 85% hydrazine hydrate (6.8 g., 0.18 mole) were heated with triethylglycol (60 g.) at 150°. After 1.5 hr. a solid commenced to condense upon the walls of the flask and on the condenser. This solid was shown to be LI by infrared spectral comparison and mixture m.p. After an additional hour of heating, the reaction mixture was cooled and added to water (150 ml.). A solid separated and the mixture was extracted with ether; the ethereal extracts were washed with water and dried. Evaporation of the solvent *in vacuo* gave a white solid (2.9 g., 53%) shown as above to be LI.

Hydrogenation of XI: Formation of LII and LIII.—The keto lactone XI (1.30 g., 0.0049 mole) was hydrogenated over pre-reduced platinum oxide (0.16 g.) in glacial acetic acid (30 ml.). A total of 1.5 molar equivalents of hydrogen was taken up after several hours (174 ml. = 7.1 mmoles at S.T.P.).

The solution was filtered and the filtrate was evaporated *in vacuo* giving a white solid (0.83 g.) with a band at 5.80 μ in its infrared spectrum which was very soluble in most common solvents. The material was chromatographed in benzene on silicic acid (Davison 100–200 mesh, 35 g.). Elution with 10% ether–90% benzene gave LII as a white solid (ca. 0.5 g.), m.p. 189–190°. The analytical sample had $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.80 μ , $\epsilon_{210}^{\text{EtOH}}$ 660. Recrystallization from benzene–petroleum ether did not raise the m.p. The analytical sample was dried by sublimation *in vacuo*.

Anal. Calcd. for $\text{C}_{14}\text{H}_{18}\text{O}_4$: C, 67.18; H, 7.25. Found: C, 66.94; H, 7.09.

Elution with chloroform–ethanol afforded a second white solid (ca. 0.1 g.), m.p. 210°. Crystallization from benzene–petroleum

ether and subsequent sublimation *in vacuo* gave LIII as a white solid, m.p. 213–214°; $\lambda_{\text{max}}^{\text{CHCl}_3}$ 2.80, 2.90 (shoulder), 5.80 μ ; $\epsilon_{210}^{\text{EtOH}}$ 380.

Anal. Calcd. for $\text{C}_{14}\text{H}_{18}\text{O}_6$: C, 63.14; H, 6.81. Found: C, 62.47; H, 6.71.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, HARVARD UNIVERSITY, CAMBRIDGE 38, MASS.]

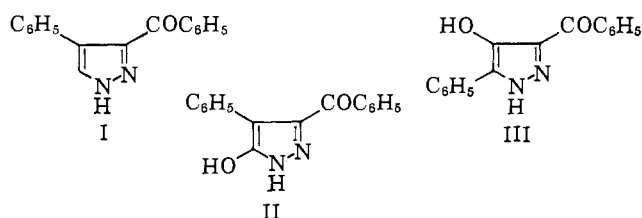
Aliphatic Diazo Compounds. VIII. The Reaction of Diazo Ketones with Bases. II^{1,2}

BY PETER YATES³ AND DONALD G. FARNUM⁴

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The reaction of α -diazoacetophenone with sodium methoxide in concentrated solutions in methanol has been found to give 3-benzoyl-4-phenylpyrazole (I), 3-benzoyl-5-hydroxy-4-phenylpyrazole (II), 3-benzoyl-4-hydroxy-5-phenylpyrazole (III), 5-benzoyltetrazole (XXV), a compound, $\text{C}_{17}\text{H}_{11}\text{N}_5\text{O}$, considered to be most probably 3-benzoyl-5-phenyl-1,2,3-triazolo[3,4-*b*]-1,2,4-triazine (XLIII), benzoic acid, and methyl benzoate. The structures of compounds I, II, III, and XXV have been established by comparisons of these products with authentic samples prepared by rational, independent syntheses. The assignment of structure XLIII to the product $\text{C}_{17}\text{H}_{11}\text{N}_5\text{O}$ has been made largely on the basis of the base-induced cleavage of this compound to 4-benzamido-5-benzoyl-1,2,3-triazole (XXXV), whose structure has been established by independent synthesis.

It has previously been found¹ that the reaction of dilute solutions of α -diazoacetophenone in hydroxylic solvents with strongly basic reagents is complex and gives rise to a mixture of products which includes benzoic acid, acetophenone, 3-benzoyl-4-phenylpyrazole (I), and 3-benzoyl-5-hydroxy-4-phenylpyrazole (II) (*vide infra*). In all cases a reaction time of several hours at 75–90° was required to ensure total, irreversible consumption of the diazo ketone.



In a further investigation of the reaction of α -diazoacetophenone with bases, we have found that the addition of concentrated methanolic sodium methoxide to a concentrated solution of α -diazoacetophenone in methanol leads to a violent, exothermic reaction. We describe here the results of an investigation of the structures of the products formed under these conditions; we shall postpone discussion of the mechanistic implications of our results until the completion of further experiments currently in progress.⁵

A 7 *M* solution of sodium methoxide in methanol was added dropwise to a 5 *M* solution of diazoacetophenone in methanol; approximately equimolar amounts of base and diazo ketone were used. The reaction was moderated by efficient external cooling, which was necessary to prevent vigorous gas evolution with excessive foaming. After completion of the reaction the mixture was poured into dilute aqueous sodium bicarbonate and the crude product was separated into three fractions: acid (bicarbonate-soluble), weak acid (bicarbonate-insoluble, hydroxide-soluble), and neutral.

Acid Fraction.—From the bicarbonate-soluble fraction were isolated a pale yellow, crystalline, water-insoluble compound, $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2$, m.p. 248.5–250°, and a colorless, crystalline, water-soluble compound, $\text{C}_8\text{H}_8\text{N}_4\text{O}$, m.p. 139.5–140°. In addition, infrared spectral evidence indicated the presence of benzoic acid.

(1) For Part I of this sub-series see P. Yates and B. L. Shapiro, *J. Am. Chem. Soc.*, **81**, 212 (1959).

(2) A preliminary report on part of this work has appeared previously: P. Yates and D. G. Farnum, *Tetrahedron Letters*, **No. 17**, 22 (1960).

(3) Department of Chemistry, University of Toronto, Toronto, Canada; Alfred P. Sloan Foundation Fellow, 1957–1960.

(4) N.I.H. Fellow, 1957–1959.

(5) We have already made some proposals in regard to the reaction routes.²

The compound $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2$ was shown to be identical with the product of this composition obtained previously¹ by the reaction of dilute solutions of diazoacetophenone with bases. The earlier work had shown that the compound is resistant to boiling aqueous ethanolic potassium hydroxide and to boiling 1:1 hydrochloric-acetic acid, dissolves readily in dilute aqueous sodium hydroxide to give a yellow solution which reduces potassium permanganate to manganate, and gives a red coloration with a solution of ferric chloride in chloroform-pyridine. On the basis of these properties and its origin it was considered to be one of the hydroxypyrazoles II or III. In the present work a choice between these alternatives was made possible on three counts. It was observed that the substance is soluble in aqueous potassium carbonate,⁶ that it fails to give a coloration with ethanolic ferric chloride, and that on oxidation with perbenzoic acid it affords an amorphous solid, which upon crystallization from solvent mixtures containing ether yields a colorless, crystalline substance, $\text{C}_{32}\text{H}_{22}\text{N}_4\text{O}_4 \cdot \text{C}_4\text{H}_{10}\text{O}$. A significant difference between structure II and III is that the latter contains a chelated hydroxyl group, while the former contains a free hydroxyl group. Both the relatively strong acidity of the compound $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2$ and its failure to give a color test with ethanolic ferric chloride are in accord with the expected properties of a *nonchelated* aromatic hydroxyl group as is present in structure II.⁷ The significance of these observations was markedly enhanced by the availability of an isomeric compound obtained from the weak acid fraction which exhibited the properties expected for the chelated hydroxyl compound III (*vide infra*). Finally, the formation of the compound $\text{C}_{32}\text{H}_{22}\text{N}_4\text{O}_4$ is readily interpreted as an oxidative coupling reaction of a type often observed with 5-pyrazolones,⁸ leading to compound IV. The infrared spectrum of the oxidation product (bands at 3.13, 3.25, 5.68, and 6.04 μ)⁹ is in accord with this assignment; the band at 6.04 μ is assigned to the benzoyl groups and that at 5.68 μ to the five-membered lactam carbonyl groups which have been modified by the inclusion of the amide nitrogen atom in a conjugated system of shorter $\text{C}_6\text{H}_5\text{C}=\text{C}-\text{N}=\text{NH}-$. An analogous shift to shorter



(6) Although the product was isolated from a bicarbonate-soluble fraction of the crude reaction product, in the pure state it is not soluble in aqueous sodium bicarbonate.

(7) H. Henecka, "Chemie der β -Dicarbonylverbindungen," Springer Verlag, Berlin, 1950, p. 111.

(8) T. L. Jacobs in "Heterocyclic Compounds," R. C. Elderfield, Ed., Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1957, pp. 124, 125, 135.

(9) The spectrum of the crystalline product has a strong band at 9.1 μ , absent in the spectrum of the amorphous material, corroborating the presence of ether of crystallization in the crystalline product.