ORGANIC AND BIOLOGICAL CHEMISTRY

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The Formation of Cyclopropanes by the Rearrangement of 4-Benzoyloxycycloalkanones[1]

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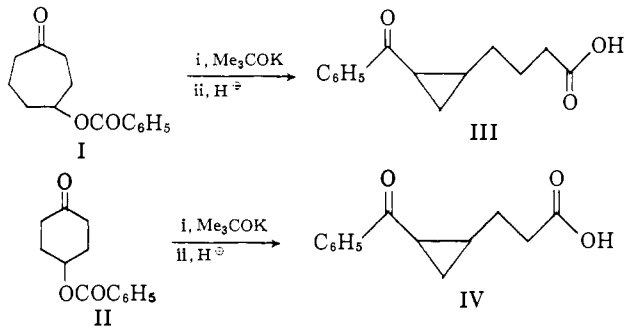
4-Benzoyloxycyclohexanone and 4-benzoyloxycycloheptanone are converted to 2-benzoylcyclopropanepropionic acid and 2-benzoylcyclopropanebutyric acid, respectively, by the action of potassium *t*-butoxide. The reaction routes for these rearrangements are discussed.

During the course of experiments concerned with the Stobbe condensation of 4-benzoyloxycycloheptanone (I), it was discovered that I rearranges to an isomeric keto acid on treatment with potassium *t*-butoxide. This keto acid was not obtained in crystalline form but was characterized by its conversion to a semicarbazone and by the formation of the 2,4-dinitrophenylhydrazones of its ethyl and methyl esters by treatment with 2,4-dinitrophenylhydrazine in acidic ethanol and methanol, respectively[4]; each hydrazone showed in its infrared spectrum an ester carbonyl-stretching band at 5.78 μ. It was subsequently found that an analogous reaction occurs in the case of the lower homolog, 4-benzoyloxycyclohexanone (II), to give an isomeric keto acid, which in this instance was obtained in crystalline form.

The infrared spectrum (CCl_4) of each keto acid has carbonyl bands at 5.84 and 5.96–5.97 μ. The band at 5.84 μ can readily be assigned to a carboxylic acid group, while that at 5.96–5.97 μ must be due to a conjugated carbonyl group. The absence of any ethylenic stretching band in these spectra and the failure of the keto acids to give positive tests for unsaturation with either bromine or potassium permanganate indicated that this conjugated carbonyl group must be a benzoyl group, yet the position of its band is significantly higher in wave length than the carbonyl bands of simple alkyl phenyl ketones; *e.g.*, acetophenone: $\lambda_{max}^{CCl_4}$ 5.91 μ. However, the carbonyl band of a cyclopropyl phenyl ketone is usually shifted approximately 0.05–0.06 μ toward longer wave lengths relative to that of a comparable alkyl phenyl ketone[5-7]; *e.g.*, cyclopropyl phenyl ketone: $\lambda_{max}^{CCl_4}$ 5.96 μ.[7] We therefore concluded that the structures of the keto acids might well contain the cyclopropyl phenyl ketone system. Consideration of plausible reaction pathways (*vide infra*) then led to the postulation of structures III and IV for the keto acids obtained by isomerization of I and II, respectively. We now present evidence which establishes these structural assignments.



Although the presence of a phenyl group in these compounds makes impossible the confirmation of the presence of the cyclopropyl ring on the basis of absorption in the 3.2–3.3 and 9.5–10 μ regions of their infrared spectra, the near-infrared region can be utilized for this purpose. Washburn and Mahoney[8] have found two bands near 1.64 and 2.24 μ to be characteristic for monosubstituted and 1,2-disubstituted cyclopropanes; they consider, furthermore, that the presence of aromatic rings does not lead to ambiguity in the use of this criterion. The near-infrared spectrum of the keto acid III in carbon tetrachloride has such bands at 1.63 and 2.23 μ (*cf.* cyclopropyl phenyl ketone: $\lambda_{max}^{CCl_4}$ 1.64 and 2.27 μ[8]) and thus strongly supports the postulated presence of a cyclopropyl ring in the structure of the keto acid.

The ultraviolet spectra of III and IV in ethanol each have a maximum at 244 mμ with extinction coefficients of 14,700 and 16,700, respectively. The location and intensities of these maxima are compatible with the presence of a cyclopropyl phenyl ketone system [*cf.* cyclopropyl phenyl ketone: λ_{max}^{EtOH} 244 mμ (ϵ 14,100)[9]], but do not distinguish unambiguously between this and an alkyl phenyl ketone system [*cf.* acetophenone: λ_{max}^{EtOH} 242 mμ (ϵ 12,300)[9]] since the ultraviolet spectra, in contrast to the infrared spectra, of aromatic or α,β-ethylenic ketones are little affected by attachment of a cyclopropyl ring to the ketonic group.[5,10] Neither do these ultraviolet spectra provide definite evidence for the exclusion of an α,β-ethylenic phenyl ketone system, since, although some alkenyl phenyl ketones have longer wave length or higher intensity maxima than those of comparable alkyl phenyl ketones [*e.g.*, crotonophenone: λ_{max}^{EtOH} 256 mμ (ϵ 17,400)[9]; acrylophenone: λ_{max}^{EtOH} 242 mμ (ϵ 20,900)[11]], many do not [*e.g.*, 1-cyclohexenyl phenyl ketone: λ_{max}^{EtOH} 245 mμ (ϵ 10,900)[12]]. The ultraviolet spectra of the 2,4-dinitrophenylhydrazones of the esters of III and IV are more informative. The ethyl ester of III has λ_{max}^{EtOH} 377 mμ (ϵ 24,400) and the methyl ester of IV has $\lambda_{max}^{CHCl_3}$ 384 mμ (ϵ 29,400). These maxima lie at slightly longer wave lengths than those of phenyl alkyl ketone 2,4-dinitrophenylhydrazones; thus, the 2,4-dinitrophenylhydrazone of acetophenone has λ_{max}^{EtOH} 373 mμ,[13] and the 2,4-dinitrophenylhydrazones of C_6H_5COR (R = CH_3, CH_2CH_3, or $CH_2CH_2CH_3$) have $\lambda_{max}^{CHCl_3}$

(1) A preliminary account of this work has appeared: P. Yates and C. D. Anderson, *J. Am. Chem. Soc.*, **80**, 1264 (1958); see also R. L. Clarke and W. T. Hunter, *ibid.*, **80**, 5304 (1958).

(2) Department of Chemistry, University of Toronto, Toronto, Canada.

(3) N.S.F. Fellow, 1952–1953.

(4) Esterification of a keto acid during 2,4-dinitrophenylhydrazone formation under these conditions has considerable precedent; *cf.*, for example, D. W. Mathieson, *J. Chem. Soc.*, 3251 (1953).

(5) *Cf.* R. J. Mohrbacher and N. H. Cromwell, *J. Am. Chem. Soc.*, **79**, 401 (1957).

(6) R. C. Fuson and F. N. Baumgartner, *ibid.*, **70**, 3255 (1948).

(7) N. Fuson, M.-L. Josien, and E. M. Shelton, *ibid.*, **76**, 2526 (1954).

(8) W. H. Washburn and M. J. Mahoney, *ibid.*, **80**, 504 (1958).

(9) R. P. Mariella and R. R. Raube, *ibid.*, **74**, 521 (1952).

(10) E. J. Corey and H. J. Burke, *ibid.*, **78**, 174 (1956).

(11) A. L. Nussbaum, O. Mancera, R. Daniels, G. Rosenkranz, and C. Djerassi, *ibid.*, **73**, 3263 (1951).

(12) A. I. Kosak and H. M. Leyland, *J. Org. Chem.*, **21**, 733 (1956).

(13) C. J. Timmons, *J. Chem. Soc.*, 2613 (1957).

379 ± 1 mμ.[14] It is relevant that Roberts and Green[15] have found the maximum of the 2,4-dinitrophenylhydrazone of cyclopropyl methyl ketone in ethanol lies at 367 mμ, 4–6 mμ higher than the maxima of the 2,4-dinitrophenylhydrazones of simple alkyl ketones.[16]

Excellent physical evidence corroborating the assignment of structures III and IV to the keto acids was provided by a comparison of their nuclear magnetic resonance spectra[17] with the spectrum of cyclopropyl phenyl ketone (V)[18] (Table I). The signals at very low field in the spectra of III and IV which have no counterpart in the spectrum of V are assigned

TABLE I

NUCLEAR MAGNETIC RESONANCE DATA[a]

Compound	τ (p.p.m.)[b]					
Cyclopropyl phenyl ketone (V)		2.17 (2.0)	2.60 (3.1)	7.50 (1.0)		9.05 (4.2)
III	−1.18 (1.0)	2.10 (1.9)	2.60 (2.9)	7.60 (2.8)	8.45 (5.2)	9.12 (2.1)
IV	−0.98 (1.0)	2.10 (1.9)	2.50 (2.9)	7.52 (2.8)	8.42 (3.1)	9.12 (2.1)

[a] Low resolution spectra measured at 40 Mc. on solutions in carbon tetrachloride. [b] The figures in parentheses under the τ-values are the approximate relative areas of the peaks.

to the carboxylic acid hydrogen atoms; those with τ = 2.1–2.2 p.p.m. in all three spectra are assigned to the *ortho* hydrogen atoms on the phenyl rings, and those with τ = 2.5–2.6 to the *meta* and *para* hydrogen atoms.[19] The signal with τ = 7.50 p.p.m. of relative intensity 1 in the spectrum of V must be assigned to the single hydrogen atom on the cyclopropane ring α to the carbonyl group and that of relative intensity 4 with τ = 9.05 p.p.m. to the four cyclopropyl hydrogen atoms β to the carbonyl group. The signal given by the hydrogen atoms of cyclopropane itself is well known to appear at appreciably higher field (τ = 9.78 p.p.m.) than the signals of methylene hydrogen atoms in alkanes and other cycloalkanes.[20] Thus, it is to be anticipated that the signal of the tertiary hydrogen atom in V would appear at higher field than that of the tertiary hydrogen atom in $C_6H_5COCHR_2$. Although the spectrum of a compound of this type was not available to us, comparison can be made with the position of the signal due to the primary hydrogen atoms in acetophenone, *i.e.*, τ = 7.45 p.p.m.[21] Since it is anticipated that the tertiary hydrogen signal would be shifted to lower field by *ca.* 0.5 p.p.m. relative to the primary hydrogen signal,[22] it can be seen that the position of the signal for the tertiary cyclopropyl hydrogen atom of V is in accordance with expectation. The signal due to the secondary cyclopropyl hydrogen atoms of V is shifted by 0.7 p.p.m. to lower field relative to that of cyclopropane; this shift may be interpreted in terms of significant overlap between the C–C orbitals of the cyclopropane ring in V and the π-orbitals of the carbonyl group[23] leading to electron withdrawal from the cyclopropane carbon atoms β to the carbonyl group and thus to the observed shift to lower field of the signal due to the hydrogen atoms attached to these carbon atoms.[24] On this basis the spectra of the keto acids are in full accord with the structures assigned. Each shows a signal of relative intensity 3 with τ = 7.5–7.6 p.p.m. which can be attributed to the overlap of signals due to the tertiary cyclopropyl hydrogen atom α to the carbonyl group and the hydrogen atoms in the side chain on the methylene group α to the carboxylic acid group.[22] Each shows a signal of relative intensity 2 with τ = 9.1 p.p.m. which can be assigned to the secondary cyclopropyl hydrogen atoms situated on a carbon atom β to the carbonyl group. Finally, the signals at τ = 8.4 p.p.m. can be attributed to the overlap of signals due to the tertiary cyclopropyl hydrogen atom situated on a carbon atom β to the carbonyl group and the hydrogen atoms of the remaining side chain methylene groups,[25] the relative intensities for III and IV being 5 and 3, as required.

These spectral studies provide considerable support for the structural assignments III and IV. Full confirmation was obtained by the following degradative experiments with the keto acid derived from 4-benzoyloxycyclohexanone. On treatment of this acid with zinc chloride in acetic acid–acetic anhydride at reflux, a noncrystalline neutral product was obtained with carbonyl bands in its infrared spectrum (CCl_4) at 5.60 μ (γ-lactone) and 5.66 μ (enol ester) which is formulated as VI. This on basic hydrolysis followed by acidification gave a crystalline product with carbonyl bands in its infrared spectrum (KBr) at 5.59 μ (γ-lactone) and 5.92 μ (alkyl phenyl ketone) which was shown to be 6-benzoyl-4-hydroxyhexanoic acid lactone (VII) in the following ways. Conversion of the lactone to the sodium salt of the corresponding hydroxy acid VIII followed by oxidation with chromium trioxide–pyridine gave 4,7-dioxo-7-phenylheptanoic acid (IX), identified by comparison with an authentic sample prepared from 3-(2-furyl)-acrylophenone (X) by the method of Kehrer.[26] Also, reduction of IX with sodium borohydride in aqueous isopropyl alcohol gave 4,7-dihydroxy-7-phenylheptanoic acid γ-lactone (XI) (infrared bands of liquid film at 2.86 and 5.64 μ) which on oxidation with chromium trioxide in acid medium gave the keto lactone VII, identical with the product obtained by hydrolysis of VI. These results can only be interpreted in terms of structure IV or XII for this keto acid[27]; the latter is excluded by the spectral data and IV is therefore established. The close spectral similarity between the two keto acids then leaves no doubt that III must be the structure of the keto acid derived from 4-benzoyloxycycloheptanone.

The stereochemistry of III and IV has not been rigorously established. In the case of the liquid III, it might seem likely that the material is a mixture of *cis* and *trans* isomers. However, this possibility is contraindicated by the fact that the properties of III were unchanged when it was regenerated under mild conditions from its sharply-melting semicarbazone. We consider it probable that both III and IV are the *trans* isomers since they have been obtained under conditions which have been found sufficient to effect deuterium exchange by methyl 2-*t*-butoxycyclopropanecarboxylate.[28] Since the α-hydrogen of a ketone is

(14) E. A. Braude and E. R. H. Jones, *J. Chem. Soc.*, 498 (1945); F. Ramirez and A. F. Kirby, *J. Am. Chem. Soc.*, **75**, 6026 (1953).

(15) J. D. Roberts and C. Green, *ibid.*, **68**, 214 (1946).

(16) *Cf.* M. F. Hawthorne, *J. Org. Chem.*, **21**, 1523 (1956).

(17) We thank Dr. E. A. Chandross for these measurements and Dr. J. N. Shoolery, Varian Associates, Palo Alto, Calif., for valuable discussions.

(18) We thank Dr. W. J. Close, Abbott Laboratories, for a generous sample of this compound.

(19) *Cf.* L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959, p. 62.

(20) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, N. Y., 1959, p. 236; *cf.* also, for example, K. B. Wiberg, B. R. Lowry, and T. H. Colby, *J. Am. Chem. Soc.*, **83**, 3998 (1961).

(21) G. V. D. Tiers, "Characteristic Nuclear Magnetic Resonance 'Shielding Values' for Hydrogen in Organic Structures," 1958.

(22) *Cf.* ref. 19, p. 57.

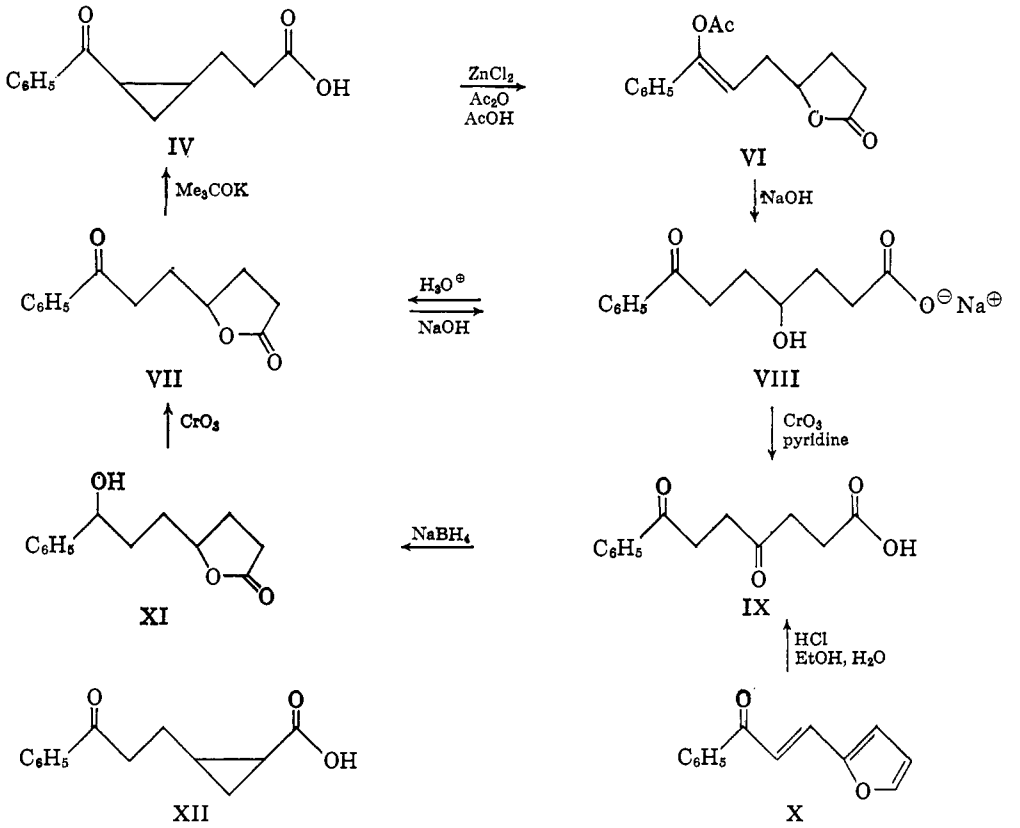
(23) *Cf.* R. H. Eastman, *J. Am. Chem. Soc.*, **76**, 4115 (1954).

(24) A purely inductive effect of the carbonyl group would be expected to give rise to a much smaller shift.[25]

(25) *Cf.* ref. 19, p. 53.

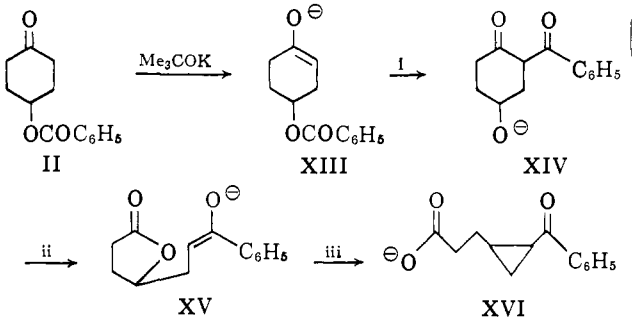
(26) E. A. Kehrer, *Ber.*, **34**, 1263 (1901).

(27) The possibility that formation of the keto acid involves substitution in the aromatic ring is excluded by the observation that oxidation of the keto acid with perbenzoic acid, followed by hydrolysis, yielded phenol, identified as 2,4,6-tribromophenol, and by the nuclear magnetic resonance data.



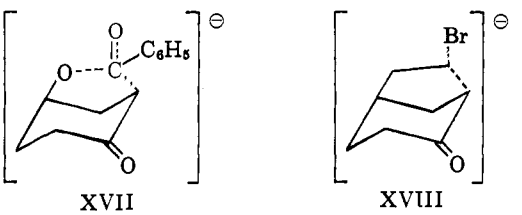
in general more acidic than that of an ester[29] and cyclopropyl carbanions are incapable of maintaining their configuration,[30] it would be expected that the more stable *trans* isomers would be obtained from these reactions.

The reaction sequence which is considered best to represent the pathway involved in the isomerization of 4-benzoyloxycyclohexanone (II) to XVI, the anion of IV, is as shown below.

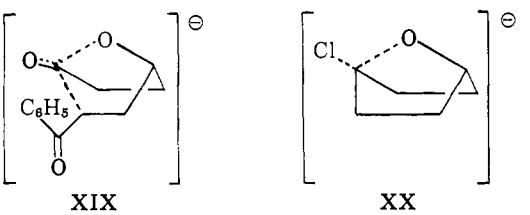


The scheme consists of formation of the enolate anion XIII followed by three intramolecular steps: (i) migration of the benzoyl group from oxygen to carbon giving the β-diketone XIV, (ii) cleavage of the β-diketone system to give the enolate anion XV of the keto lactone VII, and (iii) formation of the cyclopropane ring by 1,3-displacement of the acyloxyl group.

Step i is analogous to the Baker–Venkataraman reaction.[31] It involves a transition state (XVII)[32] which is geometrically comparable to that involved in the intramolecular alkylation of 4-(2-bromoethyl)-cyclohexanone (XVIII).[33] A closely analogous acyl migration in the reverse direction has been postulated to occur in a related system.[34]



Step ii may be considered in relation to the intermolecular, base-catalyzed cleavage of 2-benzoylcyclohexanones; these have been found to undergo predominant cleavage of the endocyclic carbonyl–carbon bond.[35] Here, the transition state XIX[32] may be compared to that involved in the conversion of *trans*-4-chlorocyclohexanol to 1,4-epoxycyclohexane (XX).[36]



Step iii is analogous to the many known cyclopropyl ketone syntheses that involve base-induced γ-elimination,[37] although none of these appears to have involved previously an acyloxyl function as the leaving group.

(28) K. B. Wiberg, R. K. Barnes, and J. Albin, *J. Am. Chem. Soc.*, **79**, 4994 (1957).

(29) R. G. Pearson and R. L. Dillon, *ibid.*, **75**, 2439 (1953).

(30) H. M. Walborsky and F. M. Hornyak, *ibid.*, **77**, 6026 (1955).

(31) J. E. Gowan and T. S. Wheeler, *J. Chem. Soc.*, 1925 (1950); M. P. O'Farrell, D. M. S. Wheeler, M. M. Wheeler, and T. S. Wheeler, *ibid.*, 3986 (1955).

(32) It is suggested that in both steps i and ii the breaking and making of the carbon–oxygen and carbon–carbon bonds is concerted, thus minimizing strain energy. Reaction paths *via* intermediates analogous to those which have been shown to be involved in normal base-catalyzed ester hydrolysis [M. L. Bender, *J. Am. Chem. Soc.*, **73**, 1626 (1951)] are expected to be of higher energy in the present cases.

(33) M. S. Newman and Y. T. Yu, *ibid.*, **74**, 507 (1952).

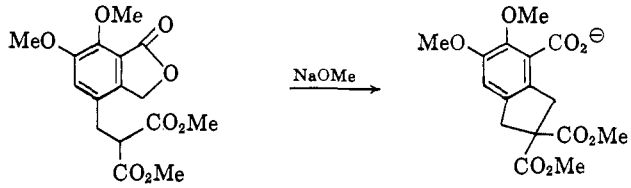
(34) R. M. Lukes, G. I. Poos, R. E. Beyler, W. F. Johns, and L. H. Sarett, *ibid.*, **75**, 1707 (1953).

(35) C. R. Hauser, F. W. Swamer, and B. I. Ringler, *ibid.*, **70**, 4023 (1948).

(36) H. W. Heine, *ibid.*, **79**, 6268 (1957).

(37) *Cf.* E. Vogel, *Fortschr. chem. Forsch.*, **3**, 430 (1955).

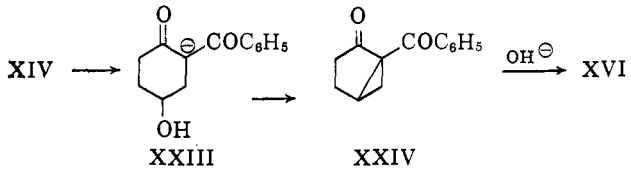
Related reactions are known, however, in which this is the case. An intermolecular example is the conversion of γ-butyrolactone to γ-cyanobutyric acid by potassium cyanide,[38] while the base-induced isomerization of the phthalide XXI to the indan derivative XXII[39] provides an intramolecular analog.



XXI XXII

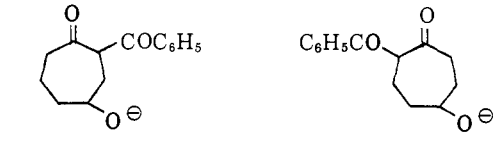
The feasibility of step iii is demonstrated by the observation that treatment of the lactone VII with potassium *t*-butoxide under the conditions used for the rearrangement of II afforded the keto acid IV in 64% yield.

An alternative pathway, subsequent to step i, could involve conversion of the anion XIV to the anion XXIII followed by intramolecular displacement of hydroxide ion to give the bicyclic compound XXIV. Cleavage of this with hydroxide ion would then lead to XVI. This route is considered to be unlikely, however, because the hydroxide ion is a very poor leaving group in displacement reactions at saturated carbon atoms.[40]

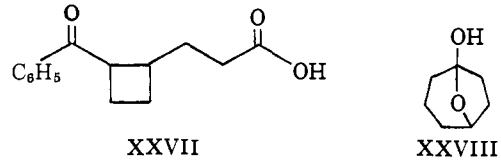


XXIII XXIV

A route analogous to that proposed for the formation of IV is suggested for the formation of III from I. In this case, two variants of step i are possible, since the two methylene groups adjacent to the ketone group in I are nonequivalent. The cyclopropane derivative III is derived from the intermediate β-dicarbonyl species XXV, formed by migration of the benzoyl group to C.2. Migration to C.7 would lead to the β-dicarbonyl species XXVI which by steps analogous to ii and iii would give the cyclobutane derivative XXVII. The nuclear magnetic resonance and other spectroscopic data show that III, not XXVII, is the structure of the isomerization product.[41] The direction of the isomerization may reflect more rapid formation of XXV *via* a five-membered cyclic transition state than of XXVI *via* a six-membered cyclic transition state[42]; however, it is possible that both β-diketones are formed reversibly and that the nature of of the final product is determined at some subsequent stage of the reaction. It may be noted that the tendency for 4-hydroxycycloheptanone to exist in the hemi-ketal form XXVIII[43,44] suggests that little strain energy would be involved in the formation of the transition state required for step ii in the case of either XXV or XXVI.

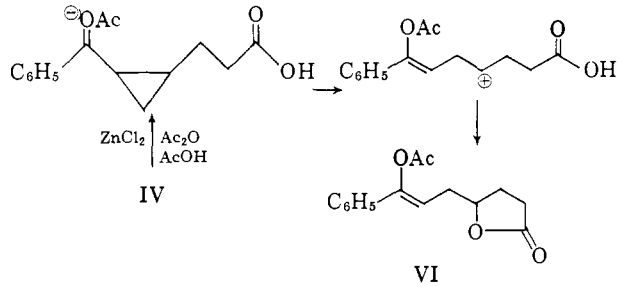


XXV XXVI



XXVII XXVIII

The cleavage of the cyclopropane ring of IV on treatment with zinc chloride and acetic anhydride can be formulated as shown below.



IV VI

Several modifications of this general scheme are possible; thus, the cationic intermediates may be formulated as bicyclobutonium ions,[45] and varying degrees of concert may be envisaged in the breaking of the cyclopropane ring and formation of the lactone ring. The mode of cleavage of the cyclopropane ring is that leading to the more stable cation. The reaction may be compared with the *p*-toluenesulfonic acid-catalyzed ring opening of cyclopropyl phenyl ketones[46] and their aluminum chloride-catalyzed reactions with aromatic hydrocarbons.[6,9]

Experimental[47]

Isomerization of 4-Benzoyloxycycloheptanone (I); Formation of 2-Benzoylcyclopropanebutyric Acid (III). (a) During Attempted Stobbe Condensation.—The apparatus and general procedure used in this and the subsequent experiments employing potassium *t*-butoxide was that recommended by Johnson and Daub,[49] except that provision was made for mechanical stirring. A potassium *t*-butoxide solution was prepared from 1.08 g. (0.028 g.-atom) of freshly cut potassium by refluxing it in 25 ml. of *t*-butyl alcohol (dried by refluxing over calcium hydride and distilling therefrom) under a dry nitrogen atmosphere. To the resulting hot solution was added a solution of freshly distilled 4-benzoyloxycycloheptanone (I,[44] 5.96 g., 0.0257 mole) and dimethyl succinate (5.15 ml., 0.0395 mole) in an additional 30 ml. of the dried *t*-butyl alcohol, and the mixture was refluxed for 2.0 hr. (reflux periods as short as 35 min. were also tried and gave similar results). Within the first 10 min., the color of the reaction mixture became a clear brown and remained unchanged thereafter. At the end of the reflux period, the cooled mixture was neutralized by the addition of a solution of 1.0 g. of ammonium sulfate in 10 ml. of water. About three-fourths of the *t*-butyl alcohol was distilled *in vacuo*, and the residue was diluted with 20 ml. of 2 *N* hydrochloric acid. The organic product was separated by extraction with four 40-ml. portions of ether. The combined extracts were washed with eight 30-ml. portions of aqueous 5% sodium bicarbonate. The bicarbonate washes were combined, washed once with ether, and acidified with 16

(38) G. Paris, R. Gaudry, and L. Berlinguet, *Can. J. Chem.*, **33**, 1724 (1955).

(39) J. Blair, W. R. Logan, and G. T. Newbold, *J. Chem. Soc.*, 3608 (1956).

(40) A. Streitwieser, Jr., *Chem. Rev.*, **56**, 571 (1956).

(41) Thus, for example, cyclobutyl hydrogen atoms do not show the unusually high shielding characteristic of cyclopropyl hydrogen atoms: *cf.* M. C. Caserio, W. H. Graham, and J. D. Roberts, *Tetrahedron*, **11**, 171 (1960).

(42) *Cf.* E. L. Eliel in "Steric Effects in Organic Chemistry," ed. by M. S. Newman, John Wiley and Sons, Inc., New York, N. Y., 1956, p. 116.

(43) W. von E. Doering and A. A.-R. Sayigh, *J. Org. Chem.*, **26**, 1365 (1961).

(44) P. Yates and C. D. Anderson, *Can. J. Chem.*, **41**, 1033 (1963).

(45) E. F. Cox, M. C. Caserio, M. S. Silver, and J. D. Roberts, *J. Am. Chem. Soc.*, **83**, 2719 (1961).

(46) H. M. Walborsky and L. Plonsker, *ibid.*, **83**, 2138 (1961).

(47) Melting points are corrected, unless otherwise indicated. Boiling points are uncorrected and pressure values <0.1 mm. are nominal. The drying agent was magnesium sulfate and the chromatographic adsorbent Woelm "non-alkaline" alumina, Grade III.[48] The infrared spectra were calibrated against water vapor or polystyrene.

(48) R. A. Boissonnas, *Helv Chim. Acta*, **30**, 1689 (1947).

(49) W. S. Johnson and G. H. Daub in "Organic Reactions," Vol. VI, ed. by R. Adams, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 1.

ml. of concentrated hydrochloric acid. The acids liberated were extracted with four 40-ml. portions of chloroform. The combined extracts were washed with saturated aqueous sodium chloride and dried. The chloroform was distilled from the filtered extract, and the last traces of volatile material were removed at 50–60° and oil-pump pressure. The slightly yellowish residue, a viscous oil, weighed 5.63 g.; infrared bands (CCl_4): 3.0–3.5, 5.62, 5.74, 5.84, 5.97, 6.26, 6.34 μ; ultraviolet maximum (95% ethanol): 243 mμ ($E^{1\%}_{1cm}$ 208), which indicates that the product contains 33% of III.

Partition chromatography[50] of a 312-mg. portion of the acidic product on a silicic acid column buffered at pH 6.4 indicated that it was a complex mixture. No crystalline product was obtained, but the early fractions (eluted with chloroform in carbon tetrachloride) afforded 147 mg. (47% of the sample applied) of oil having carbonyl bands at 5.85 and 6.00 μ (in $CHCl_3$). This material, relatively pure III, was converted to its **p-bromophenacyl ester** in the usual way.[51] The derivative, obtained in 59% yield (159 mg.), could not be obtained crystalline even after chromatography on Florisil; infrared bands (CCl_4): 5.74, 5.86, 5.99, 8.23 μ.

Another portion of the crude acidic product was esterified with ethereal diazomethane. The resulting oily mixture of **methyl esters**, dried at 80–90° and 9 mm., had principal infrared bands (CCl_4) at 5.64 (weak), 5.74 (very strong), 5.97 (medium), 6.26 μ.

A third portion of the crude acidic product (133 mg.) was treated with 108 mg. of 2,4-dinitrophenylhydrazine in aqueous ethanolic sulfuric acid,[52] and the mixture was left for 20 hr. The crystals which formed were collected, washed with 1:1 ethanol–water, and dried. This crude **2,4-dinitrophenylhydrazone of the ethyl ester of III** (128 mg.) was recrystallized three times from ethanol–ethyl acetate to give 67 mg. (27%) of red-orange needles, m.p. 127.5–128.5°. The melting point was unchanged by an additional recrystallization; infrared bands ($CHCl_3$): 3.02, 5.78, 6.18, 6.26 μ; ultraviolet maximum (95% EtOH): 377 mμ (ϵ 24,400).

Anal. Calcd. for $C_{22}H_{24}N_4O_6$: C, 59.99; H, 5.49; N, 12.72. Found: C, 59.79; H, 5.58; N, 12.91.

Similarly, treatment of 149 mg. of a crude acidic product prepared in another run (in which the dimethyl succinate was added before the addition of I) with 128 mg. of 2,4-dinitrophenylhydrazine in aqueous methanolic sulfuric acid afforded the **2,4-dinitrophenylhydrazone of the methyl ester of III**. Application of the crude derivative (83 mg.) to a column of 4.3 g. of alumina and elution with benzene gave 59 mg. of material, m.p. 142–145°, obtained from the second and third (20-ml.) fractions. Two recrystallizations from methanol–ethyl acetate yielded 51 mg. (19%) of orange crystals, constant m.p. 144–146°; infrared bands ($CHCl_3$): 3.04, 5.78, 6.18, 6.26 μ.

Anal. Calcd. for $C_{21}H_{22}N_4O_6$: C, 59.15; H, 5.20; N, 13.14. Found: C, 59.27; H, 5.37; N, 13.00.

The yield of the latter derivative was unchanged by preliminary esterification of the crude acidic product with diazomethane.

(b) **By Treatment with Potassium *t*-Butoxide Alone.**—The apparatus and procedure employed were the same as in the attempted Stobbe condensation with I. A potassium *t*-butoxide solution was prepared from 50 ml. of *t*-butyl alcohol (dried as before) and 1.00 g. (0.026 g.-atom) of potassium. To the resulting hot solution was added I (5.42 g., 0.0234 mole), with the use of 10 ml. of dried *t*-butyl alcohol for rinsing. The mixture was refluxed under dry nitrogen for 30 min., during which time it became slightly yellow. It was then cooled with ice, 10 ml. of 6 *N* hydrochloric acid was added, and the *t*-butyl alcohol was distilled *in vacuo*. Sufficient water was added to dissolve the potassium chloride present, and the organic product was extracted with four 50-ml. portions of ether. The combined extracts were washed twice with saturated aqueous sodium chloride and dried. Filtration and evaporation of the ether afforded a residue that was stirred with 50 ml. of saturated aqueous sodium bicarbonate for 1 hr. The undissolved neutral product was extracted with three 25-ml. portions of ether. The combined, dried extracts afforded 1.27 g. (23%) of residual liquid on evaporation of the solvent (completed at about 30 mm. pressure). The infrared spectrum of this material indicated that it was recovered I of high purity. The ether-extracted aqueous layer was acidified with hydrochloric acid, and the oily acid liberated was collected by extraction with four 50-ml. portions of ether. After the combined extracts were dried and filtered, evaporation of the ether (completed at about 30-mm. pressure) yielded 4.46 g. (82%) of III as a nearly colorless oil. Molecular distillation of a 2.71-g. portion at 65–75° (bath temperature) and 10^{-3} mm. afforded a colorless oil which was collected in two fractions: (a) n^{20}D 1.5390, 616 mg., and (b) n^{20}D 1.5430, 1.310 g. These represent a 58% yield. A middle fraction, n^{20}D 1.5416, from a similar distillation of another portion of the crude acidic product was used for analysis. This product gave negative unsaturation tests with both bromine and potassium permanganate; the procedures used were those of Cheronis[53]; infrared bands (CCl_4): 3.0–3.5, 5.84, 5.96, next band at 6.25, 6.33 μ; near-infrared bands (CCl_4): 1.633, 2.234 μ (spectrum measured on a 3.1% solution in a 1.0-cm. cell); ultraviolet maximum (95% ethanol): 244 mμ (ϵ 14,700).

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94; equiv. wt., 232. Found: C, 72.43; H, 7.10; neut. equiv., 241.

A portion of the undistilled III thus obtained (899 mg., 0.00387 mole), 812 mg. of semicarbazide hydrochloride, and 1.24 g. of anhydrous sodium acetate were dissolved in 9 ml. of 95% ethanol plus about 6 ml. of water. The mixture was heated in a water-bath at 75–80° for 20 min. Cooling, scratching, and subsequent storage at about 5° afforded 731 mg. of a crystalline **semicarbazone**. Recrystallization from 3 ml. of aqueous 65% ethanol yielded 633 mg. (57%) of white needles, m.p. 133.5–135° (unchanged by further recrystallization).

Anal. Calcd. for $C_{15}H_{19}N_3O_3$: C, 62.27; H, 6.62; N, 14.52. Found: C, 62.51; H, 6.72; N, 14.53.

When 550 mg. (0.00190 mole) of the semicarbazone was placed in 54 ml. of 8 *N* hydrochloric acid at room temperature, an ether-soluble oil appeared immediately. The oil was collected by continuous extraction with ether for 6 hr. The extract (volume 50 ml.) was washed with four 10-ml. portions of saturated aqueous sodium chloride and dried. Filtration and evaporation *in vacuo* (completed at 0.15 mm.) afforded 435 mg. of residual oil. Molecular distillation at about 100° (bath temperature) and 10^{-3} mm. afforded an 82% yield of regenerated III as a slightly yellowish oil. It was collected in two fractions: (a) n^{28}D 1.5417, 242 mg., and (b) n^{28}D 1.5415, 120 mg. Neither this distillate nor those described earlier could be induced to crystallize.

In another experiment, 525 mg. of I treated with potassium *t*-butoxide as above, but with a 45-min. reflux period, gave 518 mg. of undistilled III and 28 mg. of neutral product. A 36-mg. portion of this sample of III was treated with 2,4-dinitrophenylhydrazine (32 mg.) in aqueous methanolic sulfuric acid. Purification of the crude derivative (49 mg.) on alumina as previously described afforded 37 mg. (56%) of orange, crystalline **2,4-dinitrophenylhydrazone**, m.p. 143–145° (after recrystallization from methanol–ethyl acetate), whose infrared spectrum was identical with that of the 2,4-dinitrophenylhydrazone of the methyl ester of III derived from the acidic product from the attempted Stobbe reaction with I. The mixture m.p. of the twice-recrystallized hydrazone obtained here and that obtained earlier was 144–146°.

Isomerization of 4-Benzoyloxycyclohexanone (II); Formation of 2-Benzoylcyclopropanepropionic Acid (IV).—The apparatus and procedure used here were the same as in the attempted Stobbe condensation with 4-benzoyloxycycloheptanone. Freshly cut potassium (0.20 g., 0.0051 g.-atom) was added to 20 ml. of *t*-butyl alcohol (dried over calcium hydride), and the mixture was refluxed under dry nitrogen until the potassium dissolved (1.3 hr.). The resulting potassium *t*-butoxide solution was cooled slightly, and 4-benzoyloxycyclohexanone (II)[54] (0.98 g., 0.0045 mole, dried under high vacuum at room temperature) was added, with the use of 2.5 ml. of dried *t*-butyl alcohol for rinsing. The mixture, which became light yellow almost immediately, was refluxed for 45 min. with little further change in color. After being cooled quickly to room temperature, the mixture was acidified with 2.2 ml. of 6 *N* hydrochloric acid, which destroyed the yellow color and precipitated potassium chloride. Most of the *t*-butyl alcohol was distilled at 30–40 mm. pressure. The residue was diluted with just enough water to dissolve the potassium chloride and extracted with three 35-ml. portions of ether. The combined extracts were washed with four 25-ml. portions of aqueous 5% sodium bicarbonate and dried. Evaporation of the ether (completed at 30–40 mm. pressure over 8 hr.) afforded 221 mg. of crude neutral product as a pale yellow oil; infrared bands (CCl_4): 5.59 (medium), 5.80 (strong), 5.92 (medium) μ; there was negligible absorption in the region of 3 μ.

The combined sodium bicarbonate washes were acidified and extracted with three 35-ml. portions of ether. The combined, dried extracts on evaporation of the ether (completed at 30–40 mm. pressure) furnished 0.80 g. of crystalline 2-benzoylcyclopropanepropionic acid (IV), m.p. 59–66°. Recrystallization from aqueous acetic acid yielded three crops: (a) 0.22 g., m.p. 67–68°; (b) 0.17 g., m.p. 66.5–68°; and (c) 0.13 g., m.p. 65.5–67°. These represent a 53% yield. Two recrystallizations of a

(50) T. Higuchi, N. C. Hill, and G. B. Corcoran, *Anal. Chem.*, **24**, 491 (1952).

(51) 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. 157.

(52) Reference 51, p. 171.

(53) N. D. Cheronis, "Micro and Semimicro Methods," Vol. VI of "Technique of Organic Chemistry," ed. by A. Weissberger, Interscience Publishers, Inc., New York, N. Y., 1954, pp. 456 and 472.

(54) E. R. H. Jones and F. Sondheimer, *J. Chem. Soc.*, 615 (1949).

portion of the first crop from benzene–hexane gave white needles of unchanged m.p. This product gave negative unsaturation tests with both bromine and potassium permanganate[53]; infrared bands (CCl_4): 3.0–3.5, 5.84, 5.97, 6.25, 6.33, 9.48, 9.79 μ; (KBr): 3.0–3.5, 5.84, 6.00 and 6.03 (doublet), 6.25, 6.32, 9.74, 9.95, 10.08 μ; ultraviolet maximum (95% ethanol): 244 mμ (ϵ 16,700).

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.46; equiv. wt., 218. Found: C, 71.68; H, 6.55; neut. equiv., 219.

A 2,4-dinitrophenylhydrazone of the methyl ester of IV was prepared from 50 mg. each of IV and 2,4-dinitrophenylhydrazine in aqueous methanolic sulfuric acid. The crude derivative (98 mg., m.p. 137–147°) was dissolved in benzene, applied to 6.0 g. of alumina, and eluted with benzene. The last 30 of the first 40 ml. of eluate contained material that on recrystallization from methanol–ethyl acetate gave 57 mg. (60%) of orange-red crystals, m.p. 171.5–172.5°. A second recrystallization from the same solvents yielded 46 mg. of crystals having the double m.p. 161–162° and 171–172°. A final recrystallization from ethyl acetate alone gave 44 mg., double m.p. 162° and 172–173°; infrared bands ($CHCl_3$): 3.03, 5.77, 6.19, and 6.28 μ; ultraviolet maximum ($CHCl_3$): 384 mμ (ϵ 29,400).

Anal. Calcd. for $C_{20}H_{20}N_4O_8$: C, 58.25; H, 4.89; N, 13.58. Found: C, 58.43; H, 5.09; N, 13.74.

Oxidation of IV (500 mg.) with perbenzoic acid in chloroform followed by reduction of unconsumed oxidant with ferrous sulfate, removal of benzoic acid by sublimation, and hydrolysis of the crude product with aqueous potassium hydroxide gave a liquid phenolic fraction (23 mg., 10%). Bromination[55] of this material (20 mg.) gave **2,4,6-tribromophenol** (44 mg.), m.p. 89–92°; after molecular distillation at 0.20 mm. and 50–55° (bath temperature), this derivative had m.p. 91–92.5°, and was identified by a mixture m.p. with an authentic sample. The noncrystalline carboxylic acid fraction from the hydrolysis of the crude oxidation product was oxidized with aqueous potassium permanganate at pH 6.5–7.4, but no crystalline product, other than benzoic acid and unconsumed IV, could be isolated.

6-Benzoyl-4-hydroxyhexanoic Acid Lactone (VII). (a) From 2-Benzoylcyclopropanepropionic Acid (IV).—2-Benzoylcyclopropanepropionic acid (1.008 g., 0.00462 mole) was dissolved in 10 ml. of glacial acetic acid containing 2.0% of zinc chloride and 10 ml. of acetic anhydride. The solution was refluxed under nitrogen for 3 hr., cooled, and evaporated to dryness *in vacuo*. The residue was stirred with 10 ml. of water containing 2.0 g. of sodium bicarbonate, and the resulting suspension (pH 8) was extracted with three 10-ml. portions of chloroform. The combined extracts were washed with 5 ml. of aqueous 1 *N* sodium bicarbonate and dried. The filtered chloroform solution was evaporated *in vacuo*, and two 10-ml. portions of toluene were evaporated from the residue, finally at 40–50° and 0.25 mm. The residual brown gum (VI) weighed 1.13 g. (94%); infrared bands (CCl_4): 5.60, 5.66 (shoulder), 8.33, 8.51 μ.

The crude VI (1.07 g., 0.00410 mole) was dissolved in 12 ml. of water and 6 ml. of methanol containing 0.63 g. of potassium hydroxide and the solution was refluxed under nitrogen for 12 hr. The cooled solution was neutralized with acetic acid and evaporated *in vacuo*. The residual potassium salts were dissolved in 4.0 ml. of glacial acetic acid and 2.5 ml. of water containing 0.30 ml. of concentrated sulfuric acid. After being stirred at room temperature for 20 hr., the mixture was extracted with four 15-ml. portions of ether. The combined extracts were washed with two 15-ml. portions of saturated aqueous sodium chloride and dried. The filtered solution was evaporated, finally at 40° and 0.8 mm., leaving a residual yellow oil (0.89 g., 93%). A small portion was crystallized from water and then had m.p. 72–74°. Seeding the main portion of yellow oil with this material induced complete crystallization, the resulting solid having m.p. 60–67°. A 354-mg. portion was recrystallized from 45 ml. of water containing 2 drops of 0.1 *N* hydrochloric acid. This afforded 200 mg. (53%) of 6-benzoyl-4-hydroxyhexanoic acid lactone (VII) as white needles, m.p. 74–75.5°; infrared bands (KBr): 5.59, 5.92, 6.25, 6.32, 8.40 μ. The mixture m.p. with a sample prepared from 4,7-dihydroxy-7-phenylheptanoic acid γ-lactone (see below) was 74.5–76°.

(b) From 4,7-Dihydroxy-7-phenylheptanoic Acid γ-Lactone (XI).—A solution of 4,7-dihydroxy-7-phenylheptanoic acid γ-lactone (4.47 g., 0.0203 mole) in 16 ml. of glacial acetic acid and 5 ml. of water containing 0.50 ml. of concentrated sulfuric acid was cooled in an ice-bath. Chromium trioxide (2.30 g.) dissolved in 8 ml. of glacial acetic acid and 7 ml. of water was added dropwise with stirring. The reaction mixture was then allowed to warm slowly to room temperature. After 10 hr., stirring was discontinued and the mixture was stored at 5° for 12 additional hours. After dilution with 40 ml. of water, the mixture was extracted with four 25-ml. portions of ether. The combined extracts were washed with seven 25-ml. portions of saturated aqueous sodium bicarbonate; during the extraction, 25 ml. of ethyl acetate had to be added to prevent crystallization of the oxidation product. After being washed with a 25-ml. portion of saturated aqueous sodium chloride and dried, the organic layer was evaporated *in vacuo*, affording a slightly pink, crystalline residue (3.99 g.), m.p. 67–72°. Recrystallization from 45 ml. of 1:1 benzene–hexane yielded 1.91 g. (43%) of VII as fine crystals, m.p. 74.5–75.5°. A portion was purified for analysis by a second recrystallization from the same solvents and then had m.p. 75–76°.

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.46. Found: C, 71.71; H, 6.49.

The mother liquor from the first recrystallization above was evaporated *in vacuo*, and the residue was recrystallized from ethanol–water. This afforded 0.75 g. (17%) of additional crude VII, m.p. 57–71°.

4,7-Dioxo-7-phenylheptanoic Acid (IX). (a) From 6-Benzoyl-4-hydroxyhexanoic Acid Lactone (VII).—A portion (508 mg., 0.00233 mole) of the crude, crystalline 6-benzoyl-4-hydroxyhexanoic acid lactone (VII) of m.p. 60–67° obtained from 2-benzoylcyclopropanepropionic acid (IV) as described above was suspended in 23.3 ml. of 0.1 *N* sodium hydroxide solution and stirred at 70° under nitrogen for 10.5 hr. The lactone had by then completely dissolved, and the reaction mixture had pH *ca.* 7. The mixture was evaporated to dryness, finally at 30° and 0.5 mm. The white residual solid was suspended in 6 ml. of pyridine. To this was added a suspension of chromium trioxide–pyridine complex (prepared by adding 0.73 g. of chromium trioxide to 7 ml. of pyridine), with the use of an additional 7 ml. of pyridine for rinsing. The mixture was left at room temperature for 10.5 hr., diluted with 20 ml. of saturated aqueous sodium bicarbonate, and extracted with four 20-ml. portions of chloroform. The first extraction resulted in an emulsion which was broken by filtration through Celite. The combined extracts were washed with 25 ml. of saturated aqueous sodium chloride and dried. Evaporation of the filtered extracts *in vacuo*, followed by evaporation of two portions of toluene to remove the last traces of pyridine, unexpectedly yielded 0.26 g. of crude 4,7-dioxo-7-phenylheptanoic acid (IX), m.p. 87–107°. Recrystallization from benzene–hexane and then from water afforded 108 mg. of material, m.p. 112.5–114.5°. A mixture m.p. with an authentic sample of IX prepared as described in (b) was identical.

The aqueous alkaline layer from the chloroform extraction was acidified with concentrated hydrochloric acid and extracted with four 20-ml. portions of chloroform. During the first extraction, an emulsion was obtained here also and was broken by filtration through Celite. The combined extracts were washed with four 25-ml. portions of saturated aqueous sodium chloride, dried, filtered, and evaporated *in vacuo*. This afforded 350 mg. of crystalline residue, m.p. 97–106°, that was dissolved in 5 ml. of hot benzene and filtered through Celite. Evaporation of the filtrate yielded 229 mg. of greenish white crystals, m.p. 98–109°. Recrystallization from water followed by recrystallization from benzene–hexane afforded 153 mg. of still slightly greenish IX, m.p. 112–113.5°. Thus, the total yield of twice-recrystallized IX was 45% over-all from IV. Three further recrystallizations yielded 131 mg. of white crystals, m.p. 113.5–114.5°. The m.p. was not changed on admixture with an authentic sample of IX. Comparison of the infrared spectra of the two samples corroborated their identity; infrared bands (KBr): 3.0–3.5, 5.83, 5.95, 6.08, 6.25, 6.32 μ; in chloroform solution, the band at 6.08 μ was absent and the alkyl phenyl ketone band occurred at 5.92 μ and was of increased relative intensity.

(b) From 3-(2-Furyl)-acrylophenone (X).—An authentic sample of 4,7-dioxo-7-phenylheptanoic acid (IX) was prepared from 3-(2-furyl)-acrylophenone (25.8 g.) by the acid-catalyzed hydrolysis procedure of Kehrer.[26] A 48% yield (14.7 g.) of once-recrystallized product (m.p. 107–110°) was obtained. Several recrystallizations from water and benzene gave IX having the constant m.p. 113.5–114.5° (lit.[26] m.p. 115–116°). The infrared spectrum, which was measured in potassium bromide, was identical with that of the above sample prepared from IV *via* VII.

4,7-Dihydroxy-7-phenylheptanoic Acid γ-Lactone (XI).—4,7-Dioxo-7-phenylheptanoic acid (IX) (6.00 g., 0.0256 mole) was dissolved in 300 ml. of isopropyl alcohol and 12 ml. of water containing 1.20 g. of sodium borohydride, and the solution was stirred at room temperature. After 11 hr., the mixture was found to be gelatinous. The addition of 30 ml. of isopropyl alcohol and 10 ml. of water again gave complete solution. After a total of 39 hr., the solution was evaporated *in vacuo*. The white residual solid was dissolved in 30 ml. of methanol plus 60 ml. of water and acidified by the addition of 25 ml. of concentrated hydrochloric acid. After 19 hr. at room temperature, the volume of the mixture was reduced to 70–75 ml. by evaporation at 35° and 30–40 mm. pressure. The concentrate was extracted with three 25-ml. portions of chloroform. The combined extracts were washed with 25 ml. of saturated aqueous sodium bicarbonate and dried. The yellowish solution was fil-

(55) Reference 51, p. 211.

tered and evaporated at 35° and 30–40 mm. pressure yielding 5.52 g. of residual oil. This was combined with 0.83 g. of a corresponding crude product obtained in a preliminary experiment using 1.00 g. of IX. Distillation through a short Vigreux column furnished 4.19 g. (64%) of 4,7-dihydroxy-7-phenylheptanoic acid γ-lactone (XI) as a slightly yellowish oil, b.p. 170–174° at 0.13 mm., $n^{20}D$ 1.5390; infrared bands (liq. film): 2.86, 5.64, 6.26, 6.33, 8.46 μ.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.08; H, 7.16.

Conversion of 6-Benzoyl-4-hydroxyhexanoic Acid Lactone (VII) to 2-Benzoylcyclopropanepropionic Acid (IV).—A solution of potassium *t*-butoxide was prepared in the usual manner by dissolving freshly cut potassium (0.30 g., 0.0077 g.-atom) in 30 ml. of dried *t*-butyl alcohol at the reflux temperature. This required 1.5 hr. The solution was cooled slightly, and 6-benzoyl-4-hydroxyhexanoic acid lactone (VII, 1.50 g., 0.00689 mole, dried over phosphorus pentoxide at reduced pressure) was added. The mixture was refluxed under dry nitrogen for 45 min., cooled to 15–20°, and treated with 3.3 ml. of 6 *N* hydrochloric acid. The pale yellow mixture was evaporated, finally at 30° and 30–40 mm. pressure. Water (10 ml.) was added to the residue, and the insoluble yellow oil was collected by extraction with three 15-ml. portions of ethyl acetate. The combined extracts were washed with three 20-ml. portions of aqueous 1 *N* sodium bicarbonate. Evaporation of the washed ethyl acetate solution and recrystallization of the waxy residue (206 mg.) from benzene–hexane yielded 83 mg. of recovered VII, m.p. 72–74°. A further recrystallization from water afforded 69 mg., m.p. 75–76°; mixture m.p. with starting material, 74.5–75.5°.

The combined sodium bicarbonate washes were acidified with concentrated hydrochloric acid and extracted with three 20-ml. portions of chloroform. Evaporation of the combined, dried extracts yielded 1.25 g. of crude 2-benzoylcyclopropanepropionic acid (IV), m.p. 63–68°. Recrystallization from 33% aqueous acetic acid afforded two crops: (a) 0.76 g., m.p. 67.5–68.5°, mixture m.p. with IV prepared from II 67.5–68.5°; and (b) 0.20 g., m.p. 66–67.5°. These together represent a 64% yield. The infrared spectrum of the first crop was identical with that of IV prepared from II.

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

3-Furanones. I. The Yellow Compound of Kleinfeller and Fiesselmann[1]

BY PETER YATES[2a] AND JERRY A. WEISBACH[2b]

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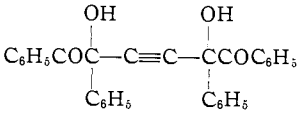
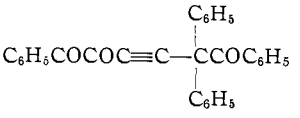
The yellow compound obtained by Kleinfeller and Eckert by the action of hydrogen chloride or bromine on 2,5-dihydroxy-1,2,5,6-tetraphenyl-3-hexyne-1,6-dione (I) and by Fiesselmann and co-workers by the action of bromine on methylenedeoxybenzoin dimer (III) has been shown to be 2-desylidene-4,5-diphenyl-3(2*H*)-furanone (IX). Its reactions have been investigated and its infrared and ultraviolet spectra and those of its tetrahydro derivative, 2-(2-hydroxy-1,2-diphenylethyl)-4,5-diphenyl-3(2*H*)-furanone (XII), compared with the spectra of a series of model compounds containing the 4,5-diphenyl-3-furanone system. A new, rational synthesis of the yellow compound has been effected *via* the action of oxalyl chloride on the sodium derivative of deoxybenzoin.

Kleinfeller and Eckert[3] observed that when 2,5-dihydroxy-1,2,5,6-tetraphenyl-3-hexyne-1,6-dione (I) is treated with saturated alcoholic hydrogen chloride, it is converted to a yellow compound, $C_{30}H_{20}O_3$. This product, which was reported to form a trioxime, was suggested to have structure II.



I

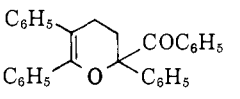


II

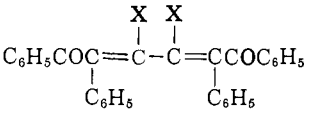
In the course of further work, Kleinfeller[4] found that the yellow compound is also formed, together with benzil, by the action of bromine in chloroform or acetic acid on I, that it forms a monosemicarbazone, fails to give a quinoxaline derivative, and is converted by concentrated sulfuric acid to a white, isomeric compound.

Fiesselmann and Ribka,[5] in the course of an investigation of the structure and reactions of methylenedeoxybenzoin dimer (III), discovered that treatment of this dimer with bromine in acetic acid gives a yellow compound, $C_{30}H_{20}O_3$, and two white compounds, one of which is isomeric with the yellow compound. They showed that this yellow compound, which forms a mono-2,4-dinitrophenylhydrazone, is identical with the yellow compound obtained by Kleinfeller and Eckert[3] from I, and that the isomeric white compound formed from III is identical with the compound obtained by the action of sulfuric acid on the yellow compound.

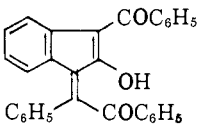
Fiesselmann and Meisel[6] investigated the oxidative degradation of the yellow compound with ozone and with chromic acid; the major products were found to be benzoic acid and benzil, which were the only products identified. They also carried out an investigation of the course of the bromination by isolation of reaction intermediates and were able to establish that the formation of the yellow compound very probably proceeds *via* the consecutive formation of the 1,3-dienes IV and V. They suggested that its formation from the acetylenic



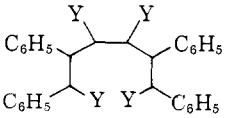
III



IV, X = H
V, X = Br
VI, X = OAc



VII



VIII

diol I also proceeds *via* V or an equivalent intermediate,[7] and Fiesselmann and Lindner[8] subsequently showed that it can be formed in high yield by the action of warm 47% hydrobromic acid on the diene VI. The conversion of V to the yellow compound was considered[6] to involve substitution into a phenyl ring[9] and structure VII was assigned to it.

We have reinvestigated these compounds and in this and the following paper[10] discuss new experimental

(1) A preliminary report on part of this work has appeared previously: P. Yates and J. A. Weisbach, *Chem. Ind.* (London), 1482 (1957).

(2) (a) Department of Chemistry, University of Toronto, Toronto, Canada; Alfred P. Sloan Foundation Fellow, 1957–1960; (b) Eastman Kodak Co. Fellow, 1958–1959.

(3) H. Kleinfeller and F. Eckert, *Ber.*, **62**, 1598 (1929).

(4) H. Kleinfeller, *ibid.*, **72**, 249 (1939).

(5) H. Fiesselmann and J. Ribka, *ibid.*, **89**, 40 (1956).

(6) H. Fiesselmann and F. Meisel, *ibid.*, **89**, 657 (1956).

(7) *Cf.* J. Salkind and A. Kruglow, *ibid.*, **59**, 1936 (1926).

(8) H. Fiesselmann and H. J. Lindner, *ibid.*, **89**, 1799 (1956).

(9) *Cf.* H. Wieland and H. Kloss, *Ann.*, **470**, 201 (1929).

(10) P. Yates and J. A. Weisbach, *J. Am. Chem. Soc.*, **85**, 2950 (1963).