

Aldoketene Dimers and Trimers from Acid Chlorides. A Synthesis of Substituted 3-Hydroxycyclobutenones

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The literature on ketene dimerizations is examined in reference to some new data presented. The following generalization of ketene dimerizations is suggested: "with the single exception of ketene itself, spontaneous dimerizations of ketenes probably afford 1,3-cyclobutanediones as major primary products." Several catalysts are implicated as favoring the formation of β -lactone dimers. Possible mechanistic interpretations are offered for these results as well as for the base-catalyzed rearrangement of the β -lactone dimers of arylketenes (11 and 12) to the 3-hydroxycyclobutenone dimers (7 and 9). It is demonstrated that, although reaction of propionyl chloride and triethylamine in ether forms the β -lactone dimer (4, R = CH₃) of methyl ketene, the reaction in methylene chloride provides a useful synthesis of the 3-hydroxycyclobutenone dimer (2, R = CH₃). A similar reaction of arylacetyl chlorides is exploited as a convenient synthesis of 2,4-diaryl-3-hydroxycyclobutenones (7 and 9).

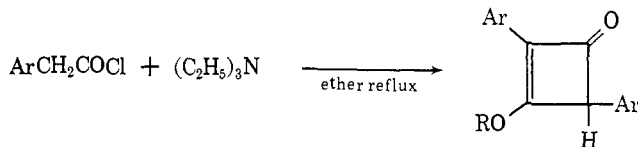
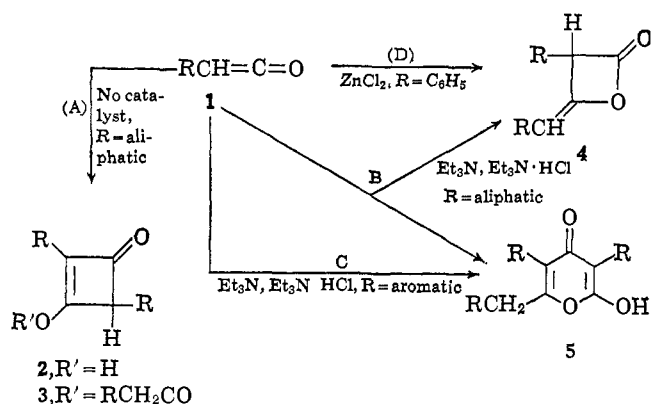
The formation of at least two types of aldoketene dimers and two types of aldoketene trimers has been established by several groups of workers.²⁻⁷ Review of the voluminous and sometimes confusing literature on the subject yields the following reasonably accurate generalizations, as summarized in Chart I. (A) Spontaneous dimerization of dilute solutions of "pure"⁸ aliphatic aldoketenes (1) yields, predominantly, 3-hydroxycyclobutenone-type dimers (2),² or their acyl-

ated trimers (3).⁶ (B) *In situ* preparation and dimerization of aliphatic aldoketenes by dehydrohalogenation of acid chlorides with triethylamine in ether affords the β -lactone-type dimers (4)^{4,5} predominantly, or low yields of the pyronone-type trimers (5).³ (C) Dehydrohalogenation of arylacetyl chlorides with triethylamine affords pyronone-type trimers (5). (D) Dimerization of phenylketene, prepared by zinc dehalogenation of α -chlorophenylacetyl chloride (and still contaminated with zinc chloride), affords mainly the β -lactone type dimer (4).²

It was our intent in this work to exploit the synthetic possibilities of these reactions further, and to examine some of the factors which lead to the diverse types of reactions. Sauer⁴ and Hill⁵ have developed path B, the reaction of aliphatic acid chlorides with triethylamine, into a useful preparation of the β -lactone-type ketene dimers (4). The corresponding reaction with arylacetyl chlorides, however, was reported to give a 50% yield of the pyronone-type trimer (5) by Wedekind.³ It seemed desirable to examine the dehydrohalogenation of phenylacetyl chloride with triethylamine more closely in order to understand this different behavior.

In order to compare the reaction of phenylacetyl chloride and triethylamine more directly with that of the aliphatic acid chlorides, the procedure used by Sauer for the aliphatic acid chlorides was followed reasonably closely. Thus, 1 equiv. of triethylamine was added dropwise to 1 equiv. of phenylacetyl chloride in ether at the reflux temperature. Concentration of the ether filtrate afforded a crystalline precipitate of 2,4-diphenyl-3-phenylacetoxycyclobutenone (6), m.p. 120–122°, in 65% yield.

Chart I



6, R = C₆H₅CH₂CO; Ar = C₆H₅
 7, R = H; Ar = C₆H₅
 8, R = *p*-CH₃OC₆H₄CH₂CO; Ar = *p*-CH₃OC₆H₄
 9, R = H; Ar = *p*-CH₃OC₆H₄

The structure of the product is established by its analysis, infrared spectrum ($\lambda_{\text{max}}^{\text{Nujol}}$ 5.60, 5.70, and 6.08 μ ; cf. the corresponding trimer of methyl ketene, $\lambda_{\text{max}}^{\text{heat}}$ 5.6–5.8 and 6.0–6.1 μ ⁶), its hydrolysis in aqueous sodium hydroxide to approximately molar equivalent amounts of phenylacetic acid and 2,4-diphenyl-3-hydroxycyclobutenone (7), m.p. 149–150°^{2,7} ($\lambda_{\text{max}}^{\text{Nujol}}$ 4.0 (very broad), 5.9 (broad), and 6.5 μ (broad)), and its regeneration in 67% yield by treatment of the triethylamine salt of 7 with phenylacetyl chloride. The Wedekind pyronone-type trimer (5) could be isolated in only a few per cent yield from the reaction of phen-

(1) Fellow of the Alfred P. Sloan Foundation, 1962–1965.

(2) H. Staudinger and S. Bereza, *Ber.*, **44**, 533 (1911); see also H. Staudinger, "Die Ketene," Enke, Stuttgart, Germany, 1912.

(3) E. Wedekind, J. Häussermann, W. Weisswange, and M. Miller, *Ann.*, **378**, 261 (1911).

(4) J. C. Sauer, *J. Am. Chem. Soc.*, **69**, 2444 (1947); W. E. Hanford and J. C. Sauer, *Org. Reactions*, **3**, 108 (1946).

(5) C. M. Hill and G. W. Senter, *J. Am. Chem. Soc.*, **71**, 364 (1949).

(6) E. Enk and H. Spes, *Angew. Chem.*, **73**, 834 (1961).

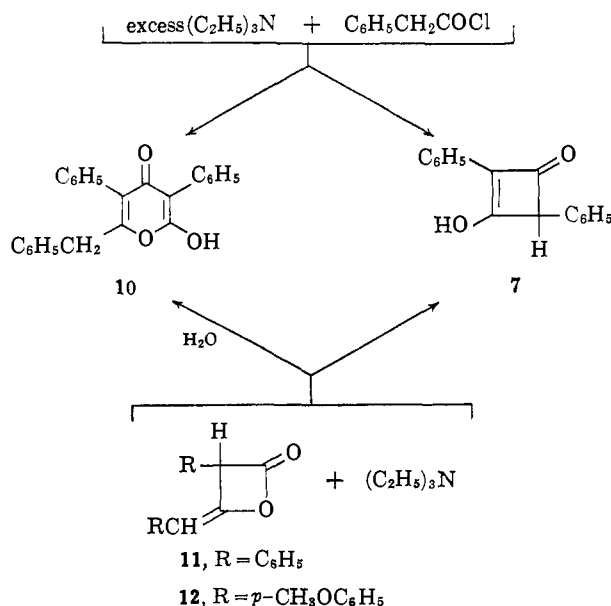
(7) J. E. Baldwin and J. D. Roberts, *J. Am. Chem. Soc.*, **85**, 2444 (1963).

(8) These solutions were prepared by distillation of the aldoketenes and were, thus, free from the zinc salts generated in their preparation.

ylacetyl chloride and triethylamine. Reaction of *p*-methoxyphenylacetyl chloride with triethylamine afforded a 40% yield of the corresponding cyclobutenone trimer of *p*-methoxyphenylketene (8), m.p. 114–114.5°. This substance was similarly identified by its analysis, infrared spectrum ($\lambda_{\text{max}}^{\text{Nujol}}$ 5.59, 5.70, and 6.07 μ), and hydrolysis to 2,4-di-*p*-methoxyphenyl-3-hydroxycyclobutenone (9), m.p. 152–154° ($\lambda_{\text{max}}^{\text{Nujol}}$ 4.0 broad and 5.8, 6.18 μ), in 90% yield. The enol 9 could also be converted to a methyl ether, m.p. 122–123° (λ_{max} 5.71, 6.15, and 6.24 μ), upon treatment with diazomethane, and could be recovered from this methyl ether by hydrolysis in aqueous methanolic potassium hydroxide. Thus, the reaction of arylacetyl chlorides with triethylamine seems to provide a useful synthesis of ketene trimers of type 3 and dimers of type 2 (*i.e.*, 3-hydroxycyclobutenones), in contrast to the behavior of aliphatic acid chlorides, which give type 4 dimers (*i.e.*, β -lactones).

The different behavior of aryl and alkylacetyl chlorides, as well as the discrepancy between Wedekind's observation of the formation of pyronones (type 5 trimers) and our observation of the formation of type 3 trimers from arylacetyl chlorides, prompted us to examine these reactions further. Addition of phenylacetyl chloride to excess triethylamine in boiling ether did, indeed, result in the formation of Wedekind's pyronone (10) in 25% yield,⁹ in addition to some hydroxycyclobutenone 7. Furthermore, the β -lactone dimer, 11, of phenylketene² reacted instantly with triethylamine in ether to give a mixture of the pyronone 10⁹ and the hydroxycyclobutenone 7 (*cf.* ref. 2 and 7). The amount of pyronone formed was quite small when moisture was rigorously excluded, but appreciable when it was not. These reactions are summarized in Chart II.

Chart II



The above observations suggest that the pyronone 10, trimer 6, and hydroxycyclobutenone 7 formed in the reactions of phenylacetyl chloride with triethylamine

(9) The pyronone could be obtained only after base hydrolysis of an unisolated base-insoluble precursor, possibly an acylated derivative analogous to dehydroacetic acid.

could all arise from secondary reactions of an initially formed β -lactone dimer 11. This interpretation would also be compatible with the observation that neither trimer 6 nor hydroxycyclobutenone 7 was converted to pyronone 10 under the Wedekind conditions, and thus could not be its precursors. Although the intermediacy of the β -lactone 11 could not be demonstrated in the particular reaction of phenylacetyl chloride with triethylamine, the corresponding β -lactone 12, m.p. 154–156°, could be isolated in low yield from the reaction of *p*-methoxyphenylacetyl chloride with triethylamine. The substance was characterized by analysis, molecular weight determination, and determination of its infrared spectrum ($\lambda_{\text{max}}^{\text{Nujol}}$ 5.40 and 5.86 μ ; *cf.* diketene,¹⁰ $\lambda_{\text{max}}^{\text{Solid}}$ 5.30, 5.41, and 5.87 μ). The β -lactone 12 could also be converted to the corresponding hydroxycyclobutenone 9 by reaction with potassium hydroxide in aqueous dioxane (*cf.* ref. 7). However, it was not converted to 9 in the presence of triethylamine hydrochloride under the conditions of its preparation. Thus it seems that, in the case of *p*-methoxyphenylacetyl chloride, and probably in the case of phenylacetyl chloride, reaction with 1 equiv. of triethylamine does lead to the trimer 8 directly, in contrast to the behavior of aliphatic acid chlorides.¹¹

Interpretation of these sundry reactions of acid chlorides and their derived ketenes must, then, account for the following observations: (A) formation of 3-hydroxycyclobutenone-type dimers (2) or the acylated trimers (3) by polymerization of solutions of "pure" aldoketenes; (B) formation of β -lactones (4) by dimerization of aliphatic aldoketenes in the presence of triethylamine hydrochloride; (C) formation of the acylated trimers (3) by polymerization of arylketenes in the presence of triethylamine hydrochloride; (D) formation of pyronone-type trimers (5) from aryl ketenes in the presence of excess triethylamine; and (E) formation of the β -lactone 11 from phenylketene in the presence of zinc chloride.¹² We suggest the following simplifying interpretation of these reactions. Spontaneous dimerization of aldoketenes, like that of ketoketenes, affords cyclobutane-1,3-diones. The formation of β -lactone-type dimers can be promoted by certain catalysts, triethylamine hydrochloride being effective for aliphatic aldoketenes, but triethylamine or zinc chloride being required for arylaldoketenes. These catalyzed dimerizations are, thus, similar to the aluminum chloride catalyzed dimerization of the ketoketene, dimethylketene, to its β -lactone dimer,¹³ and the Lewis acid catalyzed additions of ketenes to carbonyl functions to give β -lactones.¹⁴ At the very least, the sometimes-stated principle that monosubstituted aldoketenes differ from ketoketenes in yielding, predominantly,

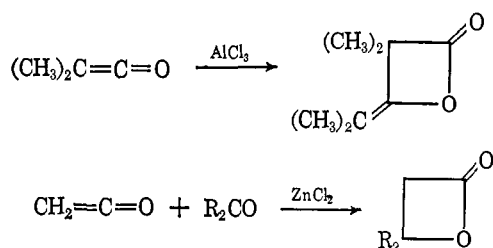
(10) F. A. Miller and G. L. Carlson, *J. Am. Chem. Soc.*, **79**, 3995 (1957).

(11) A clear distinction must be made between these reactions, in which the ketene is generated in the presence of triethylamine hydrochloride, but not free triethylamine, and the reaction leading to pyronone 10, in which a large excess of triethylamine is present.

(12) The catalytic action of zinc chloride in this reaction is consistent with Staudinger's observation² that, if the solution is diluted to a large volume with low boiling petroleum ether before dimerization is allowed to proceed, the major product is the hydroxycyclobutenone 7, as in case A.

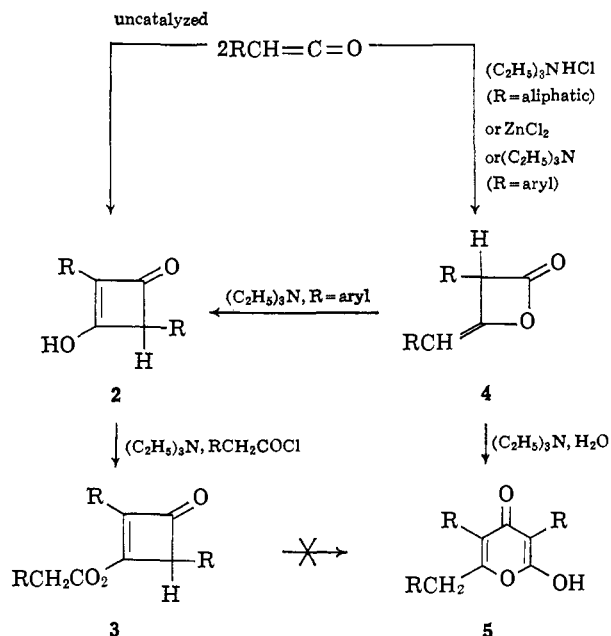
(13) R. H. Hasek, R. D. Clar, E. U. Elam, and J. C. Martin, *J. Org. Chem.*, **27**, 60 (1962).

(14) R. N. Lacey in "Advances in Organic Chemistry," Vol. II, R. A. Raphael, E. C. Taylor and H. Wynberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1960, p. 226.



β -lactone dimers¹⁵ refers to reactions which are not spontaneous dimerizations, and may involve intermediates other than, or in addition to, ketenes. The several reactions of the aldoketenes and their dimers are interpreted in summary in Scheme I.

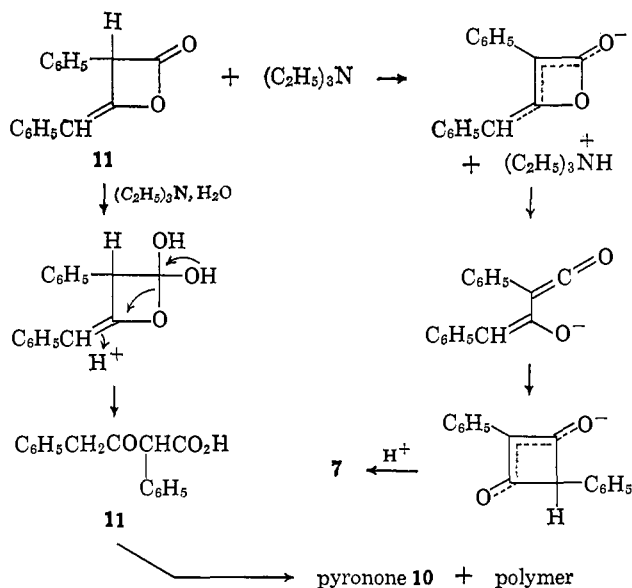
Scheme I



Presentation of these data on aldoketene dimerizations in the form of Scheme I calls attention to some further interesting points. Thus, why is an aryl rather than an alkyl substituent required for facile base-catalyzed rearrangement of the β -lactone dimer **4** to the hydroxycyclobutenone dimer **2**? This point was checked further in this work by specific attempts to rearrange the β -lactone dimer of methylketene to the hydroxycyclobutenone dimer with triethylamine under anhydrous conditions. Only nonvolatile base-insoluble polymeric material and a small yield of pyronone were obtained in a comparatively slow reaction. Mechanisms which can accommodate the different behavior of aryl- and alkylaldoketene dimers have already been advanced for the rearrangement in aqueous base.⁷ We outline in Scheme II one which takes advantage of the increased acidity of the α -hydrogen in aryl dimers, and which we feel is also able to account for the effect of small amounts of water on the triethylamine-catalyzed rearrangement.¹⁶

(15) C. R. Noller, "Chemistry of Organic Compounds," 2nd Ed., B. Saunders, Co., Philadelphia, Pa., 1957, p. 762; R. A. Raphael in "Chemistry of Carbon Compounds," Vol. II, E. H. Rodd, Ed., Elsevier Publishing Co., New York, N. Y., 1953, p. 48; Y. Etienne and N. Fischer in "Heterocyclic Compounds with Three- and Four-Membered Rings," Part II, A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p. 803.

Scheme II



Scheme I also suggests that, if the catalytic effect of triethylamine hydrochloride could be attenuated, dehydrohalogenation of aliphatic acid chlorides might also give type **2** hydroxycyclobutenone dimers or their acylated type **3** trimers. We first confirmed that dehydrohalogenation of propionyl chloride with triethylamine in refluxing ether⁴ gave only small amounts of trimer **3** ($\text{R} = \text{CH}_3$) as judged by proton magnetic resonance (n.m.r.) analysis of the crude product and distilled fractions, and no base-soluble dimer **2** ($\text{R} = \text{CH}_3$). The n.m.r. analysis depended upon the observation that the trimer **3** ($\text{R} = \text{CH}_3$) prepared in another reaction (*vide infra*) exhibited a doublet ($J = 2.5$ c.p.s.) for the vinyl methyl hydrogens (*cf.* ref. 17) at τ 8.42. The lower field component of this doublet overlapped with one of the components of the vinyl methyl quartet of the β -lactone dimer **4** ($\text{R} = \text{CH}_3$). The higher field component was in a relatively clear region of the spectrum. Thus, it was possible to establish an upper limit to the ratio of trimer **3** ($\text{R} = \text{CH}_3$) to dimer **4** ($\text{R} = \text{CH}_3$) by integrating through the vinyl methyl region of the n.m.r. spectrum. By this technique the ratio of trimer **3** ($\text{R} = \text{CH}_3$) to dimer **4** ($\text{R} = \text{CH}_3$) in the reaction of propionyl chloride with triethylamine in refluxing ether was shown to be no greater than 0.06–0.09. When the reaction was conducted at 0° the ratio was less than 0.02 (the minimum detectable). When the reaction was run at 0° in methylene chloride, a poorer solvent for triethylamine hydrochloride, the ratio rose to 0.2–0.3, while in refluxing methylene chloride it climbed to 0.4. The presence of large amounts of trimer **3** ($\text{R} = \text{CH}_3$) in these latter reactions was amply confirmed by the presence of other characteristic peaks in the n.m.r. spectrum and by isolation of a sample of material whose n.m.r. spectrum (τ 6.4, multiplet, 1 H; 7.4,

(16) In this mechanism, the ratio of rearrangement to polymerization is dependent upon the "ratio" of the base strength to the activity of water in the medium. Thus, the scheme can accommodate the observed rearrangement without polymerization in aqueous base⁷ by suggesting that the strong base, hydroxide ion, competes successfully with water in aqueous solution to give rearrangement, while water competes successfully with the weak base, triethylamine, in ether solution to cause polymerization.

(17) D. G. Farnum, M. A. T. Heybey, and B. Webster, *J. Am. Chem. Soc.*, **86**, 673 (1964).

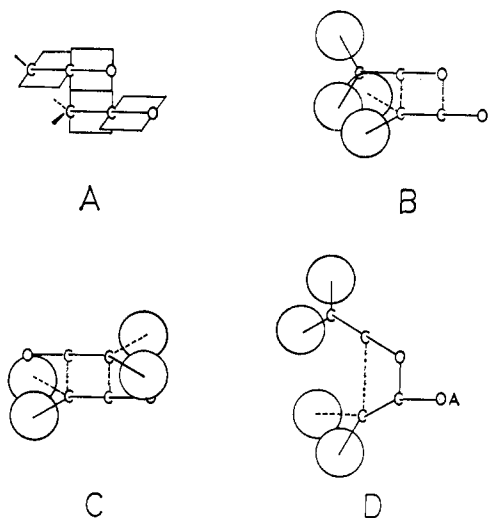


Figure 1.

quartet, 2 H; 8.42, doublet, 3 H; 8.77, triplet; and 8.84, doublet, 6 H) was quite compatible with structure **3** ($R = \text{CH}_3$). Furthermore, the trimer **3** could also be prepared by reaction of the triethylamine salt of 2,4-dimethyl-3-hydroxycyclobutenone (**2**, $R = \text{CH}_3$)¹⁷ with propionyl chloride. The infrared spectrum of the material was identical with that reported in the literature for **3** ($R = \text{CH}_3$).⁶

We therefore conclude that a consistent, useful interpretation of the sundry "dimerizations" of ketenes is the following. *With the single exception of ketene itself, spontaneous dimerizations of ketenes probably afford 1,3-cyclobutanediones as major primary products. The formation of β -lactone-type dimers can be facilitated by the presence of catalysts, triethylamine or its hydrochloride being effective for aldoketenes, but a strong Lewis acid, such as aluminum chloride, being required for ketoketenes.*¹⁸ In Figure 1, we illustrate one factor which may be of prime importance in the reluctance of substituted ketenes to give β -lactones by spontaneous dimerization. Figure 1A shows the most favorable orientation of π -orbitals in an idealized transition state for concerted β -lactone-type dimerization of ketene. Only with this orientation can the ketene carbon-carbon double bond which ultimately becomes the β -lactone double bond be maintained throughout the reaction. In Figure 1B the resultant steric crowding of the substituent groups about the ketene is shown. Examination of Courtauld molecular models suggests that, if any one of the three crowded groups is a methyl group, rather than hydrogen, restricted rotation of that group is significant. Larger groups, of course, encounter severe steric crowding. In a transition state for concerted cyclobutanedione-type dimerization (Figure 1C), steric interactions are essentially absent by comparison. A possible effect of acid catalysts in

(18) The only apparent exception to this generalization, of which we are aware, is the observation by Jenkins¹⁹ of the formation of the β -lactone dimer of methyl ketene in unspecified yield in a heterogeneous vapor phase reaction. The author admits the possibility of a catalytic reaction taking place on the surface of the vessel and packing. Furthermore, the dimerization of "pure" methyl ketene in solution apparently gives the β -diketone-type dimer and trimer.² For these reasons we believe that this apparent exception could well turn out to be consistent with our generalization upon further scrutiny. We thank a referee for reminding us of this observation.

(19) A. D. Jenkins, *J. Chem. Soc.*, 2563 (1952).

facilitating β -lactone-type dimerization is illustrated in Figure 1D. Coordination of a ketene oxygen atom with an acid would increase the electrophilicity of the carbonyl carbon atom, and, thus, both favor C-O bond formation and tighten the C-O bond in the transition state for dimerization. The resultant dissymmetry would relieve steric compression, as suggested in the extreme by Figure 1D. Other explanations involving, for example, trigonal adducts of the ketene carbonyl group with triethylamine or its hydrochloride can be imagined, as suggested by Anet²⁰ for the methoxide-induced formation of the β -lactone dimer from diphenylketene.²¹

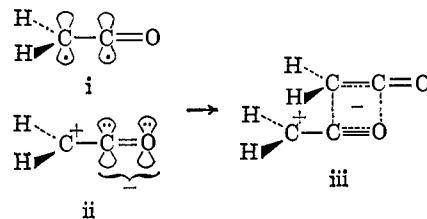
Experimental Section²³

2,4-Diphenyl-3-phenylacetoxycyclobutenone (6). *A. From Triethylamine and Phenylacetyl Chloride.* Triethylamine (30.0 g., 0.297 mole) in anhydrous ether (500 ml.) was added dropwise over 4 hr. to phenylacetyl chloride (50.5 g., 0.32 mole) in refluxing anhydrous ether (500 ml.) with vigorous stirring. The mixture was boiled under reflux a further 1.5 hr. The triethylamine hydrochloride was removed by suction filtration. The bright yellow ether filtrate was concentrated by rotary evaporation and the precipitate was filtered to give a crude white crystalline solid (24.5 g., 65%), m.p. 116.5–117°. Recrystallization from ether raised the melting point to 120–122°.

B. From 2,4-Diphenyl-3-hydroxycyclobutenone (7). The enol **7** (1.0 g., 4.3 mmoles) was dissolved in a little ether. An excess of triethylamine was added, causing the enol salt to precipitate as an oil. The ether and excess amine were removed by decantation, the oil was washed with another portion of ether, and a solution of excess phenylacetyl chloride in ether was added to the oil. The mixture was stirred and heated briefly on the steam bath, then transferred to a separatory funnel. The amine hydrochloride which had formed was removed by two extractions with water. The ether solution was shaken with 10% aqueous sodium

(20) R. Anet, *Chem. Ind. (London)*, 1313 (1961).

(21) These mechanisms assume a reasonably symmetrical transition state for uncatalyzed β -lactone formation from ketene, and, therefore, imply a concerted cyclization. This would seem to violate the Woodward-Hoffmann rules.²² Three possible resolutions of this conflict follow. (1) A six-electron transition state (iii), formally derivable by combination of i and ii, would abide by the rule, although it alleviates



the steric problem which we suggest to be present. (2) The electronegativity of the oxygen and the presence of its extra electron pairs introduces a polar dissymmetry in the transition state. Thus, the Woodward-Hoffmann rules, derived for symmetric carbon-carbon double bonds, need not apply. (3) The cyclization may not be concerted, but may still be subject to steric interference and solvent effects. The last two possibilities apply equally well to the formation of the β -diketone-type dimers.

(22) R. Hoffmann and R. B. Woodward, *J. Am. Chem. Soc.*, **87**, 2046 (1965).

(23) Melting points and boiling points are uncorrected. Analyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, N. Y., and Scandinavian Microanalytical Laboratories, Herlev, Denmark. N.m.r. spectra were determined with a Varian A-60 spectrometer. Infrared analyses were run on a Perkin-Elmer Infracord.

bicarbonate. Upon concentration of the ether solution, fine, white needles were deposited. Filtration and recrystallization from ether afforded the phenylacetyl derivative **6** (1.0 g., 67%), m.p. 121–123°, undepressed upon admixture with the product obtained in part A.

Anal. Calcd. for $C_{24}H_{18}O_3$: C, 81.31; H, 5.12. Found: C, 81.47, 81.37; H, 5.04, 5.21.

The infrared spectrum showed λ_{\max}^{Nujol} 5.60, 5.70, and 6.08 μ .

Although the substance was insoluble in sodium bicarbonate, it dissolved slowly in aqueous sodium hydroxide with hydrolysis. Thus, trimer **6** (1.0 g., 2.8 mmoles) was heated for 1 hr. on a steam bath with 10% aqueous sodium hydroxide (100 ml.). The mixture was cooled and washed with ether. The alkaline solution was acidified with concentrated hydrochloric acid. The white precipitate was removed by filtration and dried to give white crystals (0.41 g., 62%), m.p. 146–147°, identified as the enol (**7**)^{2,7} by a mixture melting point determination. The acidic filtrate was extracted three times with a total of 125 ml. of ether. The combined ether extracts were dried over magnesium sulfate, filtered, and evaporated to dryness. Crystals of phenylacetic acid (0.27 g., 79%), m.p. 76.5°, identified by a mixture melting point with an authentic sample, remained.

Reaction of the trimer **6** (5.93 g., 0.017 mole) in anhydrous ether (350 ml.) with triethylamine (2.5 ml., 0.018 mole) slowly afforded a finely divided, white precipitate. Additional triethylamine (15 ml., 0.106 mole) was added. After 1 hr., precipitation had practically ceased and the white solid was removed by filtration and dried in a vacuum desiccator to a constant weight of 3.34 g.

The solid was dissolved in water, and the solution was decanted from a small amount of greenish oil (0.1 g.) and acidified with concentrated hydrochloric acid. The white precipitate was filtered (2.3 g., 58%), m.p. 147–150° (undepressed upon mixture with an authentic sample of 2,4-diphenyl-3-hydroxycyclobutenone).

The ethereal filtrate was shaken with dilute hydrochloric acid (200 ml.), water (200 ml.), and 5% potassium carbonate (200 ml.). The ether was evaporated on a steam bath and the residual oil was heated and stirred with 5% sodium hydroxide (100 ml.) for 35 min. The alkaline solution was cooled and extracted with ether (200 ml.) in three portions. Acidification of the alkaline solution gave 0.4 g. of impure solid which did not afford any pyrone (*vide infra*) upon attempted crystallization from benzene.

The β -Lactone Dimer (11) of Phenylketene. In a 1-l., three-necked, round-bottomed flask equipped with an efficient condenser, carrying a calcium chloride tube, a motor-driven centrifugal stirrer, and a 50-ml. graduated dropping funnel, was placed granular zinc (60 g., 0.92 g.-atom) and anhydrous ether (300 ml.). Stirring was started, the reaction flask was heated gently on a hot plate, and α -chlorophenylacetyl chloride (70.0 g., 0.37 mole) was added dropwise from the funnel. The reaction proceeded smoothly with the development of the yellow color and turbidity observed by Staudinger. The heating was discontinued at once. That the α -chlorophenylacetyl chloride was taken up quickly was evidenced by a rapid drop in the ether reflux rate which was interrupted momentarily. At the end of the addi-

tion stirring was continued and the solution was refluxed gently over the hot plate for 30 min. At the end of this time, pure dry *n*-pentane (600 ml.) was added quickly, and a light brown oil was precipitated. Stirring was continued for 20 min. and the mixture was allowed to stand for 2 hr.

At the end of 2 hr., the two layers had completely separated and the clear pentane solution was decanted into a 2-l. separatory funnel in which it was shaken successively with 5% hydrochloric acid (500 ml. in two portions), water (200 ml.), 10% sodium carbonate (500 ml. in two portions), and water (500 ml. in two portions). Acidification of the combined sodium carbonate extracts with concentrated hydrochloric acid resulted in the precipitation of the acidic dimer of phenylketene (0.65 g.), m.p. 147–150°. The pentane solution was dried over magnesium sulfate and filtered into a 2-l., round-bottomed flask. The solvent was removed by evaporation under reduced pressure. The product separated as an oil which formed a fine, crystalline mass when the last of the pentane was removed. The neutral dimer of phenylketene did not crystallize from saturated solutions of pentane but separated as an oil. It could be obtained as a white solid, however, by the partial evaporation of such solutions under reduced pressure and was removed by filtration. Two repetitions of this process resulted in a white substance (10.0 g., 23%), m.p. 63–70° (lit.² m.p. 73°).

2,4-Diphenyl-3-hydroxycyclobutenone (7). A. From the β -Lactone Dimer 11 and Sodium Hydroxide. In agreement with Staudinger's observations the action of 5% sodium hydroxide on the neutral dimer of phenylketene resulted in solutions containing the sodium salt of the acidic dimer of phenylketene and a certain amount of undissolved oil. By ether extraction of the alkaline solutions, removal of the remaining ether on the steam bath, and acidification of the alkaline solution with concentrated hydrochloric acid, a white precipitate was obtained which melted at 149–150° without further purification.

B. From the β -Lactone Dimer and Triethylamine. Dimer **11** (1 g.) was dissolved in technical ether, and triethylamine (3 drops) was added. A crystalline precipitate formed immediately, but the addition of 5 more drops of the amine caused further precipitation of an oil. After the mixture had been allowed to stand overnight, the clear ethereal solution was decanted from the precipitate and treated with an excess of triethylamine. Further precipitation occurred and both the ethereal solution and its precipitate yielded 2-hydroxy-3,5-diphenyl-6-benzyl- γ -pyrone (0.3 g.) upon treatment with 5% sodium hydroxide and subsequent acidification. The pyrone melted at 168–168.5° and a mixture melting point with an authentic sample³ showed no lowering. The original precipitate was largely dissolved by water and upon acidification of the solution, the acidic dimer of phenylketene, m.p. 144–145°, was precipitated. The acidic dimer of phenylketene could be prepared free from the pyrone when moisture was rigorously excluded. Thus, triethylamine (10 ml.) in dry ether (60 ml.) was added dropwise over 1 hr. to a solution of the β -lactone (2.0 g.) in dry ether (25 ml.). As each drop was added, precipitation of a white, crystalline solid, m.p. 98–100°, occurred. It was removed by filtration and dissolved in water. Acidifi-

cation of the solution resulted in the precipitation of the acidic dimer: 1.7 g.; 85%; m.p. 147–150°; $\lambda_{\text{max}}^{\text{Nujol}}$ 4.0 (very broad), 5.9 (broad), and 6.5 μ (broad). The ether filtrate was evaporated and the oil remaining was heated with 5% sodium hydroxide. The alkaline solution was freed from undissolved oil by extraction with ether, heated to drive off any residual ether, cooled, and acidified. The dark-colored precipitate which appeared afforded less than 0.1 g. of pyrone (m.p. 167–169°) upon crystallization from benzene.

p-Methoxyphenylacetyl Chloride. Thionyl chloride (19.0 g., 0.16 mole) was added to *p*-methoxyphenylacetic acid (21.0 g., 0.126 mole), maintained at 45–50° in an oil bath. The mixture was heated for 2 hr. to give a yellow oil. The product was fractionated under reduced pressure and *p*-methoxyphenylacetyl chloride (20.49 g., 88%) was collected at 125° (9 mm.).

2,4-Di-*p*-methoxyphenyl-3-*p*-methoxyphenylacetoxy-cyclobutenone (8) and β -Lactone Dimer 12. Triethylamine (9.4 g., 0.093 mole) in anhydrous ether (170 ml.) was added dropwise over a period of 1.75 hr. to *p*-methoxyphenylacetyl chloride (19 g., 0.103 mole) in refluxing anhydrous ether (170 ml.). The reaction mixture was stirred vigorously during the addition and for an additional 45 min. The white precipitate (21.1 g.) was removed by suction filtration. The yellow filtrate was concentrated until heavy white crystals began to coat the inside of the flask. The mixture was chilled in the refrigerator and filtered. The crystalline product was recrystallized from acetone to give a colorless crystalline product 8 (6.1 g., 40%), m.p. 114–114.5°.

The ethereal filtrate on further concentration and long standing deposited additional crystalline material, which, upon recrystallization from acetone afforded a substance (12), m.p. 143–145° (0.75 g., 5%). The material of m.p. 114–114.5° was recrystallized several times from acetone and sent for analysis.

Anal. Calcd. for $\text{C}_{27}\text{H}_{24}\text{O}_6$: C, 72.96; H, 5.44. Found: C, 72.92; H, 5.46.

The infrared spectrum showed $\lambda_{\text{max}}^{\text{Nujol}}$ 5.59, 5.70, and 6.07 μ .

The higher melting material (143–145°) was recrystallized several times from acetone. The melting point was raised to 154–156°.

Anal. Calcd. for $\text{C}_{18}\text{H}_{16}\text{O}_4$: C, 72.96; H, 5.44; mol. wt., 296. Found: C, 72.98; H, 5.47; mol. wt., 240.

The infrared spectrum showed $\lambda_{\text{max}}^{\text{CH}_2\text{Cl}_2}$ 5.40, 5.86, and 6.24 μ .

2,4-Di-*p*-methoxyphenyl-3-hydroxycyclobutenone (9). *A. From the Trimer 8.* The trimer 8 (0.89 g., 2.0 mmoles) was dissolved in a mixture of 20 ml. of ethanol and 20 ml. of water containing sodium hydroxide (1 g.). After 0.5 hr. at 40° the solution was filtered and acidified with concentrated hydrochloric acid. The sparkling white platelets which collected were filtered and recrystallized from acetone. Small, white prisms (0.49 g., 89%), m.p. 152–154°, $\lambda_{\text{max}}^{\text{Nujol}}$ ca. 4 (very broad), 5.85 (broad), 6.19, and 6.5 μ (broad), were thus obtained.

Anal. Calcd. for $\text{C}_{18}\text{H}_{16}\text{O}_4$: C, 72.96; H, 5.44. Found: C, 72.40; H, 5.52.

B. From β -Lactone 12. The β -lactone obtained above (11 mg., 0.037 mmole) was dissolved in a few

milliliters of 10% potassium hydroxide in 1:1 water-dioxane. After 1 hr. at room temperature, the solution was acidified with concentrated hydrochloric acid and diluted with cold water, and the crystalline precipitate was filtered. Colorless crystals of 9 (7 mg., 64%), m.p. 150–152°, were thus obtained. The infrared spectrum of this material was identical with that of the substance obtained from part A.

Treatment of the enol 9 with slightly in excess of 1 equiv. of diazomethane in ether (undistilled, but dried over NaOH pellets) gave a quantitative yield of a colorless crystalline solid, m.p. 122–123°, recrystallized from ether.

Anal. Calcd. for $\text{C}_{19}\text{H}_{18}\text{O}_4$: C, 73.55; H, 5.81. Found: C, 73.87; H, 5.83.

The infrared spectrum showed λ_{max} 5.71, 6.15, and 6.24 μ .

Reaction of β -Lactone 12 with Triethylamine Hydrochloride. Triethylamine hydrochloride (0.456 g., 3.32 mmoles) was added to the β -lactone 12 (0.49 g., 1.66 mmoles) in ether (14 ml.) under a dry nitrogen blanket. The reactants were refluxed on a water bath with vigorous stirring for 4 hr. at 40–45°. Ether (5 ml.) was added after 2 hr. to make up for losses. A white precipitate was separated from the yellow ethereal solution by suction filtration. The infrared spectrum of the precipitate was essentially that of a mixture of β -lactone and triethylamine hydrochloride. The filtrate was concentrated by rotary evaporation and refrigerated overnight. The white precipitate (0.12 g.) which formed in the yellow ethereal solution had an infrared spectrum identical with that of the β -lactone 12.

The triethylamine- β -lactone precipitate was washed six times with boiling ether in an attempt to remove the β -lactone. Only a small amount of this lactone was precipitated in the filtrate even though it was concentrated by rotary evaporation. Boiling water was added to the triethylamine hydrochloride- β -lactone precipitate in an attempt to dissolve the triethylamine hydrochloride and separate it from the β -lactone. The resulting white precipitate (0.17 g.) had an infrared spectrum identical with that of the β -lactone 12.

Reaction of Phenylacetyl Chloride with Excess Triethylamine. 2-Hydroxy-3,5-diphenyl-6-benzyl- γ -pyrone. Phenylacetyl chloride (40.0 g., 0.259 mole) in ether (15 ml.) was added dropwise to a stirred refluxing solution of triethylamine (20.0 g., 0.259 mole) in anhydrous ether (300 ml.). The addition required 30 min. and stirring was continued for an additional 45 min. The reaction mixture was filtered and the white precipitate was washed with two 100-ml. portions of ether. The combined filtrate and washings were evaporated to dryness to afford a honey-colored oil (25.4 g.). The oil was dissolved in a small amount of ether and added to an aqueous solution of 10% sodium hydroxide (1 l.), and the mixture was heated on the steam bath for 2 hr. with stirring. The mixture was cooled in an ice bath and the undissolved dark red oil was extracted into ether (250 ml.) in two portions. During the second extraction, threadlike crystals began to appear in the alkaline solution and soon the entire aqueous layer was a semisolid mass of crystals.

The white, threadlike crystals were removed by filtration and redissolved in distilled water, and the resulting solution was acidified. The white solid which pre-

precipitated (7.5 g., 24%), m.p. 169–170°, crystallized from benzene in the form of fine threads: m.p. 170–171° (lit.³ m.p. 173–174°); neut. equiv.: 354 (calcd.) 358, 349 (found); benzoyl derivative m.p. 124–125° (lit.³ m.p. 126°); monoxime, m.p. 157–158° dec. (lit.³ m.p. 157° dec.).

The alkaline filtrate from the pyrone salt was extracted once again with ether (100 ml.). The residual ether was removed by heating on a steam bath and the solution was cooled and acidified. The granular precipitate was removed by filtration and redissolved in 10% aqueous potassium carbonate (75 ml.). A small amount of undissolved oil was removed by extraction with ether and several grams of additional potassium carbonate was added. More of the pyrone separated as its potassium salt and it was removed and worked up as before to give additional pyrone (0.4 g., total yield 25%).

The alkaline solution was now essentially free from pyrone. It was acidified and the white precipitate was removed by filtration and dried in a vacuum desiccator. The hydroxycyclobutenone **7** (3.5 g.), m.p. 140–145°, thus was obtained.

Reaction of Methylketene Dimer with Triethylamine. The forerun fractions obtained in the distillation of crude methylketene β -lactone dimer, prepared by the procedure of Sauer,⁴ contained triethylamine as well as β -lactone dimer, as evidenced by infrared and n.m.r. analysis. Upon standing for several days, these fractions set up to a viscous yellow involatile polymeric substance.

Hydrolysis of this polymer (20 g.) with concentrated sulfuric acid (50 ml.) was accompanied by solution and carbon dioxide evolution. After 1 week at room temperature the resultant solution was poured over ice and made alkaline by concentrated sodium hydroxide. The alkaline solution was extracted with ether and acidified with hydrochloric acid. After the solution had been allowed to stand overnight, crystals were deposited. One recrystallization from ether afforded 2-hydroxy-3,5-dimethyl-4-ethyl- γ -pyrone, m.p. 148–151° (lit.³ m.p. 151°).

The polymer could also be hydrolyzed with boiling aqueous 10% sodium hydroxide. When the sodium hydroxide solution was acidified, a brown tar was formed which developed crystals upon standing. These crystals could be removed and had a melting point of 145–148°.

Reactions of Propionyl Chloride with Triethylamine.

A. In Ether at 0°. Triethylamine (29.0 g., 0.287 mole) was added dropwise over a period of about 1 hr. with vigorous stirring at 0° to a solution of propionyl chloride (26.5 g., 0.286 mole) in anhydrous ether (75 ml.). The solution was stirred for 2 days while the temperature was permitted to warm up to room temperature. The solid amine hydrochloride precipitate was filtered and washed three times with ether. Most of the ether was removed from the solution and washings by distillation through a Vigreux column at atmospheric pressure. The n.m.r. spectrum of the residual orange oil was determined. There was no evidence for a peak at τ 8.44, later shown to be characteristic of the trimer **3** (R = CH₃). The absorption characteristic of the β -lactone dimer was present (see

D). Integration through the region τ 8–8.5 indicated a trimer to dimer ratio of less than 0.02.

B. In Ether at Reflux. The procedure above was followed except that the addition of triethylamine was made while the solution was boiling under reflux. Reflux was continued for 7 hr. after completion of the addition. The residual oil obtained after distillation had peaks in its n.m.r. spectrum characteristic of both the β -lactone dimer and the trimer. Integration of the n.m.r. spectrum through the region τ 8–8.5 indicated that the trimer to dimer ratio was 0.06–0.09.

C. In Methylene Chloride at 0°. Essentially the same procedure was used as the above except that methylene chloride was used as solvent and the reaction was conducted at 0°. The reaction mixture was stirred for 2 days at room temperature. Integration of the τ 8–8.5 region in the n.m.r. of the methylene chloride solution of the crude product as before indicated a trimer to dimer ratio of 0.23–0.33.

D. In Methylene Chloride at Reflux. The reaction was carried out as before except that methylene chloride was used as solvent, and the addition was carried out at reflux temperature. The mixture was then boiled under reflux for an additional 6 hr. N.m.r. analysis of the methylene chloride solution of the total product as before revealed a trimer to dimer ratio of 0.38–0.42. The methylene chloride was removed by fractional distillation at atmospheric pressure. The crude residual oil was then fractionally distilled at 4 mm. The material distilling up to 50° was collected as a colorless oil (5.6 g., 37%), $\lambda_{\text{max}}^{\text{N}_{20}}$ 5.56, 5.64, and 6.0 μ . The n.m.r. spectrum showed τ 5.34 (quartet of doublets, $J_1 = 7.0$ c.p.s., $J_2 = 1.5$ c.p.s., area = 1.0), 6.07 (quartet of quintets, area = 1.0), 8.35 (doublet of doublets, $J_1 = 7.0$ c.p.s., $J_2 = 1.5$ c.p.s., area = 3.3), and 8.62 (doublet, $J = 7.8$ c.p.s., area = 3.3). The residue was then molecularly distilled at 60–85° (3mm.). The faintly yellow distillate (1.05 g., 14%) had an infrared spectrum identical with that reported for the trimer **3** (R = CH₃). The n.m.r. spectrum in carbon tetrachloride exhibited a multiplet at τ 6.4, a quartet ($J = 2.5$ c.p.s.) at 8.42, a triplet ($J = 7.5$ c.p.s.) at 8.77, and an overlapping doublet ($J = 6.5$ c.p.s.) centered at 8.84. The integrated area ratios were 1.0:2.0:2.9:5.8.

Preparation of Trimer 3 (R = CH₃) from 2,4-Dimethyl-3-hydroxycyclobutenone and Propionyl Chloride. The enol **2** (R = CH₃; 1.65 g., 14.7 mmoles) was slurried in methylene chloride (25 ml.). The material dissolved upon the addition of triethylamine (1.52 g., 15.0 mmoles) in methylene chloride (10 ml.). Propionyl chloride (1.38 g., 14.9 mmoles) in methylene chloride (10 ml.) was added dropwise over a period of 0.5 hr. The originally colorless solution became very faintly yellow. After 2.25 hr. at room temperature, the methylene chloride was removed by rotary evaporation. The residual oil was filtered free from the precipitated triethylamine hydrochloride and fractionally distilled to give a colorless liquid, b.p. 80–82° (0.55 mm.) (0.85 g., 34%), with an infrared and n.m.r. spectrum identical with that of the trimer obtained above.

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