Novel Condensation Products of Diketene

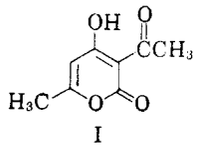
E. MARCUS AND J. K. CHAN

Research and Development Department, Union Carbide Corporation, Chemicals and Plastics, South Charleston, West Virginia

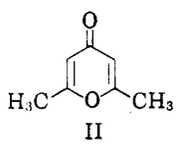
Received March 9, 1967

A study of some self-condensation products of diketene has been undertaken. In addition to dehydroacetic acid (I), we have been able to isolate and identify 3,9-diacetyl-4,5,10-trimethyl-2H,8H-benzo[1,2-*b*:3,4-b']-dipyran-2,8-dione (A), 3,6-diacetyl-4,7-dimethyl-5-hydroxycoumarin (B), and 3,8-diacetyl-4,7-dimethyl-5-hydroxycoumarin (C) as condensation products of diketene. Support for these proposed structures has been obtained by degradations, rearrangements, independent syntheses, and spectral data. A mechanism that rationalizes the formation of A, B, and C is suggested. A newly discovered reaction by which A, B, and C can be made directly from diketene in 26, 13, and 10% yields, respectively, is also reported.

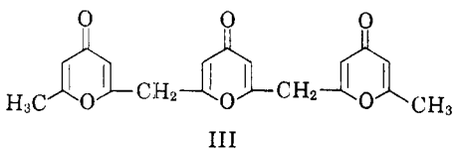
In 1949, Steele, Boese, and Dull[1] reported that, during the preparation of dehydroacetic acid (I) from diketene in the presence of a catalytic amount of sodium phenoxide, two by-products were found in the reactant solution. They described them as 2,6-dimethyl-4H-pyranone (II) and 2,6-bis(6-methyl-4-oxo-2-pyranylmethyl)pyrone (III). The former compound (II),



I



II



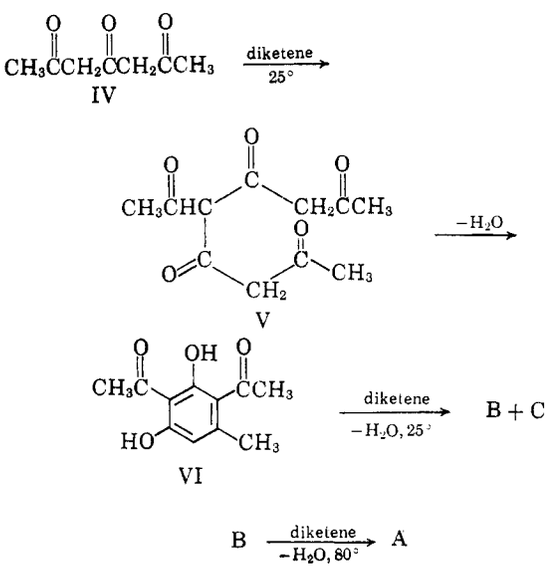
III

mp 130–132°, was formed in 4% yield by dehydration of 2,4,6-heptanetrione (IV); the latter compound (III), mp 235–236°, was obtained in 8% yield. Interest in these compounds has led us to repeat the experiment under the same conditions as reported.[1] The compound believed to be III was then characterized by infrared, nmr, and mass spectroscopy as well as by elemental analyses. While the molecular formula and the melting point of the compound were identical with those reported,[1] the proposed structure (III) was not consistent with our spectral data. The nmr spectrum indicated that the compound had about 15 protons of the allylic methyl and the acetyl type with only one aromatic proton. The spectral data were in good agreement with a compound having structure XXII. This paper presents a study of the formation of this compound and the related precursors obtained from the self-condensations of diketene.

In a recent publication,[2] we reported that diketene would react with water in the presence of a tertiary amine catalyst to give 2,4,6-heptanetrione (IV). Later experiments conducted by us showed that, under mild conditions in the presence of a catalytic amount of a tertiary amine, IV could further react with diketene to give two unknown $C_{15}H_{14}O_5$ isomers (B and C). One of these isomers (B) could be converted under more vigorous conditions into A, which was found by mixture melting point as well as by spectral analyses to be identical with the compound believed to be III as proposed by Steele, Boese, and Dull.[1] Isomer A is also the same compound which we isolated as a by-product from the reaction of diketene with ethyl acetoacetate.[2,3]

According to the results from our experiments, it was postulated that diketene would react with IV to give the unknown intermediate (acetoacetyl)heptanetrione (V) which then could cyclize to form 2,4-diacetylorcinol (VI). Compound VI could in turn react with another mole of diketene to give the two isomers B and C (Scheme I).

SCHEME I



Compound VI itself has not been isolated from the reaction of IV with diketene. However, VI made separately from acetyl chloride and IV[4] could again be converted into the two $C_{15}H_{14}O_5$ isomers B and C. This result supported our view that VI was indeed an intermediate in the formation of compounds A, B, and C.

The reaction of VI with diketene could conceivably produce four different $C_{15}H_{14}O_5$ isomers (VII, VIII, IX, and X) (Scheme II). Attack of diketene at the OH group of VI in the 1 position might produce VII and IX, while attack at the OH group in 3 position could afford VIII and X.

Most informative were isomerization experiments with potassium hydroxide in methanol followed by acidification.[5] When either B or C was treated carefully with 5% methanolic potassium hydroxide solution at 50°, a mixture of B and C in which B predominated

(1) A. B. Steele, A. B. Boese, and M. F. Dull, *J. Org. Chem.*, **14**, 460 (1949).

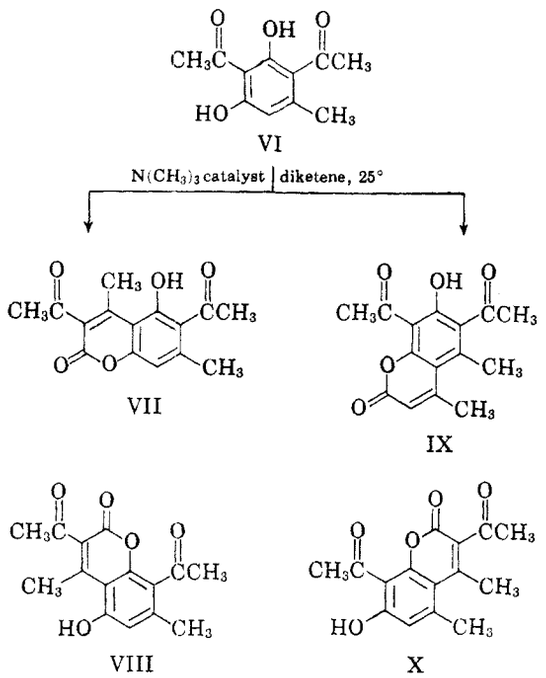
(2) E. Marcus, J. K. Chan, and C. B. Strow, *ibid.*, **31**, 1369 (1966).

(3) In ref 2 we suggested the tentative structure X, which differs slightly from the correct structure XXII proposed in this publication.

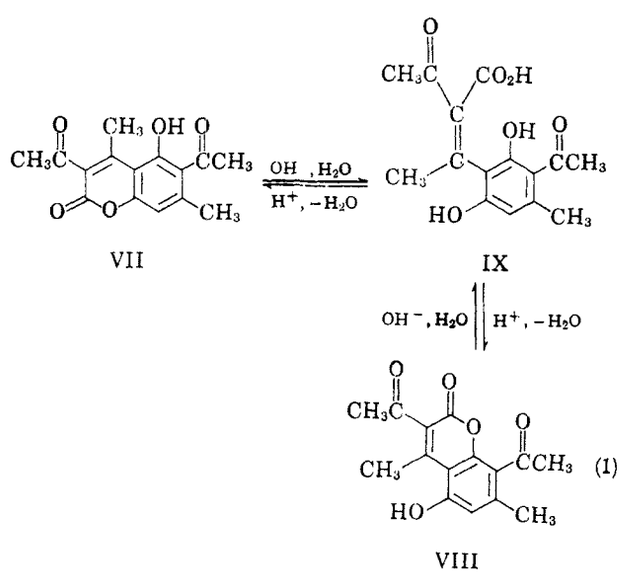
(4) J. N. Collie, *J. Chem. Soc.*, **85**, 971 (1904).

(5) For similar rearrangements, see L. Crombie and D. E. Games, *Tetrahedron Letters*, No. 2, 145 (1966).

SCHEME II



could be obtained after acidification. Of the compounds having the four possible structures (VII, VIII, IX, and X), only VII and VIII are interconvertible *via* XI in this fashion assuming an initial opening of the lactone ring under basic conditions (eq 1).



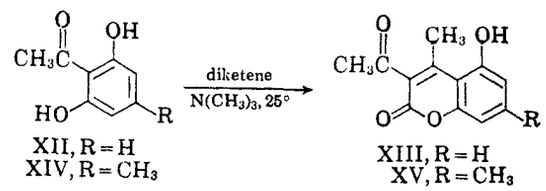
The infrared spectrum of B in KBr exhibited a broad weak band between 3.7 and 4.4 μ indicating a chelated hydroxyl group. Isomer C in KBr absorbed strongly at 3.1 μ; a very dilute solution of C in deuterated chloroform absorbed at 2.81 μ, which suggested the absence of intramolecular hydrogen bonding. Therefore, B and C should be described by VII and VIII, respectively.

In order to obtain further confirmation and comparison of spectral properties, the analog XIII and XV

(6) A. Russell and J. R. Frye, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 281.

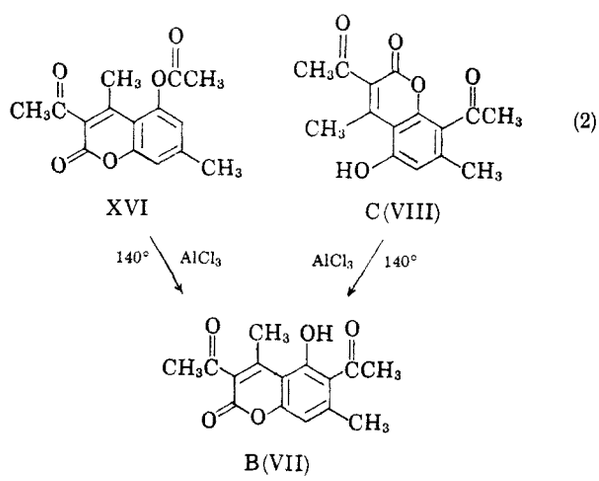
(7) P. R. Saraiya and R. C. Shah, *Proc. Indian Acad. Sci.*, **31**, 213 (1950); *Chem. Abstr.*, **46**, 5013 (1952).

SCHEME III



were synthesized by the method given in Scheme III (see ref 6 and 7 for syntheses of compounds XII and XIV). Both XIII and XV in KBr also absorbed strongly at 3.1 μ; their dilute solutions in deuterated chloroform exhibited the free OH band in the 2.8-μ region. The other essential features of their infrared as well as their nmr spectra were also very similar to those of compound C.

Compound XV could be converted easily with acetic anhydride into its acetate XVI, which by a Fries reaction afforded B. Compound B was also produced by a Fries rearrangement of C (eq 2). In general, high

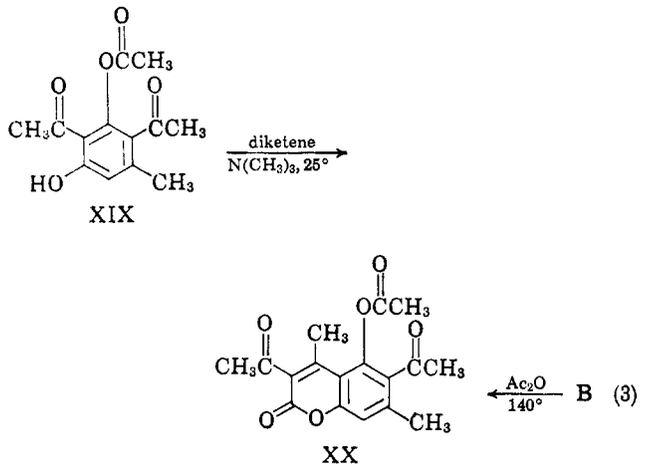


temperatures in these Fries reactions favor the formation of the thermodynamically more stable *o*-acetylphenols; *e.g.*, treatment with aluminum chloride at 170° converted 4-acetyl-3-methylphenol to 2-acetyl-5-methylphenol.[8]

Further information was obtained from an only partially successful attempt to make the two monoacetates of 2,4-diacetylorcinol (VI) and converting them with diketene to the acetates of B and C. A comparison of the acetates made in this fashion with the acetates made from B and C should answer the question whether B and C are formed by attack of diketene at the same or different OH groups of VI. So far only one monoacetate (XVII), mp 138–140°, could be made which upon reaction with diketene gave an ester that was identical with the acetate (XVIII) made from C (Scheme IV). It is reasonable to assume that esterification by 1 mole of acetic anhydride would occur at the less hindered OH group of VI. This result is, of course, in agreement with all the other data.

The other monoacetate (XIX) of VI should give rise to an ester XX upon reaction with diketene which ought to be identical with the acetate made from B (eq 3). However, all of our attemps to obtain XIX by

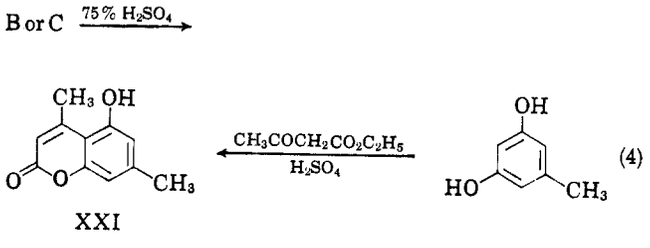
(8) K. W. Rosenmund and W. Schnurr, *Ann.*, **460**, 56 (1928).



partial esterification of VI or by partial hydrolysis of the diacetate of VI have been unsuccessful. This diacetate, mp 72–74°, was made from VI and acetic anhydride in the presence of pyridine. Collie[9] reported that a monoacetate of VI, mp 75°, was formed when VI was heated with acetic anhydride. However, we could isolate only a monoacetate (XVII) of a much higher melting point, 138–140°, and a diacetate, mp 72–74°.

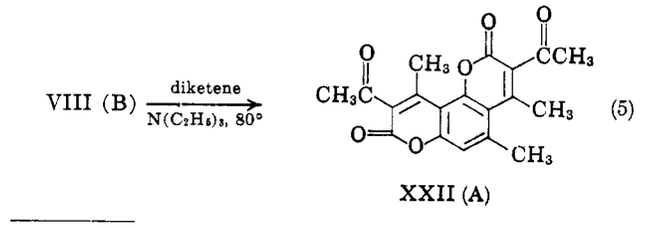
Degradation of B as well as C with boiling aqueous sodium hydroxide solution gave 2′,6′-dihydroxy-4′-methylacetophenone (XIV). This result can be rationalized by assuming an initial opening of the lactone ring giving XI followed by a reverse aldol condensation leading to VI. The further conversion of VI into XIV has been described previously[7] and also in this paper.

Degradation in 75% sulfuric acid also furnished interesting results. This reagent has been used to effect deacylations of somewhat related systems.[10] Both B and C afforded a product that was identical with the hydroxycoumarin (XXI) made from orcinol and ethyl acetoacetate by the Pechmann reaction[11] (eq 4). Double deacylation of VII and VIII leading



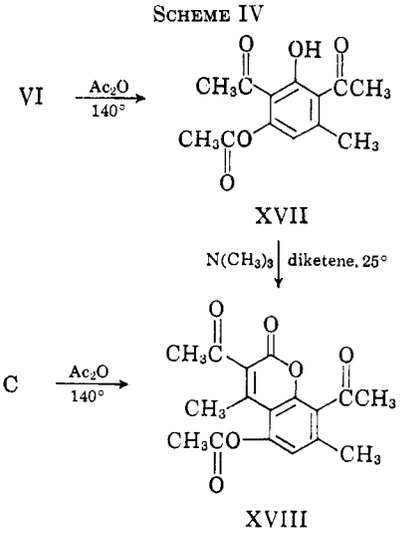
to XXI is, of course, again consistent with the assigned structures for B and C.

As stated previously, B was found to be the precursor of A. Therefore, further reaction of B, identified as VII, with diketene should lead to the dilactone XXII (eq 5).



(9) J. N. Collie, *J. Chem. Soc.*, **85**, 978 (1904).

SCHEME IV



The nmr spectrum of A showed the presence of 15 protons between 2.54 and 2.80 ppm (five acetyl and allylic methyl groups) and one aromatic proton at 7.12 ppm.

The mass spectra of A, B, and C taken with a time-of-flight mass spectrometer are noteworthy. In the case of B, the most abundant ion was the mass 43 acetyl ion followed closely by the molecular ion (mass 274). The next most prominent ions were formed by the loss of an acetyl group (parent minus 43), the loss of a methyl group (parent minus 15), and the loss of a combination of an acetyl and a methyl group followed by the addition of a hydrogen (parent minus 57). The mass spectrum of C was very similar to that of B. In the case of the dilactone A, the most abundant ion was again the acetyl ion. The loss of an acetyl group and a carbonyl group gave the second most abundant ion (parent minus 71). The third most intense peak in the spectrum was caused by the molecular ion (mass 340). The fourth largest peak represented the parent molecule minus a methyl group and the fifth peak corresponded to the parent minus an acetyl group.

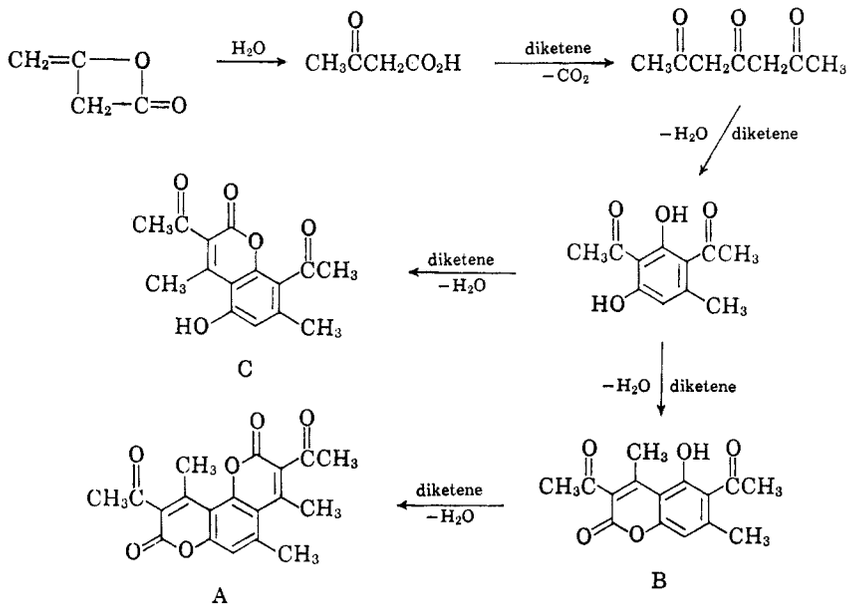
Small amounts of B and C could also be isolated as by-products when dehydroacetic acid (I) was made by dimerization of diketene at 25° in toluene using trimethylamine as catalyst. After the major product (I) had been removed by filtration, a more insoluble product gradually precipitated from the mother liquor. Recrystallization of this second crop afforded the two hydroxycoumarins B and C as by-products. When the dimerization was carried out at higher temperatures, the dilactone A could also be isolated as an impurity. Furthermore, increasing amounts of A, B, and C were formed with larger catalyst concentrations. For this reason we have investigated the reaction of diketene in triethylamine in the absence of an inert solvent. The major product was now compound A (26% yield); besides, isomers B and C were formed in yields varying from 7 to 15% each.

On an over-all basis, the self-condensation products A, B, and C are made from diketene according to

(10) C. Djerassi, E. J. Eisenbraun, R. A. Finnegan, and B. Gilbert, *J. Org. Chem.*, **25**, 2164 (1960); R. A. Finnegan, M. P. Morris, and C. Djerassi, *ibid.*, **26**, 1180 (1961).

(11) For references, see S. Sethna and R. Phadke, *Org. Reactions*, **7**, 35 (1953).

SCHEME V



eq 6 and 7, but, in detail, Scheme V rationalizes the formation of these products.

$$\text{B and C: } 4C_4H_4O_2 \longrightarrow C_{15}H_{14}O_5 + CO_2 + H_2O \quad (6)$$

$$\text{A: } 5C_4H_4O_2 \longrightarrow C_{19}H_{16}O_6 + CO_2 + 2H_2O \quad (7)$$

According to this proposed mechanism, the presence of some water is necessary initially to form acetoacetic acid from diketene, then B and C and finally A. However, on the basis of the over-all mechanism, the sequence of reactions generates water, which helps to propagate the reaction.

Experimental Section

All melting points are uncorrected. The nmr spectra were obtained from a Varian A-60 spectrometer with tetramethylsilane as an internal standard. The infrared spectra (KBr pellet) were taken on Baird-Atomic Models 4-55 and AB-2 and Perkin-Elmer Model 21. The high-dilution infrared spectra for the determination of free OH were taken on a Beckman DK-2 spectrophotometer. The solvent (CCl_4) used commonly for the determination of free OH was not suitable because of the extreme insolubility of the compounds of interest; the $CHCl_3$ available contained undesirable impurities, but $CDCl_3$ gave satisfactory results. The mass spectrometer employed was a Bendix time-of-flight Model 12. Microanalyses were performed by Union Carbide European Research Associates, Brussels, Belgium.

Apparatus.—The polymerizations of diketene were carried out in a four-necked flask equipped with a stirrer, dropping funnel, thermometer, and condenser; the condenser was connected to a gas trap for detection of carbon dioxide.

Polymerization of Diketene at 25° Using Trimethylamine as Catalyst. Compounds I, B, and C.—A solution of diketene (1000 g) in acetone (1000 g) was added to a stirred mixture of toluene (1000 ml) and 150 ml of a solution containing 5% by weight of trimethylamine in toluene. The addition required 2 hr and the temperature was maintained at 15–24°. After the addition, the mixture was stirred for 1 hr longer, cooled to −8°, and then filtered. The solid collected was immediately washed with chilled toluene (1700 ml). The wash was allowed to stand at 25° for several hours. The washed product (I) weighed 683 g (68%), mp 108.5–110°. The solid which had precipitated from the toluene wash on standing was separated by filtration and weighed 4 g, mp 252–256°. This solid was found to be impure C.

The original mother liquor was evaporated *in vacuo*. The residue product was extracted twice with acetone. The insoluble material amounted to 11 g, mp 249–252°. Recrystallization from methanol gave a fluffy white solid, mp 262–264°. The total yield of C was 1.8%. The nmr spectrum of C in deuterated acetone exhibited a slightly broadened singlet at 2.23 (3 H, 7-methyl group), sharp singlets at 2.45, 2.53, 2.55 (9 H, methyl and acetyl groups), and a broad singlet at 6.72 ppm (1 H at C-6). The expected broad peak corresponding to the hydroxyl group of this very insoluble compound could not be seen, probably because of exchange with the solvent. The infrared spectrum (KBr pellet) showed very strong absorption at 3.08 (OH), 5.92 (C=O, conjugated lactone), and 6.01 μ (C=O, conjugated acetyl); it also contained peaks at 6.18, 6.30, 6.66, 6.93, 7.33, 7.95, 8.38, 8.95, 9.11, 11.65, 12.71, and 13.04 μ. A 5.83×10^{-4} M solution in $CDCl_3$ showed the presence of free OH at 2.810 μ, ϵ_{max} 116.5. For comparison, the extinction coefficient of the free OH band of 1-naphthol was determined in $CDCl_3$; a 4.81×10^{-3} M solution had ϵ_{max} 115 at 2.792 μ. For further comparison, see also ϵ_{max} of free OH of XV.

Anal. Calcd for $C_{15}H_{14}O_5$ (C): C, 65.69; H, 5.15; mol wt, 274.3. Found: C, 65.84; H, 5.41; mol wt (largest parent peak by mass spectroscopy), 274.

In a similar but smaller run using 3.2 moles of diketene, after the mother liquor was evaporated to dryness and the residue extracted with acetone, the insoluble material was boiled with 50 ml of chloroform and filtered hot. The solid (0.8 g) filtered off was found to be C, mp 250–258°. Concentration of the chloroform filtrate gave a small amount of a pale yellow solid, mp 180–185°. It was identified as impure B by spectral methods as well as by mixture melting with a pure sample of B obtained by the reaction of diketene in triethylamine.

Polymerization of Diketene at 80° Using Sodium Phenoxide as Catalyst. Compounds I and A.—The procedure used in this experiment was the same as that reported by Steele, Boese, and Dull.[1] From a mixture of diketene (135 g), sodium phenoxide (0.15 g), and benzene (150 ml), 74 g of dehydroacetic acid (I) and 2 g of impure A were obtained. The latter compound, upon recrystallization from glacial acetic acid, gave a white solid, mp 234–236° (lit.[1] mp 235–236°).

The nmr spectrum of A in $CDCl_3$ showed sharp singlets at 2.54 (3 H), 2.57 (6 H), and 2.74 (3 H), a slightly broadened singlet at 2.80 (3 H) for methyl and acetyl groups, and a broad singlet at 7.12 ppm (1 H, aromatic). The infrared spectrum (KBr pellet) showed very strong absorption at 5.83 and 5.88 μ (C=O); it also contained peaks at 6.19, 6.24, 6.38, 6.97, 7.08, 7.21, 7.40, 8.12, 8.90, 9.58, 10.47, 11.30, 12.70, and 13.10 μ.

Polymerization of Diketene in Triethylamine in the Absence of an Inert Solvent. Compounds A, B, and C.—Diketene (84 g, 1.0 mole) was added dropwise into triethylamine (101 g, 1.0 mole) at 25–30°. The reaction was exothermic and a large volume of carbon dioxide was given off. After the addition was complete, the mixture was kept at room temperature for 1 hr and then at 40–45° for 1.5 hr until carbon dioxide stopped evolving. The lower layer of the reaction mixture was separated and diluted with methanol (180 ml). The compound which precipitated was filtered and washed with more methanol to give

18 g (26%), mp 228–230°. Recrystallization from chloroform gave a white solid, mp 235–236°. This was identified by spectral and elemental analyses as well as by mixture melting point to be the same as compound A obtained from the previous experiment.

Anal. Calcd for $C_{19}H_{16}O_6$ (A): C, 67.05; H, 4.75; mol wt, 340.3. Found: C, 66.91; H, 4.80; mol wt (largest parent peak by mass spectroscopy), 340.

The upper layer of the reaction mixture was combined with the methanol filtrate and the methanol wash. The mixture was evaporated under reduced pressure, leaving a brown syrupy residue (53 g). The residue was slurried with chloroform (100 ml) and the mixture was allowed to stand for 1 hr at 25°. Upon filtration, 9.2 g of a pale yellow solid (B) was obtained, mp 194–197° (13%). Recrystallization from hot chloroform afforded pure B, mp 199–201°. The nmr spectrum of B in $CDCl_3$ showed a slightly broadened singlet at 2.66 (3 H, 7-methyl group), sharp singlets at 2.52, 2.60, 2.70 (9 H, methyl and acetyl groups), a broad singlet at 6.62 (1 H, aromatic), and a sharp singlet at 14.74 ppm (1 H, chelated hydroxyl group). The infrared spectrum (KBr pellet) showed broad weak absorption at 3.7–4.4 (OH, chelated), strong absorption at 5.83 and 5.93 (C=O, conjugated lactone and conjugated acetyl), and 6.23 μ (C=O, chelated); it also contained peaks at 6.45, 6.72, 7.05, 7.21, 7.62, 7.91, 8.19, 8.46, 8.95, 9.24, 9.61, 9.70, 10.43, 11.39, 12.62, 12.94, and 14.07 μ.

Anal. Calcd for $C_{15}H_{14}O_5$ (B): C, 65.69; H, 5.15; mol wt, 274.3. Found: C, 65.41; H, 5.21; mol wt (largest parent peak by mass spectroscopy), 274.

After separation of B by filtration, the filtrate was evaporated again *in vacuo*. The residue obtained was diluted with about 100 ml of methanol. On standing, the mixture precipitated 7.0 g (10%) of C which was removed by filtration: mp 245–255°. A mixture melting point with a pure sample of C obtained as a by-product in the preparation of I showed no depression.

Compounds B and C. From Reaction of Diketene with 2,4,6-Heptanetrione (IV).—Diketene (8.4 g) was added dropwise over a period of 1.5 hr at 25° to a stirred mixture of IV (7.1 g), toluene (30 ml), and a solution of 4% trimethylamine in toluene (8 ml). After the addition, the reaction mixture was stirred for another 4 hr. It was then cooled to 5° and filtered to give 2.5 g of a solid, mp 170–177°. The solid was suspended in 50 ml of methanol and the mixture heated to boiling and filtered hot. The insoluble material amounted to 1.5 g (11%), mp 197–199.5°. This solid was identified as B by mixture melting with a pure sample of B obtained by the reaction of diketene in triethylamine. The methanol filtrate, on cooling, gave 0.5 g of impure C, mp 250–255°. A mixed melting point with a pure sample of C obtained as by-product in the preparation of I showed no depression. Concentration of the methanol filtrate afforded additional 0.4 g of C of poorer quality, mp 235–245°. The total yield of C was 6%.

2,4-Diacetylorcinol (VI).—The procedure for the preparation of VI from IV was the same as that reported by Collie.[4] The nmr spectrum of VI in $CDCl_3$ showed a slightly broadened singlet at 2.55 (3 H, 5-methyl group), sharp singlets at 2.62 and 2.72 (6 H, acetyl groups), a singlet at 6.27 (1 H, aromatic), and sharp singlets at 14.04 and 15.55 ppm (2 H, chelated OH groups). The infrared spectrum (KBr pellet) showed broad weak absorption at 3.60–3.95 and 4.10–4.40 (OH, chelated), strong absorption at 6.14 and 6.27 μ (C=O, conjugated acetyl); it also contained peaks at 6.87, 6.98, 7.30, 7.52, 7.70, 7.86, 8.36, 10.16, 11.03 and 11.79 μ.

Compounds B and C. From the Reaction of VI and Diketene.—Diketene (0.55 g) was added dropwise over a 25-min period at 25° to a stirred mixture of VI (1.0 g), toluene (15 ml), and a solution of 4% trimethylamine in toluene (0.3 g). After stirring for 3 hr, the reaction mixture was filtered to give 0.7 g of a solid, mp 180–230°. This was extracted with boiling chloroform (20 ml) to give 0.07 g (5.3%) of B, mp 197–199°. A mixture melting point with a pure sample of B obtained by the reaction of diketene in triethylamine showed no depression. Concentration of the chloroform gave some additional amount of B. The insoluble solid after chloroform extraction was found to be C by mixture melting point with pure C isolated as a by-product in the preparation of I. The yield was 0.1 g (7.6%), mp 258–260°. Compound I was found in the original toluene mother liquor.

Isomerization of B and C with 5% Methanolic Potassium Hydroxide. A.—A mixture of C (0.4 g) and 4.4 g of a 5% methanolic potassium hydroxide solution was stirred at 50° for about 15 min until all solid dissolved. The yellow solution was then cooled and acidified with dilute hydrochloric acid. The precipitate was filtered, washed with water, and dried to give 0.35 g, mp 187–220°. The crude product was then suspended in 15 ml of chloroform, heated to boiling, and filtered hot; the insoluble solid obtained was found to be C (0.1 g), mp 258–261°. Evaporation of the filtrate gave 0.25 g of B, mp 191–194°; this solid was identified as B by its infrared spectrum and by mixture melting point with a pure sample of B obtained from the reaction of diketene in triethylamine.

B.—Under similar conditions a pure sample of B (0.4 g) was treated with 4.5 g of a 5% methanolic potassium hydroxide solution giving 0.37 g of a crude solid, which upon extraction with boiling chloroform (20 ml) gave 0.1 g of C, mp 255–258°, and 0.27 g of B, mp 191–194°. Compound C isolated was identified by its infrared spectrum and by mixture melting point with a pure sample of C obtained as a by-product in the preparation of I.

2′,6′-Dihydroxyacetophenone (XII).—Compound XII was prepared according to a procedure described by Russell and Frye.[6] A Pechmann reaction of resorcinol with ethyl acetoacetate in sulfuric acid afforded 4-methyl-7-hydroxycoumarin. The coumarin was esterified with acetic anhydride followed by a Fries rearrangement with aluminum chloride and a degradation with aqueous sodium hydroxide to give XII, mp 153–156° (lit.[6] 154–155°).

3-Acetyl-5-hydroxy-4-methylcoumarin (XIII).—A mixture of XII (2.0 g), toluene (15 ml), and a 4% solution of trimethylamine in toluene (1.0 g) was stirred while diketene (1.4 g) was added at 25° over a 15-min period. After the addition, the mixture was stirred for 10 hr longer. It was then cooled to −10° and filtered to give 1.7 g, mp 181–202°. Recrystallization from a large volume of toluene afforded 1.2 g (44%) of XIII, mp 205–208°.

The nmr spectrum of XIII in deuterated acetone exhibited sharp singlets at 2.49 and 2.60 (6 H, 4-methyl and 3-acetyl group), two doublets (J = 8 cps each) split again into doublets ($J \approx 2$ cps each) centered at 6.87 (2 H in 6 and 8 position), one skewed triplet (J = 8 cps) centered at 7.48 (1 H at C-7), and one broad singlet at 9.67 ppm (1 H, OH group). The infrared spectrum (KBr pellet) showed very strong absorption at 3.04 (OH), 5.88 (C=O, conjugated lactone), and 6.01 μ (C=O, conjugated acetyl); it also contained peaks at 6.32, 6.65, 6.81, 6.95, 7.32, 7.70, 8.24, 9.02, 9.11, 9.77, 12.50, and 13.45 μ. A very dilute solution in $CDCl_3$ showed the presence of free OH qualitatively at 2.795 μ.

Anal. Calcd for $C_{12}H_{10}O_4$ (XIII): C, 66.05; H, 4.62. Found: C, 66.36; H, 4.75.

2′,6′-Dihydroxy-4′-methylacetophenone (XIV). From VI by Deacylation.—A mixture of VI (5 g) and sodium hydroxide (5 g) in 50 ml of water was refluxed gently for 5 hr under a nitrogen atmosphere. After reflux and cooling to −10° the mixture was acidified with dilute hydrochloric acid to pH 2. The solid formed was filtered and washed with a little water. Recrystallization from hot water gave 2.6 g (65%) of XIV, mp 143–145° (lit.[7] mp 146°).

The nmr spectrum of XIV in $CDCl_3$ showed a slightly broadened singlet at 2.24 (3 H, methyl group), a sharp singlet at 2.73 (3 H, acetyl group), a slightly broadened singlet at 6.29 (2 H, aromatic), and a broad singlet at 9.63 ppm (2 H, hydroxyl groups). When the spectrum was taken in deuterated acetone, the result was similar except that the hydroxyl protons gave rise to a sharp singlet at 11.30 ppm. The infrared spectrum (KBr pellet) showed weak absorption at 3.30–4.00 (OH, chelated) and strong absorption at 3.06 (OH), 6.10, and 6.31 μ (C=C, also C=O, chelated); it also contained peaks at 6.93, 7.21, 7.35, 7.80, 8.00, 8.29, 9.24, 9.37, 9.70, 10.46, 12.10, 12.67, 13.40, and 14.21 μ.

3-Acetyl-4,7-dimethyl-5-hydroxycoumarin (XV).—Diketene (0.7 g) in 7 ml of toluene was added to a stirred mixture of XIV (1.0 g), toluene (20 ml), and a solution of 4% trimethylamine in toluene (2 g). The addition required 20 min at 25°. After the addition, the mixture was stirred for 3.5 hr longer. It was then cooled to 0° and filtered. The solid obtained was recrystallized from methanol to give 1.0 g (71%) of XV, mp 204–206°.

The nmr spectrum of XV in deuterated acetone showed one slightly broadened singlet at 2.31 (3 H, 7-methyl group), two sharp singlets at 2.46 and 2.54 (6 H, 7-methyl and 3-acetyl group), one broad singlet at 6.66 (2 H, aromatic), and one very broad singlet at 9.4 ppm (1 H, hydroxyl). The infrared spectrum (KBr pellet) showed very strong absorption at 3.12 (OH), 5.88 (C=O, conjugated lactone), and 5.99 μ (C=O, conjugated

acetyl); it also showed peaks at 6.15, 6.25, 6.42, 6.60, 7.00, 7.36, 7.76, 8.40, 9.01, 9.19, 9.60, 11.97, and 13.33 μ. A 5.17×10^{-4} M solution in $CDCl_3$ showed the presence of free OH at 2.805 μ, ϵ_{max} 118.

Anal. Calcd for $C_{13}H_{12}O_4$ (XV): C, 67.23; H, 5.21. Found: C, 67.50; H, 5.30.

3-Acetyl-4,7-dimethyl-5-acetoxycoumarin (XVI).—A mixture of XV (1.0 g) and acetic anhydride (10 ml) was refluxed at 145° for 45 min. After cooling to about 100° the mixture was poured into an ice–water mixture. The solid was filtered, washed with a little water, and dried. Recrystallization from ethanol gave 1.0 g (85%) of XVI, mp 190–191°.

The nmr spectrum of XVI in $CDCl_3$ showed sharp singlets at 2.36 (3 H), 2.44 (6 H), and 2.53 (3 H) for methyl, acetyl, and acetoxy groups, and broad singlets at 6.88 and 7.10 ppm (2 H, aromatic). The infrared spectrum (KBr pellet) showed strong absorption at 5.66 (C=O, aryl acetate), 5.88 (C=O, conjugated acetyl and lactone), and 8.35 μ (C–O, ester); it also contained peaks at 6.14, 6.24, 6.42, 6.91, 6.96, 7.24, 7.38, 7.95, 9.05, 9.26, 9.66, and 11.34 μ.

Anal. Calcd for $C_{15}H_{14}O_5$ (XVI): C, 65.96; H, 5.15. Found: C, 65.96; H, 5.03.

Rearrangement of XVI to B with Aluminum Chloride.—A mixture of XVI (1.0 g) and aluminum chloride (4.0 g) was shaken in a round-bottomed flask with stopcock closed. A condenser was then attached to the flask and the mixture was heated to 125–140° rapidly and finally kept at 140° for 2 hr. After cooling the mixture was hydrolyzed in an ice–water mixture. The yellow solid formed was filtered, washed with water, and dried. The product was then recrystallized from chloroform to give 0.4 g (40%) of B, mp 198–200°. The compound was identified by its spectrum and by mixture melting point with a sample of B obtained by the reaction of diketene in triethylamine.

Rearrangement of C to B with Aluminum Chloride.—A mixture of C (0.5 g) and aluminum chloride (2.0 g) was shaken well and heated to 125° rapidly. The mixture was finally kept at 130–140° for 2 hr. After hydrolysis in an ice–water mixture, the yellow solid was filtered off and dried. The crude solid was recrystallized from chloroform giving 0.2 g of B as first crop, mp 197–199°. Concentration of chloroform afforded additional 0.2 g of product, mp 193–196°. The combined yield was 80%. The product was identified as B by its spectra and by mixture melting point with a sample of B obtained by the reaction of diketene in triethylamine.

2,4-Diacetyl-3-hydroxy-5-methylphenyl Acetate (XVII).—A mixture of 2,4-diacetylorcinol (VI) (1.0 g) and acetic anhydride (3.0 g) was refluxed at 145–150° for 45 min. After cooling, the mixture was poured into an ice–water mixture with vigorous stirring. Filtration of the precipitate yielded 1.2 g, mp 125–132°. Recrystallization from ethanol afforded 0.8 g (67%) of XVII, mp 138–140°.

The nmr spectrum of XVII in $CDCl_3$ exhibited sharp singlets at 2.30, 2.37, 2.55, and 2.62 (12 H, methyl, acetyl, and acetoxy groups), a slightly broadened singlet at 6.53 (1 H, aromatic), and a sharp singlet at 13.31 ppm (1 H, chelated hydroxyl group). The infrared (KBr pellet) showed broad weak absorption at 3.30–4.40 (OH, chelated) and strong absorption at 5.66 (C=O, aryl acetate), 5.94 (C=O, conjugated), 6.16 (C=O, chelated), 8.34, and 8.53 μ (C—O, ester); it also contained peaks at 6.36, 6.81, 6.91, 7.16, 7.29, 7.36, 7.72, 8.03, 9.11, 9.27, 11.24, 11.91, and 13.72 μ.

Anal. Calcd for $C_{13}H_{14}O_5$ (XVII): C, 62.39; H, 5.64. Found: C, 62.60; H, 5.72.

3,8-Diacetyl-4,7-dimethyl-5-acetoxycoumarin (XVIII). From XVII and Diketene.—A mixture of XVII (1.5 g), triethylamine (0.3 g), and benzene (23 ml) was refluxed at 80°, while diketene (4.5 g) was added over a period of 20 min. Refluxing was continued for another 4–5 hr. After cooling, part of the benzene was evaporated under reduced pressure to give 1.1 g of solid, which upon recrystallization from methanol gave 0.5 g (26%) of XVIII, mp 175–179°. The product was identified by its spectra and by mixture melting point with a sample of XVIII from the reaction of C with acetic anhydride from the following experiment. The only by-product that could be isolated was dehydroacetic acid (I).

Compound XVIII. From C and Acetic Anhydride.—A mixture of C (1.5 g) and acetic anhydride (5 g) was refluxed at 140–145° for 45 min. After cooling to about 100° the mixture was poured into an ice–water mixture. The solid was filtered and washed with water. Recrystallization from ethanol gave 1.3 g (75%) of XVIII, mp 178–180°.

The nmr spectrum of XVIII in $CDCl_3$ exhibited sharp singlets at 2.35, 2.37, 2.44, 2.53, and 2.63 (15 H, methyl, acetyl, and acetoxy groups), and a slightly broadened singlet at 6.92 ppm (1 H, aromatic). The infrared spectrum (KBr pellet) showed strong absorption at 5.70 (C=O, aryl acetate), 5.85 (C=O, conjugated acetyl and lactone), 8.30, and 8.35 μ (C—O, ester); it also contained peaks at 6.18, 6.25, 6.72, 6.87, 7.03, 7.34, 7.52, 7.90, 9.03, 9.19, 10.55, and 10.96 μ.

Anal. Calcd for $C_{17}H_{16}O_6$ (XVIII): C, 64.55; H, 5.10. Found: C, 64.27; H, 5.17.

3,6-Diacetyl-4,7-dimethyl-5-acetoxycoumarin (XX). From B and Acetic Anhydride.—The procedure used for this preparation was similar to the preparation of XVIII as described in the previous experiment. The desired product (XX) was obtained in 40% yield after recrystallization from ethanol, mp 131.5–133.5°.

The nmr spectrum of XX in $CDCl_3$ showed sharp singlets at 2.31 (3 H), 2.42 (6 H), 2.50 (3 H), and 2.53 (3 H) for methyl, acetyl, and acetoxy groups, and a slightly broadened singlet at 7.20 ppm (1 H, aromatic). The infrared spectrum (KBr pellet) showed strong absorption at 5.66 (C=O, aryl acetate), 5.83 and 5.89 (C=O, conjugated lactone and acetyl), and 8.45 μ (C–O, ester); it also contained peaks at 6.17, 6.43, 6.87, 7.29, 7.34, 7.90, 9.11, 9.21, 9.45, 11.50, and 12.95 μ.

Anal. Calcd for $C_{17}H_{16}O_6$ (XX): C, 64.55; H, 5.10. Found: C, 64.27; H, 5.40.

2,4-Diacetylorcinol Diacetate. From VI and Acetic Anhydride.—A mixture of VI (4.1 g) and toluene (34 ml) was refluxed while pyridine (2 g) was added dropwise over a 10-min period followed by the addition of acetic anhydride (8 g). Refluxing was continued for 3 hr. After cooling to about 80°, the mixture was poured into an ice–water mixture. The oil layer formed was separated and evaporated to give 6.3 g of an oily residue. This residue was diluted with ethanol and cooled to −10° to give 4.2 g (73%) of the desired product, mp 72–74°. Spectral and elemental analyses indicated that this compound was the diacetate of VI.

The nmr spectrum of this compound in $CDCl_3$ exhibited a slightly broadened singlet at 2.28 (3 H, 5-methyl group), sharp singlets at 2.18, 2.25, 2.41, 2.43 (12 H, acetyl and acetoxy), and a slightly broadened singlet at 6.95 ppm (1 H, aromatic). The infrared spectrum (KBr pellet) showed strong absorption at 5.71 (C=O, aryl acetate), 5.87 (C=O, conjugated acetyl), 8.29, 8.37, and 8.51 μ (C–O, ester); it also contained peaks at 6.21, 6.41, 7.00, 7.30, 7.38, 7.90, 9.42, 9.58, and 11.15 μ.

Anal. Calcd for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52; mol wt, 292.1. Found: C, 61.85; H, 5.61; mol wt (largest parent peak by mass spectroscopy), 292.

All attempts to make the monoacetate (XIX) by partial hydrolysis of this diacetate failed. Several variations of this attempted partial hydrolysis led only to the isolation of either the completely hydrolyzed VI and/or unchanged diacetate.

Degradation of Compounds B and C with Aqueous Sodium Hydroxide.—A mixture of B (0.5 g) and sodium hydroxide (1 g) dissolved in water (20 ml) was refluxed under nitrogen for 4.5 hr. After the addition of charcoal (1.0 g), the mixture was refluxed for another 30 min. It was then filtered and the filtrate was acidified with hydrochloric acid to give 0.07 g (23%) of crude XIV, mp 138–142°. Recrystallization from boiling water afforded a pure sample of XIV, mp 145–146° (lit.[7] mp 146°). A mixture melting point with XIV made by deacylation of VI showed no depression. Under similar conditions, a mixture of C (0.90 g) and aqueous sodium hydroxide was refluxed and acidified to give 0.25 g of solid, which was also identified as XIV.

4,7-Dimethyl-5-hydroxycoumarin (XXI). From Orcinol and Ethyl Acetoacetate.—Compound XXI was prepared from orcinol and ethyl acetoacetate in sulfuric acid,[11] mp 253–256° (lit.[12] mp 258–259°).

The nmr spectrum of XXI in deuterated acetone showed a slightly broadened singlet at 2.32 (3 H, 7-methyl group), a doublet ($J \approx 1.5$ cps) at 2.62 (3 H, 4-methyl group), a broad singlet at 6.04 (1 H at C-3), and a broad singlet at 6.70 ppm (2 H in 6 and 8 position). The expected broad peak corresponding to the hydroxyl group of this very insoluble compound could not be seen, probably because of exchange with the solvent. The infrared spectrum (KBr pellet) showed strong absorption

(12) R. Adams, C. K. Cain, and S. Loewe, *J. Am. Chem. Soc.*, **63**, 1977 (1941).

at 3.07 (OH) and 5.96 μ (C=O, conjugated lactone); it also contained peaks at 6.16, 6.24, 6.64, 6.92, 7.03, 7.20, 7.31, 7.51, 7.82, 8.71, 9.18, 9.37, 11.01, and 12.00 μ.

Compound XXI. By Deacylation of B and C with 75% Sulfuric Acid.—A solution of B (0.6 g) in 6 ml of 75% aqueous sulfuric acid was kept at 25° for 2 days. The mixture was then poured onto ice. The solid formed was filtered and washed with water. After the solid had been dissolved in a large volume of ether, the solution was dried over magnesium sulfate and filtered. Evaporation of the ether to dryness gave 0.38 g (93%), mp 252–255°. It was identified as XXI by its infrared spectrum and by mixture melting point with a known sample of XXI prepared from orcinol and ethyl acetoacetate.[11]

When C (0.6 g) was treated with 75% sulfuric acid under the same conditions, 0.5 g of a solid melting at 160–180° was obtained. This solid was heated with toluene (30 ml) and filtered hot. The toluene-insoluble material was recrystallized from ethanol to give 0.2 g (49%) of impure XXI, mp 242–253°. A mixture of this compound with an authentic sample of XXI showed mp 247–253°. The compound was also identified by its infrared spectrum.

Conversion of B into Compound A.—A mixture of B (1.5 g), benzene (22 ml), and triethylamine (0.3 g) was refluxed, while diketene (4.5 g) was added dropwise over a 25-min period. After the addition, the mixture was refluxed 4 hr longer and then cooled to room temperature. The insoluble solid was filtered, yielding 2.0 g, mp 227–230°. The crude solid was then suspended in methanol, heated to boiling, and filtered hot. The insoluble solid amounted to 1.90 g, mp 234–236°. A mixture of this compound with a sample of A obtained by the reaction of diketene in triethylamine showed no depression in melting point. It was also identified as A by spectral analyses. Evaporation of the original benzene filtrate gave only 2.6 g of impure I as by-product, mp 102–108°.

When the experiment was repeated under the same conditions in the absence of B, only 0.15 g of A and 2.8 g of impure I could be obtained; therefore, the yield of A obtained from B and diketene was about 1.75 g (94%) based on B. When the same experiment was repeated in the presence of C instead of B, again only traces of A together with impure I and unchanged C were isolated.

Registry No.—I, 520-45-6; VI, 13444-19-4; VI diacetate, 13473-46-6; VII, 13449-09-7; VIII, 13449-10-0; XIII, 13473-47-7; XIV, 1634-34-0; XV, 13444-20-7; XVI, 13449-12-2; XVII, 13449-13-3; XVIII, 13449-14-4; XX, 13444-21-8; XXI, 6335-27-9; XXII, 13444-23-0; diketene, 6144-29-2.

Acknowledgment.—The authors wish to express thanks to Messrs. A. E. Gabany, H. R. Harless, H. L. Joyce, C. M. Lovell, and C. B. Strow of Union Carbide Corp. for interpretations of infrared, nmr, and mass spectral data.

The Structure of the Orange Pigment from *Pseudomonas aureofaciens*[1]

EDWIN S. OLSON AND JOHN H. RICHARDS

Contribution No. 3330 from the Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California 91109

Received March 8, 1967

The orange pigment of *Pseudomonas aureofaciens* has been characterized as 2-hydroxyphenazine-1-carboxylic acid. Three new pigments were also isolated from *Pseudomonas aureofaciens* and spectral properties of two are given.

The major pigment present in cultures of a strain of *Ps. aureofaciens* is the yellow phenazine-1-carboxylic acid.[2,3] In addition to this yellow pigment, Kluyver[2] and Haynes[3] isolated a minute amount of red acidic pigment. Kluyver showed that this second pigment also had a phenazine nucleus and speculated that it was an oxidized form of phenazine-1-carboxylic acid. Toohey, *et al.*,[4] have also isolated this pigment from a strain of *Ps. aureofaciens* and concluded, on the basis of infrared and ultraviolet spectral data and a positive Folin phenol test, that it is probably 2-hydroxyphenazine-1-carboxylic acid. Because of our interest in the biosynthesis of phenazine pigments,[5] we undertook to determine the structure of this second pigment, which is orange when pure, and have shown it to be 2-hydroxyphenazine-1-carboxylic acid (I). Recently, the isolation of 2-hydroxyphenazine from *Ps. aureofaciens* has been reported.[6]

The formula $C_{13}H_8O_3N_2$ inconclusively assigned by Kluyver[2] to the second pigment was found to be consistent with our microanalyses of the pigment and its derivatives. The pK_a of the pigment in 66.8% dioxane water was found[7] to be 7.61, a value which is reasonable for a carboxyl group attached to a phenazine ring system. The ultraviolet spectrum of the pigment in neutral ethanol is similar to that of phenazine-1-carboxylic acid.

Titration of the orange pigment in 66.8% dioxane water gave a neutralization equivalent of about 240; however, the red color did not appear at this end point but rather when almost twice the equivalent amount of base had been added. Hence the phenazine carboxylate anion is not responsible for the red color of the orange pigment in base. Since 1- and 2-phenazinol form red solutions in base, the presence of the hydroxyl group on the phenazine ring system was inferred. This was further confirmed by a positive ceric nitrate and ferric chloride test.

The presence of a carboxyl group is also supported by the strong band in the infrared spectrum at 1676 cm^{-1}. In chloroform the orange pigment shows no sharp OH stretching frequencies above 3000 cm^{-1} from which we assume that hydrogen of the hydroxyl group must be strongly hydrogen bonded to a neighboring carboxyl group. This has been confirmed by an X-ray structure determination of the orange pigment.[8] An intense carbon hydrogen out-of-plane bending absorp-

(1) Supported by Grant No. GM 10218 from the National Institute of General Medical Sciences of the U. S. Public Health Service.

(2) A. J. Kluyver, *J. Bacteriol.*, **72**, 406 (1956).

(3) W. C. Haynes, F. H. Stodola, J. M. Locke, T. G. Pridham, H. F. Conway, V. E. Sohns, and R. W. Jackson, *ibid.*, **72**, 412 (1956).

(4) J. I. Toohey, C. D. Nelson, and G. Krotkov, *Can. J. Botany*, **43**, 1055 (1965).

(5) R. E. Carter and J. H. Richards, *J. Am. Chem. Soc.*, **83**, 481 (1961).

(6) M. E. Levitch and P. Reitz, *Biochemistry*, **5**, 689 (1966).

(7) C. Tanford and S. Wawzonek, "Technique of Organic Chemistry," Vol. I, A. Weissburger, Ed., 3rd ed, Interscience Publishers, Inc., New York, N. Y., 1960, part 4, p 2942.

(8) R. Marsh, N. Jones, and J. H. Richards, unpublished results.