[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

The Reaction of Ketene with Pyridine[1]

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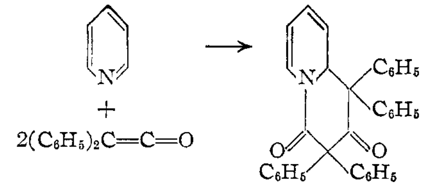
The chemistry of Wollenberg's yellow adduct of pyridine with ketene is elucidated by degradative studies. The substance is a pyronodihydroquinolizone. It disproportionates to a colorless dihydro derivative and a yellow, strongly fluorescent dehydro derivative. The mode of union of the ketene residues follows the "head-to-tail" rule.

As part of his classical survey[2] of the chemistry of the ketenes, Staudinger investigated the action of these substances on organic heterocycles. With pyridine and quinoline, ketoketenes formed adducts resulting from attack on the C=N bond of the heterocycle: *e.g.*, pyridine and diphenylketene gave I.[3] These substances were inordinately unstable. On warming or, in some cases, simple dissolution, they regenerated the addends. Acid hydrolysis gave the heterocyclic base and the carboxylic acid corresponding to the original ketene.

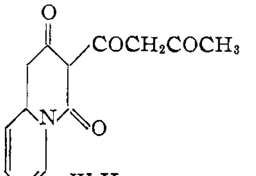


I

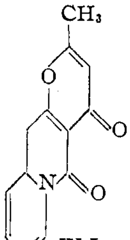
Early attempts[4] to obtain discrete nitrogenous products from the reaction of pyridine with ketene itself failed. However, Wollenberg[5] later succeeded in obtaining a pure, bright yellow, crystalline substance, $C_{13}H_{11}O_3N$, m.p. 208° (hereafter designated W-I[6]), by passing ketene gas into pyridine,[7] the stoichiometry being $C_5H_5N + 4C_2H_2O \rightarrow C_{13}H_{11}O_3N + H_2O$. He made preliminary studies but did not propose a structure.

Wollenberg's experiments showed that W-I contained two "active" hydrogens and was readily hydrolyzed by dilute alkali to a yellow monobasic acid, $C_{13}H_{13}O_4N$ (W-II), which was inert to methyl iodide and contained three "active" hydrogens. Oxidation of W-I with permanganate resulted in extensive degradation, the only isolable products being acetic and oxalic acids and acetamide. W-I rapidly absorbed one mole of hydrogen over palladium to give dihydro-W-I, $C_{13}H_{13}O_3N$, described as a yellow substance showing a blue fluorescence in solution and having two "active" hydrogens. A second mole of hydrogen was absorbed more slowly, giving tetrahydro-W-I, $C_{13}H_{15}O_3N$. Further reduction gave an uncharacterized oil. In the intervening two decades, the literature contains but one reference to W-I, Hurd, Cantor and Roe[8] having isolated a small quantity from a ketene–pyridine reaction mixture.

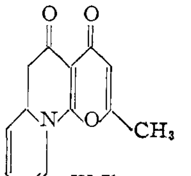
Our work leads to the conclusions that W-II is uniquely represented as shown below and that W-I is either W-Ia or W-Ib.



W-II



W-Ia



W-Ib

Our studies were initiated with the observation that W-I has the remarkable property of disproportionating at room temperature over palladium. The reaction, carried out in alcohol in an atmosphere of nitrogen, affords a mixture which can be separated by fractional crystallization into two substances: (i) a compound identical in empirical composition and properties with Wollenberg's *dihydro-W-I*, except that it is colorless and does not exhibit the reported fluorescence, and (ii) a new, bright yellow compound, *dehydro-W-I*, $C_{13}H_9O_3N$, which has the same melting point as W-I but is distinguished from it by (among other properties) a strong blue fluorescence in solution. Dehydro-W-I is also isolated from the mother liquors after *simple recrystallization* of W-I and can be obtained on a preparative scale (in 60% yield) by heating W-I in boiling butanol over palladized charcoal.

Although hydrolytic experiments with W-I and with dihydro-W-I will be described (*vide infra*), the hydrolysis of dehydro-W-I gives results which are immediately applicable to the solution of the structural question. Dehydro-W-I is weakly basic and moderately stable to acidic hydrolysis. When a warm solution of dehydro-W-I in concentrated hydrochloric acid is cooled, a crystalline hydrochloride separates. This material regenerates dehydro-W-I upon dissolution in water.[9] However, with warm 5% aqueous sodium hydroxide, dehydro-W-I readily adds one mole of water to give dehydro-W-II, $C_{13}H_{11}O_4N$, a weakly acidic, yellow substance which regenerates dehydro-W-I hydro-

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[1] Taken in part from a dissertation presented by William M. Jones in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] *Cf.* H. Staudinger, "Die Ketene," Ferdinand Enke, Stuttgart, (1912).

[3] H. Staudinger, H. W. Klever and P. Kober, *Ann.*, **374**, 1 (1910).

[4] H. Staudinger and H. W. Klever, *Ber.*, **41**, 594 (1908).

[5] O. Wollenberg, *ibid.*, **67**, 1675 (1934).

[6] Our work has been concerned with substances at three different states of oxidation. To aid the reader in following the arguments, we will refer to the parent compounds as W-I (Wollenberg's original adduct), dihyro-W-I and dehydro-W-I. Substances derived from the parent compounds by hydrolytic processes, *i.e.*, without change in oxidation state, will be referred to by changes in the Roman numeral. Thus, the hydrolysis products of dehydro-W-I are dehydro-W-II, dehydro-W-III, etc.

[7] We have observed (see the Experimental section) that the reaction gives low yields of adduct, or none at all, if the optimum conditions are not used. These we found empirically after several unsuccessful attempts.

[8] C. D. Hurd, S. M. Cantor and A. S. Roe, THIS JOURNAL, **61**, 426 (1939).

[9] This affords a convenient method of purifying dehydro-W-I.

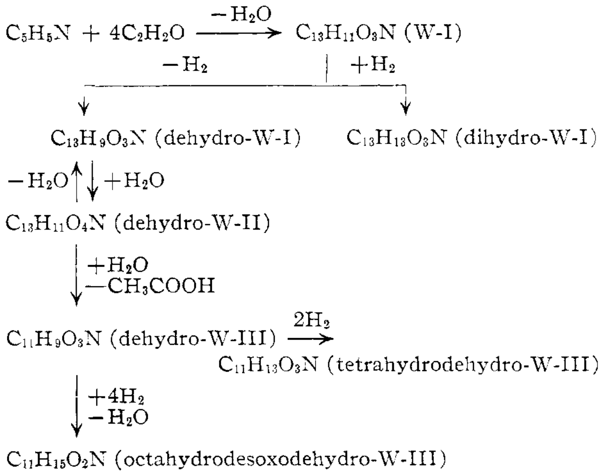
chloride with warm concentrated hydrochloric acid. Further hydrolysis of dehydro-W-II with aqueous sodium hydroxide occurs according to the stoichiometry $C_{13}H_{11}O_4N + H_2O \rightarrow C_{11}H_9O_3N$ (*dehydro-W-III*) + CH_3COOH.

Dehydro-W-III absorbs two moles of hydrogen in ethyl acetate over platinum to give *tetrahydrodehydro-W-III*, whereupon reduction stops spontaneously. This tetrahydride is colorless and appears to to be an enolic (or phenolic) ketone, since it gives a bright red color with ferric chloride, forms a fiery red 2,4-dinitrophenylhydrazone and gives a negative Schiff test.

Hydrogenation of dehydro-W-III over platinum *in acetic acid* containing *a trace of hydrochloric acid* consumes four moles of hydrogen and gives a substance *octahydrodesoxodehydro-W-III*, according to the stoichiometry $C_{11}H_9O_3N + 4H_2 \rightarrow C_{11}H_{15}O_2N + H_2O$. Two of the four moles of hydrogen are apparently used in effecting the conversion of a carbonyl group to methylene, since the product no longer reacts with 2,4-dinitrophenylhydrazine. Chart I outlines the pertinent inter-relationships.

The properties of tetrahydrodehydro-W-III and octahydrodesoxodehydro-W-III imply that these substances are substituted hydroxypyridones. This conclusion can be reached directly with a fair degree of confidence by analogical arguments, using as standards the properties of model substances (*vide infra*). However, it can also be induced more rigorously by the following systematic argument.

CHART I



$$C_5H_5N + 4C_2H_2O \xrightarrow{-H_2O} C_{13}H_{11}O_3N \text{ (W-I)}$$

$$\xrightarrow{-H_2} C_{13}H_9O_3N \text{ (dehydro-W-I)} \qquad \xrightarrow{+H_2} C_{13}H_{13}O_3N \text{ (dihydro-W-I)}$$

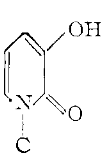
$$C_{13}H_9O_3N \text{ (dehydro-W-I)} \underset{-H_2O}{\overset{+H_2O}{\rightleftarrows}} C_{13}H_{11}O_4N \text{ (dehydro-W-II)}$$

$$C_{13}H_{11}O_4N \text{ (dehydro-W-II)} \xrightarrow[-CH_3COOH]{+H_2O} C_{11}H_9O_3N \text{ (dehydro-W-III)} \xrightarrow{2H_2} C_{11}H_{13}O_3N \text{ (tetrahydrodehydro-W-III)}$$

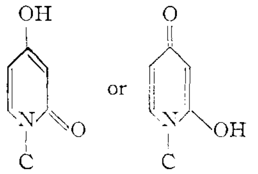
$$C_{11}H_9O_3N \text{ (dehydro-W-III)} \xrightarrow[-H_2O]{+4H_2} C_{11}H_{15}O_2N \text{ (octahydrodesoxodehydro-W-III)}$$

The octahydro compound $C_{11}H_{15}O_2N$ contains five formal units of unsaturation and is, like the tetrahydro compound, an enol. The second oxygen atom is present in a conjugated, unreactive carbonyl function (infrared absorption at 6.06 μ, no reaction with dinitrophenylhydrazine). Now, there is no combination of the groups $HO{-}\overset{|}{C}{=}\overset{|}{C}{-}$ and $-\overset{|}{C}{=}O$ which will account for the strong absorption in the ultraviolet at 289 mμ shown by the octahydro compound, so that at least one additional carbon–carbon double bond or other unsaturation must be present in a chromophorically active situation relative to the oxygen functions. However, this must be an aromatic or quasiaromatic double bond, since it is resistant to catalytic hydrogenation. (The same argument implies that there are no other isolated carbon–carbon double bonds in the molecule, and consequently that the octahydro compound contains two rings.) The nitrogen is at best feebly basic (no precipitate with ethanolic picric acid) and thus must be attached directly to the carbonyl group or conjugated with it through the double bond system. Only a hydroxypyridone can accommodate this set of requirements. From the fact that neither the octahydro nor tetrahydro compound shows the characteristic[10] broad N–H band between 3 and 4 μ, we conclude that the pyridone system is N-alkylated.[11]

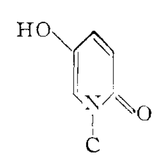
The hydroxypyridone partial formulas which must be considered for tetrahydrodehydro-W-III and octahydrodesoxodehydro-W-III are IIa–e.



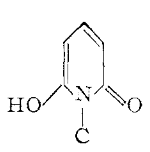
IIa



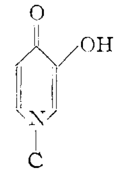
IIb



IIc

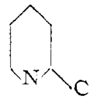


IId



IIe

Distillation of dehydro-W-III from zinc dust gives α-picoline. It is uncertain whether this substance arises from the pyridone system or from the second ring.



III

However, regardless of which of these two features is the origin of the degradation product, the part structure III is demonstrated, and IId therefore cannot be a part of dehydro-W-III or its derivatives.[12] Since the part structure IIc will be eliminated later on other grounds, we concentrate our attention upon the remaining alternatives, IIa, IIb and IIe.

A preliminary choice among these is based upon the behavior of octahydrodesoxodehydro-W-III toward Folin reagent and toward ferric chloride. Known 3- or 5-hydroxypyridines (or pyridones) give positive tests with Folin reagent, whereas 4-

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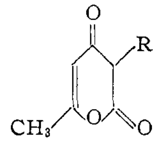
(10) F. Ramirez and A. P. Paul, This Journal, **77**, 3337 (1955).

(11) Tetrahydrodehydro-W-III shows only C–H absorption between 3 and 4 μ, despite the fact that it is an enol. We take this as evidence that the enolic O–H is internally hydrogen bonded (*cf. inter alia*, R. P. Barnes and G. E. Pinkney, This Journal, **75**, 479 (1953)). The matter is discussed further in the sequel.

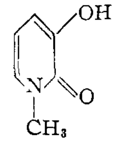
(12) This is self-evident if the α-picoline represents the skeleton of the original pyridone moiety. If it represents the second ring, the conclusion is less obvious but equally certain. Thus, in the latter case, since the nitrogen would have to be common to both rings, *both* rings must bear a carbon substituent on a ring carbon α to nitrogen.

hydroxypyridones give negative tests.[13–16] With ferric chloride, N-methyl-3-hydroxy-2-pyridone (V) gives a green-blue color[14] and N-methyl-3-hydroxy-4-pyridone (VII) gives a violet color,[15] whereas N-methyl-4-hydroxy-2-pyridone (VIa) gives a blood-red color.[16] Octahydrodesoxodehydro-W-III behaves as a 4-hydroxy-2-pyridone, giving a negative Folin test and a blood-red color with ferric chloride.

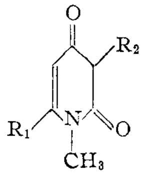
More convincing evidence that the octahydro compound contains the part structure IIb is afforded by a study of the ultraviolet spectrum. We have shown[17] that pyridones of the types IIa and IIe show bathochromic shifts of the principal maximum in alkaline solution, whereas those of type IIb show hypsochromic shifts. *The spectra of octahydrodesoxodehydro-W-III, tetrahydrodehydro-W-III and dehydro-W-III all show pronounced hypsochromic shifts in alkaline solution* (Table I). The shifts are much larger with dehydro-W-III and its tetrahydride than with the octahydro compound. This behavior parallels that observed in the dehydroacetic acid series,[17,18] in which the shift with the parent substance IVc, containing an acetyl group, is much greater than with the derivatives in which the acetyl group is reduced (IVb) or absent (IVa). Finally, the congruency in many properties of the octahydro compound and the model substance VIb (prepared[17] from IVb and methylamine) provides confirmatory evidence. Both substances show identical behavior toward ferric chloride, Folin reagent and ethanolic picric acid. The ultraviolet spectra in both neutral and basic solution are virtually superimposable (Table I) and the infrared spectra in the region 2–7 μ are also superimposable. Although IIc has not yet been formally eliminated, we consider these results strong evidence for the part structure IIb in the octahydro compound.



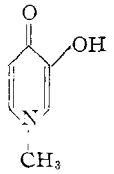
IVa, R = H
b, R = C_2H_5
c, R = $COCH_3$



V



VIa, $R_1 = R_2 = H$
b, $R_1 = CH_3$; $R_2 = C_2H_5$
c, $R_1 = CH_3$; $R_2 = H$



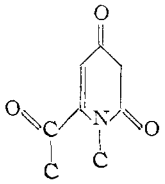
VII

TABLE I

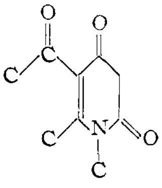
ULTRAVIOLET SPECTRA

	In methanol		In 2 × 10^{-3} *M* methanolic NaOH	
	λmax	log ε	λmax	log ε
VIb	287	3.87	279	3.86
Octahydrodesoxodehydro-W-III	289	3.87	280	3.83
Tetrahydrodehydro-W-III	232	3.96	233	4.28
	269	3.50	300	3.92
	331	4.15		
Dehydro-W-III	289	3.90	250	4.18
	315	3.46	299	3.96
	405	3.90	389	3.53

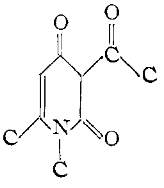
We must now place the keto group which is present in dehydro-W-III and its tetrahydride but absent in the octahydro compound. That this function is conjugated with an unsaturated system is established by the facts that (i) tetrahydrodehydro-W-III shows no absorption between 5.8 and 6.0 μ, the first band in the double bond region occurring at 6.06 μ; (ii) it forms a fiery *red* 2,4-nitrophenylhydrazone; (iii) the hydrogenolysis of the carbonyl group indicates on allylic (or benzylic) alcohol as an intermediate in the reduction. The possible part structures for the tetrahydro compound are therefore the enols of VIIIa–c.[19]



VIIIa



VIIIb



VIIIc

In order to deal with these alternatives, it is necessary to consider some additional properties of W-I, $C_{13}H_{11}O_3N$. Like dehydro-W-I, this substance adds a molecule of water when treated with dilute alkali. The product W-II, $C_{13}H_{13}O_4N$, is a weakly acidic substance which can be further degraded by basic hydrolysis to W-III, $C_{11}H_{11}O_3N$, the over-all change being exactly analogous to the hydrolytic deacetylation of dehydro-W-II to dehydro-W-III (see Chart I). Further, W-II very readily regenerates W-I upon being heated above the melting point (127°).

If VIIIa is a part structure for tetrahydrodehydro-W-III, the as yet uncharacterized second ring can be formulated in only three ways: (i) either the keto side chain is not part of a ring, (ii) the keto side chain is part of a ring fused at N–C_6 of the pyridone system, or (iii) the keto side chain is part of a ring fused at C_5–C_6 of the pyridone system.

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(13) (a) R. Kuhn and G. Wendt, *Ber.*, **72**, 305 (1939); (b) R. Adams and V. V. Jones, THIS JOURNAL, **69**, 1803 (1947).

(14) A. F. Bickel and J. P. Wibaut, *Rec. trav. chim.*, **65**, 65 (1946).

(15) A. F. Bickel, THIS JOURNAL, **69**, 1801 (1947).

(16) E. Späth and E. Tschelnitz, *Monatsh.*, **42**, 251 (1921).

(17) J. A. Berson, W. M. Jones and Sister Leo Francis O'Callaghan, THIS JOURNAL, **78**, 622 (1956).

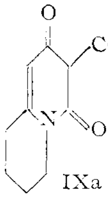
(18) J. A. Berson, *ibid.*, **74**, 5172 (1952).

(19) Several lines of evidence make an immediate choice of VIIIc intuitively attractive: (i) the spectral similarities to the dehydroacetic acid series; (ii) the striking analogy between the hydrogenolysis of a carbonyl group in the formation of octahydrodesoxodehydro-W-III and the change dehydroacetic acid (IVc) → desoxodehydroacetic acid (IVb)[18,20]; (iii) the fact that dehydroacetic acid is itself a polymer of ketene.[4,21] We have not depended upon these analogies in the main line of argument. It should be noted that W-I is not formed from IVc and pyridine under the conditions which generate W-I from ketene and pyridine.

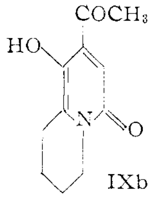
(20) R. Malachowski and T. Wanczura, *Bull. intern. acad. polonaise*, 547 (1933A); *C. A.*, **28**, 4421 (1934).

(21) E. Wedekind, *Ann.*, **323**, 246 (1902).

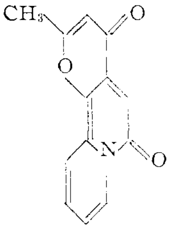
In case (i), since only three additional carbons are left uncharacterized, the second ring of tetrahydrodehydro-W-III must be three- or four-membered. This second ring is made up of carbon atoms which were originally part of the pyridine molecule employed in the formation of W-I. We are unable to reconstruct any sequence of events which would account for this bizarre mutilation of the pyridine corpus, and we consider case (i) highly improbable. In cases (ii) or (iii), eleven ring systems and over seventy detailed structures for tetrahydrodehydro-W-III are formally possible. Each of these either suffers from the same shortcomings as those derived from case (i), is inconsonant with the absorption spectra of tetrahydro-W-III or implies a structure for one of its derivatives which is unsatisfactory. Similar considerations lead to the rejection of VIIIb as a part structure.[22] We conclude that the only possible structures for tetrahydrodehydro-W-III are an enol of IXa, derived from VIIIc, and an enol of IXb, derived from IIc. IXb can be rejected on the grounds (i) that the derived expressions for dehydro-W-I (X), dehydro-W-II (XI), dehydro-W-III (XII), W-I (XIII or a double bond isomer thereof), W-II (XIV or a double bond isomer thereof) and W-III (XV or a double bond isomer thereof) are incompatible with the properties of these substances,[22] and (ii) the derived structure XIII cannot be reconciled with a satisfactory mechanism for the formation of W-I from ketene and pyridine (*vide infra* and footnote 26).



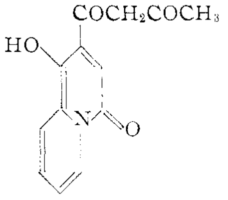
IXa



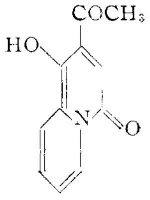
IXb



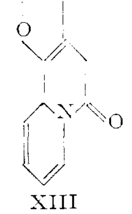
X



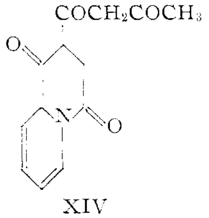
XI



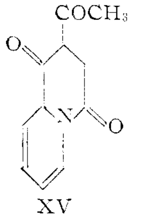
XII



XIII

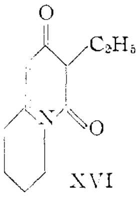


XIV

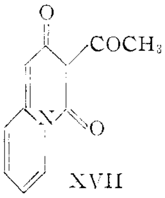


XV

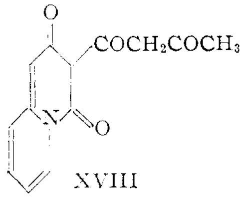
With tetrahydrodehydro-W-III uniquely identified as IXa, the chemical requirements of Chart I (and the fact that dehydro-W-II, although weakly acidic, is not a carboxylic acid), lead to the unambiguous formulation of the series: octahydrodesoxodehydro-W-III is an enol of XVI, dehydro-W-III is an enol of XVII and dehydro-W-II is an enol of XVIII. Dehydro-W-I is either XIXa or XIXb, and W-I is either XXa (≡ W-Ia) or XXb (≡ W-Ib) (or possibly a double bond isomer of either).



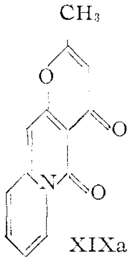
XVI



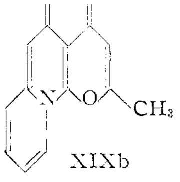
XVII



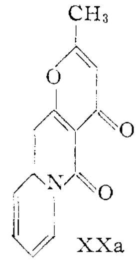
XVIII



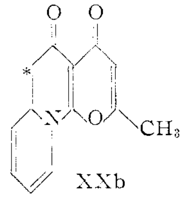
XIXa



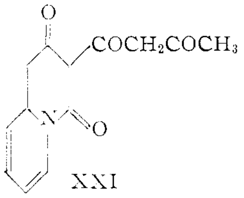
XIXb



XXa



XXb



XXI

In terms of either XXa or XXb, the facile basic hydrolysis of W-I to W-II (XXI ≡ W-II) as well as the inordinate ease of dehydrogenation are readily accommodated. The observation[5] that W-I yields two moles of methane in the Zerewitinoff determination is presumably a reflection of the activity of 2- and 6-methylene hydrogens in a γ-pyrone system.[23,24]

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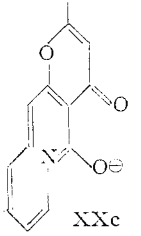
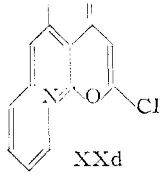
[22] The properties of any given member of the series are often satisfactorily explained by more than one structure. However, in each case it is impossible to derive structures for the *whole series* from any one of the hypothetical structures for tetrahydrodehydro-W-III based on VIIIa or VIIIb which are in harmony with the experimental observations. Some of the detailed rigorous arguments are given by W. M. Jones, Ph.D. Dissertation, University of Southern California, 1955.

(23) *Cf.* the smooth condensation of 2,6-dimethylpyrone with aromatic aldehydes (A. A. Boon, K. J. McKenzie and J. Trotter, *Proc. Chem. Soc.*, **30**, 205 (1914); A. A. Boon, F. J. Wilson and I. M. Heilbron, *J. Chem. Soc.*, **105**, 2176 (1914)).

(24) XXa has two such sets of hydrogens and XXb only one. We do not feel that this can be used as the basis of a distinction between the two possible structures, since the hydrogens at C* in both might be further "activated" by the possibility of proton abstraction being concerted with β-elimination of the weakly basic lactam nitrogen. The intriguing possibilities that such a reaction might be further aided by the establishment of a quantum mechanically stable system of ten ($2 + 4n$) π-electrons (*e.g.* as in XXc or d), and that W-I might itself be the conjugate acid of XXc or d, seem to be eliminated by the fact that a planar model of XXc or d cannot be constructed.



XXc



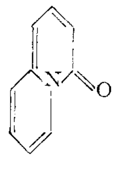
XXd

A number of other observations support the assignments. Thus, the absence of distinct O–H absorption in the infrared spectra of dehydro-W-II (XVIII), dehydro-W-III (XVII) and tetrahydrodehydro-W-III (IXa), despite the fact that these are enolic substances, is in accord with the expectation of efficient hydrogen bonding between the enolic O–H and the side chain carbonyl. When the side chain carbonyl is reduced, as in octahydrodesoxodehydro-W-III (XVI), the enol becomes free, and sharp O–H absorption at 3.18 μ is observed (compare the model substance VIb, λ_{max} 3.20 μ).

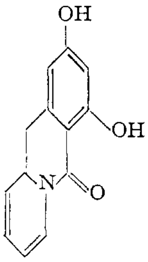
The acidic substances W-II (XXI), dehydro-W-II (XVIII) and dihydro-W-II all show strong absorption maxima in the *unconjugated* carbonyl region of the infrared spectrum (5.80–5.84 μ). This is due to the distal carbonyl group of the acetoacetyl side chain in these molecules, the absorption being absent in the deacetylated substances W-III and dehydro-W-III.

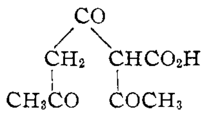
It is of interest that hydrolytic opening of the pyrone ring of W-I, dehydro-W-I and dihydro-W-I produces only relatively small changes in the long wave length ultraviolet absorption properties. Apparently the hydrogen-bonded β-diketone system is able to approximate whatever chromophoric effect the γ-pyrone nucleus contributes to the spectrum. Further, the ultraviolet spectra of W-II and W-III are substantially superimposable, as are those of dehydro-W-II and dehydro-W-III, confirming the conclusion that the distal carbonyl group is non-enolic and isolated from the chromophoric system.

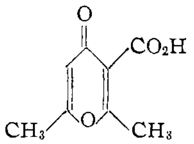
The quinolizone structure of dehydro-W-I (XIXa or b), deduced without recourse to analogy between its properties and those of the mother substance 4-quinolizone (XXII),[25] is nevertheless now supported by such analogies: both substances are but weakly basic, giving unstable hydrochlorides and picrates; both show a strong blue fluorescence in solution, and both give brown ferric chloride colors. Although these properties are not diagnostic, since close relatives of XXII are known[25b] to lack one or more of them, the correspondence is nonetheless gratifying.

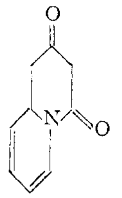

XXII

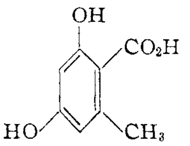
The details of the mechanism of the formation of W-I from ketene and pyridine remain obscure for the present. However, a likely intermediate is XXIII, a structure analogous to those (*e.g.*, I) established[3] for the ketoketene–pyridine adducts.[26] The subsequent stages might well involve acetoacetylation at the active methylene position to give XXI (W-II), followed by cyclodehydration[27] to give W-I (XXa or b).


XXIV


XXV


XXVI


XXIII


XXVII

Experimental[33]

Reaction of Ketene with Pyridine. Preparation of W-I.[5] —Ketene was generated by the pyrolysis of acetone over a hot wire, according to Williams and Hurd.[34] The voltage supplied to the filament, a coil of No. 24 gauge Chromel A wire, was controlled by a variable transformer. A 500-cc. three-necked flask, equipped with two efficient condensers, was charged with a mixture of 25 cc. of pyridine and 70 cc. of dry benzene and connected to the outlet of the ketene generator. The flask was cooled with a moist towel (if the reaction mixture is chilled too strongly, the principal product is dehydroacetic acid) and ketene was passed into the solution at the rate of 0.6 mole per hour for two hours. With the generator used, this rate of production of ketene was reproducibly achieved, with 75 volts supplied to the coil and vigorous ebullition of the acetone in the still-pot. (It was essential that acetone distil into the trap at the rate of 2–3 drops per second. Slower distillation of acetone apparently led to the formation of gaseous by-products which, when passed into the reaction mixture, caused a vigorously exothermic reaction from which little if any W-I could be isolated.) At the end of two hours, the ketene flow was cut off and the reaction mixture cautiously warmed on the steam-bath. After about 2 minutes, the reaction mixture turned very dark red and heat was evolved. After about 5 minutes, the exothermic reaction had ceased, whereupon the mixture was heated at reflux for 6 hours. Upon cooling, W-I usually separated as a reddish-brown precipitate, although in some cases seeding was necessary. After being washed with acetone and then with ether, this material was yellow. It darkened at 195° and melted at 199–202° dec. The yield was usually 12–15 g. Recrystallization from absolute methanol raised the m.p. to 205–207° dec., reported[5]

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[25] (a) E. Späth and F. Galinovsky, *Ber.*, **69**, 721, 761 (1936); (b) V. Boekelheide and J. P. Lodge, Jr., THIS JOURNAL, **73**, 3681 (1951).

[26] It should be noted that the mode of union of the ketene residues in W-I follows the "head-to-tail" rule. This appears to be general for ketene polymerizations,[28,30,31] and provides a strong additional argument against structure XIV for W-II, since XIV embodies one "tail-to-tail" union. This rule was a key part of the prescient speculations of Collie[32] on the biogenesis of natural products.

[27] The failure of XXI to cyclize to a resorcinol derivative (*e.g.*, XXIV) is not surprising when considered in the light of the behavior of dehydroacetic acid, which when heated with 85% sulfuric acid gives the pyrone carboxylic acid XXVI,[28] presumably *via* the intermediate XXV,[29] despite the fact that the latter is, in principle, capable of giving benzenoid products (*e.g.*, orsellinic acid, XXVII). Both orcinol and an orcinol carboxylic acid are, however, formed in small yield under alkaline conditions.[30]

[28] F. Feist, *Ann.*, **257**, 253 (1890).

[29] C. F. Rassweiler and R. Adams, THIS JOURNAL, **46**, 2758 (1924).

[30] J. N. Collie and W. S. Myers, *J. Chem. Soc.*, **63**, 122 (1893).

[31] R. B. Woodward and G. Small, THIS JOURNAL, **72**, 1297 (1950), and references cited therein.

[32] J. N. Collie, *J. Chem. Soc.*, **91**, 1806 (1907).

[33] Melting points are uncorrected. We are indebted to Mr. W. J. Schenck for microanalyses. The ultraviolet spectra were taken with the Beckman spectrophotometer, model DU. Infrared spectra were taken with the Perkin–Elmer spectrometer, model 13, rock-salt prism. In the text, the infrared bands between 2 and 7 μ are reported in μ, relative intensities on a scale of 0–20 being indicated in parentheses. Since most of the substances dealt with melt with decomposition, identity of samples from different sources was established by comparison of the infrared spectra. The ultraviolet maxima are reported in mμ, log ϵ in parentheses.

[34] J. W. Williams and C. D. Hurd, *J. Org. Chem.*, **5**, 122 (1940).

m.p. 208°; ultraviolet spectrum (in methanol) $\lambda\lambda_{max}$ 243 (4.05), 332 (3.75); infrared spectrum (in chloroform) $\lambda\lambda_{max}$ 5.92 (20), 6.05 (13), 6.14 (9), 6.29 (6), 6.98 (20), 7.05 (19).

Anal. Calcd. for $C_{13}H_{11}O_3N$: C, 68.05; H, 4.80; N, 6.10. Found: C, 67.80; H, 4.72; N, 6.35.

W-I is a pale-yellow solid which gives yellow, non-fluorescent solutions in alcohol. These solutions become fluorescent when heated, presumably due to the formation of dehydro-W-I. The latter was actually isolated from the methanolic mother liquors from a recrystallization of W-I.

Dehydro-W-I.—A mixture of 5.0 g. of W-I, 75 cc. of *n*-butyl alcohol and 0.10 g. of 30% palladium–charcoal was stirred vigorously and heated at reflux for 6 hours. During this period, the reaction mixture was occasionally swept with a stream of nitrogen. The resulting dark orange solution was filtered and evaporated to dryness *in vacuo*. The residue was taken up in chloroform and chromatographed on alumina. The first fractions (total 250 cc.) were combined, the chloroform evaporated and the residue recrystallized from 95% ethanol to give 3.0 g. of dehydro-W-I, m.p. 192–197° dec. Several recrystallizations from 95% ethanol raised the m.p. to 201–203°. To obtain very pure dehydro-W-I, 0.70 g. was dissolved in 10 cc. of concentrated hydrochloric acid and the solution refluxed for 15 minutes, cooled, diluted to 100 cc. with water and extracted with chloroform. The dried (sodium sulfate) extract was evaporated and the residue recrystallized from 95% ethanol to give 0.30 g. of dehydro-W-I as bright yellow, filamentous needles, m.p. 206–207.5° dec. Its alcoholic solutions have a strong blue fluorescence and give a reddish-brown color with ferric chloride; ultraviolet (MeOH): $\lambda\lambda_{max}$ 242 (4.15), 332 (shoulder) (3.76), 346 (3.91), 398 (4.10); infrared (chf.): 5.90 (19), 6.05 (13), 6.10 (14), 6.32 (17), 6.42 (16), 6.70 (19), 7.02 (17).

Anal. Calcd. for $C_{13}H_9O_3N$: C, 68.72; H, 3.99; N, 6.16. Found: C, 68.75; H, 4.22; N, 5.93.

Dehydro-W-I was also obtained when an ethanolic solution of W-I was stirred overnight in a nitrogen atmosphere over palladium black. The reaction mixture was filtered, evaporated and the residue fractionally crystallized from ethanol. The head fractions gave dihydro-W-I (*vide infra*). From the mother liquors, dehydro-W-I was obtained, identical in m.p. and infrared spectrum with a sample prepared as above.

Dehydro-W-I gave an immediate precipitate with ethanolic picric acid. The picrate appeared to be unstable and regenerated dehydro-W-I upon recrystallization from ethanol. Dehydro-W-I also formed an unstable, crystalline hydrochloride. A solution of 0.30 g. of dehydro-W-I in 5 cc. of concentrated hydrochloric acid was heated at reflux for 5 minutes. The resulting deep-orange solution was diluted to twice its volume with water and then cooled in an ice-bath, whereupon 0.18 g. of an orange, crystalline precipitate appeared. This material decomposed in the range 173–180° without melting. It gave a positive test for chloride ion with silver nitrate and a mineral oil mull showed O–H absorption at 3.08 μ. The hydrochloride was readily soluble in water, and its aqueous solution, upon standing a few minutes, deposited dehydro-W-I.

Dehydro-W-II (XVIII). Hydrolysis of Dehydro-W-I.—A suspension of 0.60 g. of dehydro-W-I in 15 cc. of 3% sodium hydroxide was warmed on the steam-bath until solution was complete (approximately 5 minutes). The deep orange solution was cooled in ice and acidified with 5% hydrochloric acid. The resulting yellow precipitate weighed 0.50 g. and had m.p. 120–124°. Recrystallization from ligroin raised the m.p. to 126–128°, but a persistent dark-red contaminant was not removed. This was finally separated under a hand lens and the residue recrystallized from ethyl acetate to give light yellow, clustered staves, m.p. 132–133.5°; ultraviolet (MeOH): $\lambda\lambda_{max}$ 288 (4.10), 315 (shoulder) (3.88), 408 (4.00); infrared (chf.): $\lambda\lambda_{max}$ 6.06 (13), 6.09 (13), 6.23 (14), 6.32 (10), 6.56 (7), 7.05 (11).

Anal. Calcd. for $C_{13}H_{11}O_4N$: C, 63.67; H, 4.52; N, 5.71. Found: C, 63.60; H, 4.84; N, 6.03.

The substance was weakly acidic (soluble in dilute sodium hydroxide, insoluble in bicarbonate).

Dehydration of Dehydro-W-II to Dehydro-W-I.—A solution of 0.75 g. of XVIII in 10 cc. of concentrated hydrochloric acid was heated at reflux for 30 minutes. The resulting deep-orange solution was diluted to 50 cc. with water, extracted with chloroform, the extract dried over magnesium sulfate and evaporated. The resulting gummy residue was taken up in 10 cc. of hot 95% ethanol, cooled and the precipitated solid collected to give 0.275 g. of dehydro-W-I, m.p. 205–207°, infrared spectrum identical with that of an authentic sample.

Dehydro-W-III (XVII).—A suspension of 1.5 g. of dehydro-W-I in 20 cc. of 5% sodium hydroxide was heated on the steam-bath for one hour. The deep red solution was cooled to room temperature and acidified with 5% hydrochloric acid to give 0.98 g. of dehydro-W-III, m.p. 181–187° dec. (The mother liquor had a strong odor of acetic acid.) Sublimation *in vacuo* followed by recrystallization from 95% ethanol gave felted, lanate yellow needles, m.p. 194.5–195° dec.; ultraviolet (MeOH): $\lambda\lambda_{max}$ 289 (3.90), 315 (3.46), 405 (3.90); (in 2×10^{-3} *M* methanolic NaOH): $\lambda\lambda_{max}$ 250 (4.18), 299 (3.96), 389 (3.53), infrared (chf.): $\lambda\lambda_{max}$ 5.98 (14), 6.12 (15), 6.21 (14), 6.35 (12), 6.44 (11), 6.65 (16), 6.84 (8), 7.03 (13).

Anal. Calcd. for $C_{11}H_9O_3N$: C, 65.02; H, 4.47; N, 6.89. Found: C, 65.35, 65.47; H, 4.68, 4.82; N, 7.09, 7.28.

Potentiometric titration of XVII against standard sodium hydroxide was carried out in 1:1 water–dimethylformamide. The pK_a was 9.1; XVII gave a reddish-brown color with ferric chloride.

XVII was recovered after being heated for several hours with dilute hydrochloric acid or dilute sodium hydroxide.

Tetrahydrodehydro-W-III (IXa).—A mixture of 0.520 g. of XVII (dehydro-W-III) and platinum (from 0.05 g. of platinic oxide) was stirred under hydrogen at atmospheric pressure in 50 cc. of ethyl acetate. After 6 hours, 1.95 molar equivalents of hydrogen had been absorbed, whereupon gas consumption virtually ceased. The solution was filtered, treated with Norite, filtered, evaporated and the residue recrystallized from 95% ethanol to give 0.370 g. of IXa as a colorless, fluffy, microcrystalline powder, m.p. 104–104.5°. Repeated recrystallization from 95% ethanol did not change the m.p.

Anal. Calcd. for $C_{11}H_{13}O_3N$: C, 63.74; H, 6.33; N, 6.76. Found: C, 63.44; H, 6.18; N, 6.72.

The substance gave a bright-red color with ferric chloride. It was soluble in sodium hydroxide, but insoluble in sodium bicarbonate. It gave no precipitate with ethanolic picric acid; ultraviolet (MeOH): $\lambda\lambda_{max}$ 232 (3.96), 269 (3.50), 331 (4.15); (in 2×10^{-3} *M* methanolic NaOH): $\lambda\lambda_{max}$ 233 (4.28), 300 (3.92); infrared (chf.): 6.06 (13), 6.09 (13), 6.23 (14), 6.32 (10), 6.56 (7), 7.05 (11).

The 2,4-dinitrophenylhydrazone was obtained as red needles, m.p. 214–215° dec., from absolute ethanol.

Anal. Calcd. for $C_{17}H_{17}O_6N_5$: N, 18.08. Found: N, 18.42.

Octahydrodesoxodehydro-W-III (XVI).—A mixture of 1.00 g. of dehydro-W-III (XVII), platinum (from 0.083 g. of platinic oxide), a few drops of concentrated hydrochloric acid and about 50 cc. of acetic acid was stirred under an atmosphere of hydrogen. After about 1.5 hours, two molar equivalents of gas had been consumed. The third mole of hydrogen was absorbed after an additional 2.5 hours and the fourth after approximately 10 hours. The mixture was filtered and the bulk of the solvent removed *in vacuo* at 80°. The light brown residue was triturated with 10 cc. of 5% sodium bicarbonate and the entire mixture extracted with chloroform. The dried (magnesium sulfate) extract was evaporated and the tan residue recrystallized from 95% ethanol to give 0.70 g. of a colorless solid, m.p. 197–212°. This material was leached with hot ethyl acetate and the insoluble portion recrystallized from 95% ethanol to give XVI as a white, microcrystalline powder, darkening at 222°, m.p. 230–231°; ultraviolet (MeOH): λ_{max} 289 (3.87); (in 2×10^{-3} *M* methanolic NaOH): λ_{max} 280 (3.83); infrared (Nujol mull): $\lambda\lambda_{max}$ 3.18 (13), 3.67 (6), 6.06 (14), 6.25 (12), 6.40 (17), 6.43 (17), 6.89 (15), 7.05 (17).

Anal. Calcd. for $C_{11}H_{15}O_2N$: C, 68.33; H, 7.83; N, 7.25. Found: C, 68.05; H, 8.02; N, 7.53.

The substance was soluble in sodium hydroxide, insoluble in sodium bicarbonate, gave a bright red color with ferric chloride, but gave no precipitate with phenylhydrazine or with ethanolic picric acid. The Folin test was negative.

Most of the properties of the model compound VIb have been described elsewhere.[17] The infrared spectrum (Nujol mull) had $\lambda\lambda_{max}$ 3.20 (11), 3.69 (9), 6.07 (12), 6.25 (10), 6.37 (15), 6.41 (15), 6.89 (14).

Zinc Dust Distillation of Dehydro-W-III.—A small distillation apparatus (ice-cooled receiver) was charged with an intimate mixture of 1.16 g. of dehydro-W-III and 5 g. of zinc dust. The mixture was heated cautiously over a free bunsen flame. As reaction proceeded, the heat supplied to the mixture was increased. The distillate was a mixture of a mobile oil and a bright yellow solid (presumably starting material, since this sublimes readily). After 10–15 minutes, distillation ceased. A small portion of the oil was treated with ethanolic picric acid. The yellow precipitate was recrystallized from water to give α-picoline picrate, m.p. 161–162°, alone or mixed with an authentic sample of α-picoline picrate (m.p. 162–163°). The infrared spectra of the two picrate samples were identical. Another sample of the oil was converted to the methiodide, m.p. 224–226° (reported[35] for α-picoline methiodide, m.p. 226–228°).

Hydrolysis of W-I to W-II (XXI).—A suspension of 1.00 g. of W-I in 25 cc. of 5% sodium hydroxide was warmed on the steam-bath until solution was completed (about 1 minute). The mixture was cooled to room temperature, acidified with 5% hydrochloric acid, and the resulting yellow precipitate collected, washed with water and dried in air to yield 0.83 g. of W-II, m.p. 125–127°. Recrystallization from acetone–ligroin afforded light yellow, micaceous platelets, m.p. 126–127°, reported[5] m.p. 127°; ultraviolet (MeOH): $\lambda\lambda_{max}$ 264 (4.06), 332 (3.98); (in 2×10^{-3} *N* methanolic sulfuric acid): $\lambda\lambda_{max}$ 242 (3.86) (shoulder), 330 (3.46), 392 (3.13) (shoulder); (in 2×10^{-3} *M* sodium hydroxide): $\lambda\lambda_{max}$ 259 (4.06), 342 (3.96); infrared (chf.): $\lambda\lambda_{max}$ 5.80 (17), 6.08 (20), 6.45 (20), 6.84 (19), 7.08 (17).

Anal. Calcd. for $C_{13}H_{13}O_4N$: C, 63.15; H, 5.30; N, 5.67. Found: C, 63.33; H, 5.71; N, 5.65.

W-II was soluble in sodium hydroxide. It was partially soluble in sodium bicarbonate, but solution was not accompanied by release of carbon dioxide. Attempts to determine pK_a in 50% methanol (warming was necessary to effect solution) gave results for neutral equivalent varying between 290 and 500, presumably because of some recrystalization. The infrared spectrum in chloroform, Nujol or hexachlorobutadiene mull showed no evidence of free or bonded O–H absorption between 3 and 4 μ.

When a sample of W-II was heated, it melted at 127° and vigorously evolved steam at 135°. As heating at 135° was continued, the mass solidified. After 10 minutes, the product was washed with acetone and dried to give W-I, m.p. 194–197° dec., identical in infrared spectrum with an authentic sample.

Deacetylation of W-II to W-III.—A suspension of 0.40 g. of W-II in 10 cc. of 10% barium hydroxide was warmed on the steam-bath for three hours. The mixture was cooled to room temperature, filtered from a small quantity of insoluble material and then neutralized with 5% hydrochloric acid, whereupon an oil separated. Upon standing overnight at 5°, this material solidified to give 0.15 g. of W-III, m.p. 45–54°. Several recrystallizations from ligroin gave pure W-III as a light yellow solid, m.p. 56–57°; ultraviolet (MeOH): $\lambda\lambda_{max}$ 264 (3.99), 331 (3.83); infrared (chf.): $\lambda\lambda_{max}$ 6.01 (15), 6.06 (15), 6.21 (14), 6.45 (16), 6.66 (14), 6.84 (15), 7.04 (13).

Anal. Calcd. for $C_{11}H_{11}O_3N$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.10; H, 5.42; N, 6.82.

Hydrogenation of W-I to Dihydro-W-I.—A mixture of 1.96 g. of W-I and 0.10 g. of palladium black in 150 cc. of 95% ethanol was stirred in an atmosphere of hydrogen. One molar equivalent of hydrogen was absorbed in 2 hours, at which time the rate of consumption of gas had decreased appreciably. The hydrogenation was interrupted, the solution filtered and concentrated to a small volume. When cooled, the solution deposited 1.85 g. of a light yellow solid, m.p. 234–238° dec. Recrystallization from 95% ethanol gave colorless needles, m.p. 240–242° dec., reported[5] m.p. 242–243°. The pure substance showed no fluorescence in solution; ultraviolet (MeOH): $\lambda\lambda_{max}$ 243 (4.05), 295 (very broad shoulder) (3.62); infrared (chf.): $\lambda\lambda_{max}$ 5.94 (20), 6.06 (11), 6.18 (5), 6.98 (19), 7.05 (14).

Anal. Calcd. for $C_{13}H_{13}O_3N$: C, 67.52; H, 5.66; N, 6.06. Found: C, 67.42; H, 5.48; N, 5.68.

Hydrolysis of Dihydro-W-I to Dihydro-W-II.—A sample of 0.10 g. of dihydro-W-I dissolved rapidly in 5 cc. of 5% sodium hydroxide. The solution was cooled to 5° in an ice-bath and acidified with 5% hydrochloric acid, whereupon 0.09 g. of a precipitate, m.p. 118–120°, separated. Recrystallization from acetone gave almost colorless crystals, m.p. 120–120.5°; ultraviolet (MeOH): $\lambda\lambda_{max}$ 268 (4.12), 275 (4.12), 291 (4.14); infrared (chf.): $\lambda\lambda_{max}$ 5.81 (12), 6.05 (14), 6.44 (17), 6.80 (15), 7.05 (11).

Anal. Calcd. for $C_{13}H_{15}O_4N$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.50; H, 5.79; N, 5.49.

Dihydro-W-II was re-cyclized to dihydro-W-I by heating at 140°. The product had m.p. 234–237° and its infrared spectrum was identical with that of authentic dihydro-W-I.

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[35] H. O. Jones, *J. Chem. Soc.*, **83**, 1415 (1903).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MISSOURI]

Some Reactions of N-Acetylphthalimides

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It has been shown that N-acetylphthalimide and substituted N-acetylphthalimides can acetylate butyl alcohol, in the presence of sodium butoxide, with the formation of a phthalimide or the sodium salt of a phthalimide. N-Acetylphthalimide acetylates secondary amines, but reacts with primary amines to afford N-alkyl- or arylphthalimides and acetamide. Phenylmagnesium bromide has been found to attack N-acetylphthalimide at the three carbonyl groups to yield 3-hydroxy-3-phenylphthalimidine, *o*-dibenzoylbenzene and diphenylmethylcarbinol. The reduction of N-acetylphthalimide, by means of lithium aluminum hydride, has been shown to give 3-ethylisoindoline.

The chemistry of the N-acylimides has been studied only to a limited extent. Hurd and co-workers[3] have shown that certain N-acylphthalimides of the general formula $C_6H_4(CO)_2N{-}COCH_2R$ give rise on pyrolysis to phthalimide, the acid RCH_2CO_2H, or its anhydride and the ketone $(RCH_2)_2CO$. Isobutyryl- and diphenylacetylphthalimide, in contrast, pyrolyze satisfactorily to ketenes. It has been reported also,[4] that the molecular weights of polymers which contain hydroxyl groups may be increased by heating the polymers with an N-acylpolyimide of a polycarboxylic acid. The purpose of the present work was to extend the study of the reactions of N-acetyl- and substituted N-acetylphthalimides.

It appeared to be of interest, first, to examine the reaction of N-acetylphthalimide with a representative alcohol. It was found that N-acetylphthal-

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[1] Abstracted in part from the Ph.D. thesis of M. F. Drumm.

[2] E. I. du Pont Fellow, 1949–1950.

[3] C. D. Hurd, M. F. Dull and J. W. Williams, THIS JOURNAL, **57**, 774 (1935).

[4] P. J. Flory, U. S. Patent 2,594,145; *C. A.*, **46**, 6431 (1952).