pyrone (**VIb**), m.p. 84–86°; two recrystallizations from cyclohexane yielded 0.62 g. of pure material, m.p. 86.5–87.5°, λ_{max}^{EtOH} 280 mμ (log ε 3.80), λ_{min}^{EtOH} 238 mμ (log ε 2.96); $\lambda_{max}^{CHCl_3}$ 5.85(s), 6.05(m) and 7.94(s) μ.

Further elution of the column with 1:1 ether–ethanol led to 0.27 g. (19%) of slightly yellowish crystals (m.p. 91–93°) of **6-methyl-2-methoxy-γ-pyrone** (**VIIb**); this material was obtained in a colorless state (0.17 g.) after two recrystallizations from cyclohexane and exhibited m.p. 94–94.5°, λ_{max}^{EtOH} 240 mμ (log ε 4.13); $\lambda_{max}^{CHCl_3}$ 5.98(s), 6.17(m) and 7.92(s) μ. These physical and spectral constants are in excellent agreement with those recorded in the literature.[9,10,18]

When the methylation was conducted at 0–5° exactly as described by Wiley and Jarboe[16] and the mixture processed as above by chromatography, there was isolated 52% of 6-methyl-4-methoxy-α-pyrone (VIb) (m.p. 80–84°, raised to m.p. 87–88° after one recrystallization), and 8% of 6-methyl-2-methoxy-γ-pyrone (VIIb) (m.p. 89–93°, raised to 91–93° after one recrystallization). Identity of these products with the ones isolated in the room temperature methylation experiment was established by mixture melting point determination and by coincidence of the relevant infrared and ultraviolet absorption spectra.

Methylation of 6-Phenyl-2,4-pyronone (**Vb**).—A mixture of 8.0 g. of ethyl benzoylacetate, 50 mg. of pulverized potassium bicarbonate and 50 cc. of nitrobenzene was refluxed for 2 hr., most of the nitrobenzene was distilled at 100° under reduced pressure, ether was added and the solution was extracted ten times with 30-cc. portions of 10% potassium bicarbonate solution. Acidification of the alkaline extracts followed by extraction with chloroform and evaporation left 2.68 g. of **3-benzoyl-4-hydroxy-6-phenyl-α-pyrone**,[6b] m.p. 161–168°, which was used in the next step. The analytical sample was secured from carbon tetrachloride and melted at 169–171°, λ_{Max}^{EtOH} 348 mμ (log ε 3.92), $\lambda_{max}^{CHCl_3}$ 5.72(m) and 6.10(s) μ.

Anal. Calcd. for $C_{18}H_{12}O_4$: C, 73.96; H, 4.14; O, 21.90. Found: C, 73.76; H, 4.07; O, 21.60.

6-Phenyl-2,4-pyronone (Vb)[6b,17] (1.0 g.) was heated at 120° for 10 min. with 2.85 cc. of concd. sulfuric acid and 0.15 cc. of water. The solid, obtained upon pouring into ice-water, was collected and washed with cold water and then carbon tetrachloride in order to remove benzoic acid. After drying, the cream-colored solid (0.67 g., m.p. 232–241° dec.) was recrystallized from methyl ethyl ketone whereupon it exhibited m.p. 235–236° (dec.; variable depending upon rate of heating), λ_{max}^{EtOH} 317 mμ (log ε 4.11), λ_{max}^{Nujol} 6.10(s) and 7.90(s) μ.

Anal. Calcd. for $C_{11}H_8O_5$: C, 70.21; H, 4.29. Found: C, 70.50; H, 4.40.

The methylation of 0.57 g. of 6-phenyl-2,4-pyronone was performed exactly as described above for triacetic lactone except that the reaction mixture was left at room temperature for 16 hr. Chromatography of the total reaction product (m.p. 112–121°) on 20 g. of Alcoa grade F-20 alumina (deactivated with 0.6 cc. of 10% aqueous acetic acid) and elution with benzene gave 0.33 g. of **6-phenyl-4-methoxy-α-pyrone** (**VIc**), m.p. 123–132°, raised to m.p. 129.5–131.5°[18] upon further recrystallization from cyclohexane; λ_{max}^{EtOH} 314 mμ (log ε 4.13); $\lambda_{max}^{CHCl_3}$ 5.86(s), 6.10(s) and 6.40(s) μ).

Anal. Calcd. for $C_{12}H_{10}O_3$: C, 71.28; H, 4.98; O, 23.74; OCH_3, 15.35. Found: C, 71.12; H, 5.08; O, 23.56; OCH_3, 15.13.

In a second experiment, where methylation of 0.42 g. of Vb gave 0.36 g. of 6-phenyl-4-methoxy-α-pyrone (VIc) (m.p. 125–130°), further development of the chromatogram column with ether and with chloroform yielded 60 mg. of crude **6-phenyl-2-methoxy-γ-pyrone** (**VIIc**), m.p. 84–112°. After evaporative distillation at 150° and 0.02 mm. followed by three recrystallizations from isopropyl ether, there was obtained 33 mg. of the colorless, analytical sample, m.p. 112.5–114.5°, λ_{max}^{EtOH} 276 mμ (log ε 4.29), $\lambda_{max}^{CHCl_3}$ 5.97(s), 6.10(s) and 6.20(s) μ.

Anal. Calcd. for $C_{12}H_{11}O_3$: C, 71.28; H, 4.98; O, 23.74; OCH_3, 15.35. Found: C, 71.51; H, 5.00; O, 23.45; OCH_3, 14.90.

DETROIT, MICHIGAN
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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY]

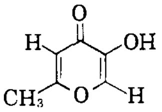
Structure of the Compound Obtained by Reaction of Acrylonitrile with α-Deoxykojic Acid

BY CHARLES D. HURD AND SWIATOSLAW TROFIMENKO[1]

RECEIVED OCTOBER 29, 1958

The major product, "D-I," from the reaction of α-deoxykojic acid with acrylonitrile has been investigated. The structure best fitting the evidence is 2-(3-hydroxy-4-oxo-6-methyl-γ-pyran-2-yl)-methyl-3-oxo-4-hydroxy-1-methyl-6-oxabicyclo-[2.2.1]heptane-2-carbonitrile. Reasons are offered for eliminating other less suitable structures.

It was shown earlier[2] that some 3-hydroxy-1,4-pyrones condense abnormally with acrylonitrile and other acrylic derivatives to yield products consisting of two molecules of the hydroxypyrone and one of the acrylic moiety. This paper deals with the structure of compound D-I, $C_{15}H_{15}NO_6$, the major product from the reaction of α-deoxykojic acid (I) and acrylonitrile. Of the more plausible structures, II agrees best with the evidence at hand and is tentatively proposed as representing D-I. For brevity in presentation of structures to follow, the two radicals from the enol and keto forms of I will be referred to as III and IV, respectively.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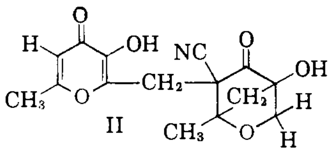
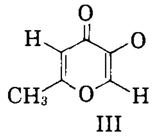
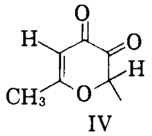

II


III


IV

D-I was a high-melting white solid, quite insoluble in ether, chloroform, ligroin, ethyl acetate and water, very sparingly soluble in alcohol, and moderately soluble in pyridine and dimethylformamide as well as dilute aqueous solution of alkali, ammonia or 10% sodium carbonate. The anion of D-I was yellow in solution, but the solid sodium salt was white; D-I was insoluble in saturated sodium bicarbonate at room temperature, but it dissolved when the suspension was heated on a steam-bath.

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[1] Allied Chemical and Dye Corporation Fellow, 1957–1958.

[2] C. D. Hurd, R. J. Sims and S. Trofimenko, THIS JOURNAL, **81**, 1684 (1959).

The infrared spectrum[2] of D-I showed strong hydroxyl absorption which could be resolved into two peaks at 3.04 and 3.14 μ. Only a rather weak band for C–H absorption could be detected at about 3.40 μ. There was a well-defined nitrile band at 4.38 and a strong, sharp carbonyl band at 5.78 μ. The region between 6.00 and 6.30 μ, characteristic of the pyrone system contained several fused peaks. The rest of the spectrum was complex but reproducible.

The nuclear magnetic resonance spectrum[3] of D-I was taken on 2 M solution of the sodium salt of D-I in water-d_2. The large peak near the center of the spectrum is due to water, the peaks labeled SB represent side bands of the same. The peak labeled Ar–H indicates the presence of one aromatic hydrogen, and the presence of an alcoholic hydroxyl is indicated from the peak adjacent to the one due to water. The other bands on the right side of the spectrum are due to methylene and methyl hydrogens. More detailed assignment has not been possible.

Functional Groups. Hydroxyls.—Support for the empirical formula of D-I was found in its titration in pyridine–methanol by potassium methoxide in benzene–methanol using brom thymol blue as indicator. In this system D-I behaved as a monobasic acid and titrated reproducibly. That this acid function was an enolic hydroxyl was supported by its pK_a of about 9 toward Davidson AI indicator[4] and a strong ferric chloride color test.

In keeping with the fact that nuclear magnetic resonance also indicated an alcoholic hydroxyl it is pertinent to note that benzoylation yielded a dibenzoate and acetylation a diacetate. In these esters, infrared spectra showed no hydroxyl bands, new carbonyl absorption at 5.73μ as well as slightly modified bands in the 5.8-region. Also, there was intensified absorption of the pyrone carbonyl at about 6μ. These changes parallel the behavior shown by the dibenzoate of kojic acid, observed by us to be 5.74 and 5.82μ with concurrent intensification of the pyrone carbonyl.

Methylation of D-I gave rise to several products. With one equivalent each of base and methyl sulfate, the almost exclusive product was a monoethyl ether, $C_{16}H_{17}NO_6$, which gave a negative ferric chloride test and still showed the presence of one hydroxyl in the infrared. When an excess of both base and methyl sulfate was used two products were obtained, both $C_{17}H_{19}NO_6$. One was insoluble in alkali and was devoid of hydroxyl bands in the infrared, thus being a simple dimethyl ether of D-I. The other material revealed a hydroxyl band at about 3.10μ and also gave a positive ferric chloride test. Kojic acid is known to produce a monoether which still contains the enolic hydroxyl group free when treated with excess alkali and methyl sulfate.[5] The nature of the second dimethylation product of D-I is uncertain.

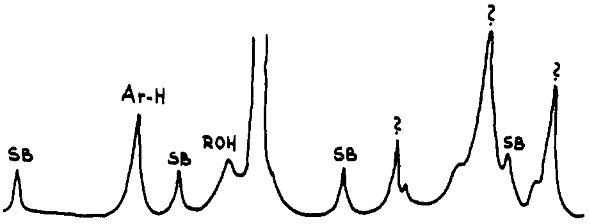

Fig. 1.—Nuclear magnetic resonance spectrum of D-I.

On treating D-I with alkali and allyl bromide a monoallylation product, m.p. 147°, was obtained, $C_{18}H_{19}NO_6$, giving a negative ferric chloride test and exhibiting one hydroxyl band at 3.02μ. From another run a material melting at 162–164° was obtained with an infrared spectrum indistinguishable from that of the 147° product except for a weak band at about 6.50μ. The material was not investigated further, although it was assumed that just a different crystalline modification was involved.

The alcoholic hydroxyl in the monomethyl ether of D–I might reasonably be adjacent to the carbonyl, hence an attempt was made to oxidize it. Cupric acetate, an excellent reagent for the oxidation of α-hydroxy ketones,[6] was completely without effect on it under conditions optimal for such oxidation. Also from a mixture of it and chromic anhydride in glacial acetic acid most of the starting material was recovered. This stability of the alcoholic hydroxyl toward oxidation would indicate that it is tertiary.

Under acid conditions most tertiary hydroxyl groups lead to relatively stable tertiary carbonium ions which give rise to dehydration or isomerization, depending on the system in question. D-I was found to be remarkably stable toward acids, which suggests that this hydroxyl occupies a bridgehead position where both carbonium ion formation and dehydration of either one alone would incur prohibitive steric strain.

Nitrile.—The band at 4.38μ in the infrared suggested very strongly a nitrile grouping in D-I. Also soda lime fusion of D-I readily gave ammonia as detected by methanolic cupric sulfate reagent.[7] Moderate acid hydrolysis of D-I yielded an amide, $C_{15}H_{17}NO_7$ (D-III), again confirming the cyanide group in D-I. D-III had no band at 4.38μ but the spectrum showed new amide bands at 2.85, 2.95 and 5.92μ. Also the melting point of D-III was considerably higher than that of D-I as is usually true of an amide over a nitrile. In fact, D-III was the most thermally stable derivative of D-I, remaining unchanged up to 300°.

When D-III was benzoylated or acetylated under the same conditions as D-I, compounds identified as the diesters of D-I were obtained. The identification was unequivocal, resting on superimposability of infrared spectra and non-depression of melting points on admixture of authentic samples. Thus both benzoyl chloride and acetic anhydride dehydrate the amide to the nitrile in the process of acylating the hydroxyls.

Compound D-III could be prepared independently starting from α-deoxykojic acid and

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(3) The determination and interpretation of the nuclear magnetic resonance spectrum of D-I was done by Dr. A. L. Allred whose cooperation is herewith gratefully acknowledged.

(4) D. Davidson, *J. Chem. Ed.*, **19**, 221, 532 (1942).

(5) A. Beélik and C. Purves, *Can. J. Chem.*, **33**, 1361 (1955).

(6) P. Ruggli and P. Zeller, *Helv. Chim. Acta*, **28**, 741 (1945); H. Bloch, H. Lehr, H. Erlenmeyer and K. Vogler, *ibid.*, **28**, 1410 (1945).

(7) S. Trofimenko and J. W. Sease, *Anal. Chem.*, **30**, 1432 (1958).

acrylamide. The above findings make the presence of a nitrile group in D-I a certainty and they also reflect on the relative stability of D-I toward acids.

Carbonyls.—The carbonyl band in the infrared spectrum of D-I falls just between the range for five-membered-ring ketones (5.72–5.75μ) and six-membered-ring ketones (5.80–5.87μ)[8] and is very close to the band found in camphor (5.77μ). Since D-I gave no Tollens and Fehling tests an aldehyde was excluded. 2,4-Dinitrophenylhydrazine and phenylhydrazine were unreactive toward D-I. Hydroxylamine formed no oxime of the monomethyl ether of D-I but it did form a sirupy material, thought to have arisen by opening of the pyrone ring. Benzoylation of this sirup gave a glass. Similarly, uncertain results were obtained under Clemmensen conditions of reduction. A non-crystalline material was isolated which appeared to be a mixture of products, judging from the presence of two infrared nitrile bands at 4.42 and 4.48μ.

Compound D-I was smoothly reduced by sodium borohydride. The product initially obtained seemed to be the boric ester of a vicinal diol. The reduced D-I could be separated from the crude product only by an acid-catalyzed transesterification with methanol and removal of the methyl borate by distillation. Boron was detected in the distillate by the characteristic green flame test. The new product analyzed for $C_{15}H_{17}NO_6$ although the values for carbon were a little low. Its infrared spectrum showed complete disappearance of the carbonyl band at 5.78μ and there were three discernible hydroxyl bands at 2.83, 2.99 and 3.12μ. The material gave an intense violet color with ferric chloride.

When the crude mixture from the borohydride reduction was treated with benzoyl chloride in pyridine two products were obtained. One of them was a monobenzoate, $C_{22}H_{21}NO_7$, that contained a band at 3.10μ which was ascribed to an enolic hydroxyl in view of the positive ferric chloride test, a carbonyl band at 5.84μ along with benzoate bands at 7.90, 9.00 and 14.00μ. The other material had two benzoate bands and gave no ferric chloride test. It changed on recrystallization from methanol to the former compound, which is not surprising in view of the acid anhydride nature of the enol benzoate.

Two experiments were carried out to test the presence of methylene adjacent to carbonyl. One of them was the Zimmerman test with alkaline *m*-dinitrobenzene[9] which came out negative, and the other was reaction with piperonal in an attempt to prepare a piperonylidene derivative from the monomethyl ether of D-I but none was formed. These results show that the carbonyl group is ketonic with a fair amount of steric hindrance, which is in accord with the negative tests for an α-methylene group.

Non-reaction on attempted bromination or hydrogenation speaks for the absence of olefinic unsaturation in D-I.

Pyrone System.—Compound D-I and all of its derivatives contained bands in the infrared between 6.00 and 6.40μ which were very similar to the bands observed in miscellaneous derivatives of kojic acid known to contain the pyrone system.

The fact that the monomethyl ether of D-I, which is insoluble in cold alkali, does dissolve on warming to give a yellow solution is readily explained in terms of the pyrone ring opening. Unlike the cold alkaline solution of D-I itself, this warm alkaline solution gave a positive Zimmerman test.[9] Also while D-I gave no haloform test under mild conditions where the opening of the pyrone ring would be unlikely, it did give a haloform test under more drastic conditions.

The above findings strongly support the pyrone system in D-I, and indeed it would be hard to rationalize the opening of two pyrone systems with only a limited amount of base present and the relatively mild conditions of the reaction when D-I is formed. A pyrone system would also account for the aromatic hydrogen peak found in the nuclear magnetic resonance spectrum of D-I.

Degradative Studies.—Considerable effort was spent in determining the behavior of D-I toward various acids, alkalies and oxidizing agents, but these experiments were less rewarding than the preceding. Refluxing with concentrated hydrobromic acid yielded only tars, and refluxing with hydriodic acid yielded tars from which ammonium iodide was obtainable. Constant boiling hydrochloric acid gave rise to a nitrogen-free product, $C_{15}H_{16}O_8$, called D-II, that could also be prepared from D-III. This suggests that D-II is the acid of which D-III is the amide, yet D-II could not be titrated successfully. It gave a positive ferric chloride test and dissolved with evolution of carbon dioxide in sodium bicarbonate, although quite slowly, and was recovered on acidification. With Davidson AI reagent a carboxylic acid test was obtained, but again only after an induction period. The spectrum of D-II lacked the customary carboxyl absorption in the 3–4μ region. The carbonyl band was shifted to 5.83 and acquired a shoulder at 5.88μ. Thus, no definite statement can be made concerning the presence of a free carboxyl group, but indications are that it is tied up to some extent. No benzoate or acetate of D-II could be made on treatment with benzoyl chloride or acetic anhydride.

Crystalline materials were obtained from D-I and potassium permanganate but in trace quantities, hence they were only examined spectrally. One of these compounds was interesting in having an infrared spectrum devoid of the bands (3.1, 6.0–6.4) due to the hydroxypyrone system but retaining the bands for alcoholic hydroxyl (2.92 with shoulder at 2.97), nitrile (4.42), carbonyl (5.82), as well as several bands at 9–12μ most of which were found also with D-I. From this, one may infer that the non-pyrone portion of D-I was largely intact in this material.

Treatment of D-I with bromine and sodium hydroxide solution gave rise to ammonium bromide

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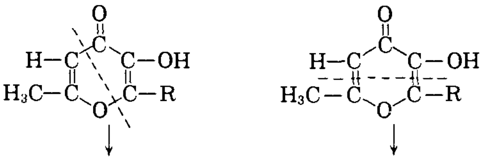
(8) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 114.

(9) W. Zimmermann, *Z. physiol. Chem.*, **233**, 257 (1935). While the Zimmerman test works well with acyclic and monocyclic carbonyl compounds, some bicyclic compounds may test negatively. This was found to be the case with camphor.

and a sirup that yielded a brick-red, high-melting 2,4-dinitrophenylhydrazone still containing the cyanide group (by infrared) but not otherwise identified. A seemingly identical 2,4-dinitrophenylhydrazone was obtained following ozonolysis of D-I and processing of the resulting sirup with dinitrophenylhydrazine.

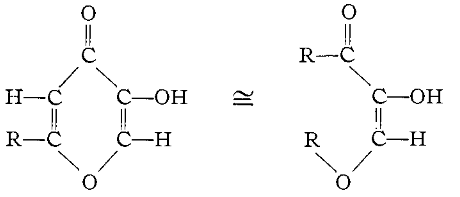
Barium hydroxide yielded useful information. To lessen the chance of side reactions in the products, the solid hydroxide was taken and was mixed with solid D-I or its monomethyl ether, then steam distilled. Acetone and pyruvaldehyde (or a precursor of it) were found in the distillate, although in poor yields. These two products suggest a dual mode of alkaline cleavage of the pyrone system in α-deoxykojic acid or its derivatives.



While isolation of acetone is in direct analogy to earlier findings,[10] the isolation of pyruvaldehyde had no precedent. Peratoner[11] had postulated its formation along the above lines but did not isolate it as secondary reactions took place.

Although chromic anhydride did not oxidize the monomethyl ether of D-I it did oxidize D-I. The dark green, glassy solid thus formed was exceedingly stable to heat and acids. It contained chromium and it revealed a nitrile band at 4.42μ.

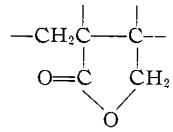
Treatment of D-I with periodic acid resulted in slow reaction with formation of iodine but with no well defined products otherwise. The reaction of periodic acid with a series of reductones and related compounds had been investigated by Hesse and Mix.[12] 3-Hydroxypyrones may be considered as analogous to a monoether of reductone, *viz.*



Testing of some model compounds under the same conditions showed that kojic acid liberates iodine almost instantaneously, 6-propyl-α-deoxykojic acid within about 24 hours, and methyl kojate not at all even after 4 days. In this respect D-I resembles the 6-substituted derivative of kojic acid.

With strong evidence supporting a pyrone moiety in D-I it would seem that the remaining 9 carbons must represent some kind of degenerate pyrone system and a cyanoethylene bridge connecting them. A terminal cyanoethyl group is unlikely since it would have to be attached to a dimer of I, for which there is no evidence. It is impossible that this linkage would involve the methyl group since pyromeconic acid had no such group yet it gave rise to F.

The fact that A, from kojic acid, contains a γ-lactone whereas compounds C, D or F do not supplies positive evidence in favor of the cyanoethylene bridge. In C, D and F the nitrogen is retained as the nitrile. To form A, therefore, the obvious conclusion is that acrylonitrile so reacts with kojic acid that the α-hydroxyl is in a position to react intramolecularly with the cyanide group. This necessitates that the α-carbon of the acrylonitrile moiety, $-CH_2-\underset{|}{\overset{\alpha}{C}}HCN$ be linked to the 2-position in kojic acid or its degenerate structure. The following partial structure would then be applicable to A

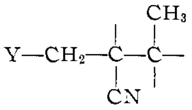


Extension of this concept to I would show this partial structure for D-I: $-CH_2\underset{|}{C}(CN)C(CH_3)<$.

In the above structures the α-hydrogen is not shown since the reaction is run under alkaline conditions and the activated α-hydrogen might be removed by base with possibilities for further reaction at this position.

The empirical formula for D-I indicates a deficiency of 18 hydrogen atoms from an open-chain saturated structure, 12 of which are accounted for by the pyrone system and the nitrile group. The remaining 6 must represent rings and carbonyls in the degenerate pyrone system since olefinic unsaturation has been ruled out. A carbonyl and hydroxyl are known to be present, leaving only one oxygen atom unaccounted for, hence the following two possibilities are permissible: two ring and one carbonyl, or one ring and two carbonyls (a choice necessitating that one of the carbonyls be completely enolized).

Differentiation between these possibilities is intimately associated with the position of linkage to the pyrone system. If one assumes that the carbon, originally β in the acrylonitrile molecule, is linked to the enolic oxygen then one obtains Va as a partial structure, and the enol, alcohol



$$Y-CH_2-\underset{CN}{\underset{|}{\overset{|}{C}}}-\underset{|}{\overset{\overset{CH_3}{|}}{C}}-$$

Va, Y = III
Vb, Y = IV

and ketone functions known to be present in D-I must be accounted for by the degenerate pyrone system. Only a cyclic isoreductive acid species containing this structure $>C{=}C(OH)COCHOH-$ would accommodate these requirements. The above statement is based on the assumption that the three remaining oxygens are linked to adjacent carbons, which is tantamount to stating than no carbon–carbon cleavage occurs under the mildly basic conditions and that the opening of

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[10] T. Yabuta, *J. Chem. Soc.*, **125**, 575 (1924); *J. Agr. Chem. Soc. Japan*, **6**, 516 (1913); H. R. V. Arnstein and R. Bentley, *J. Chem. Soc.*, 3436 (1951).

[11] A. Peratoner and G. Leonardi, *Gazz. chim. ital.*, [1] **30**, 539 (1900).

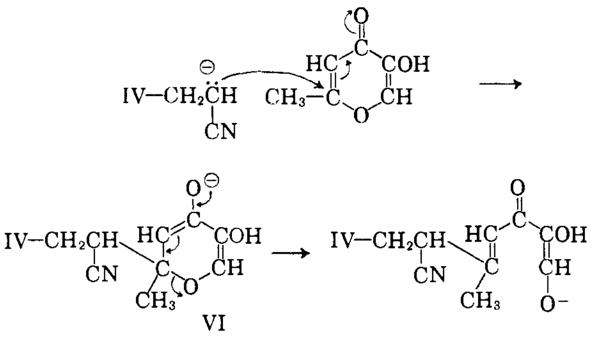
[12] K. Mix, Ph.D. Dissertation, University of Erlangen, Germany, 1958.

the deoxykojic system is initiated at the 2- rather than the 6-position. This is quite reasonable inasmuch as the 6-position is the site of attack for electrophilic reagents.

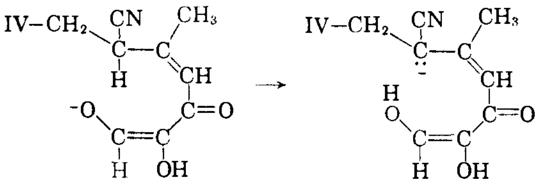
Comparison of D-I with a known isoreductic acid[13] shows that this is a quite unreasonable structure for D-I. For example, D-I is thermally stable up to its decomposition point whereas isoreductic acid is isomerized to reductic acid; D-I is unaffected by acids under not too drastic conditions but isoreductic acid readily isomerizes to reductic acid; D-I is inert toward carbonyl reagents but isoreductic acid readily gives dicarbonyl derivatives. Finally, D-I contains a non-conjugated carbonyl, as judged by the 5.78μ band, whereas isoreductic acid[14] has a carbonyl band at 5.90μ, as expected for conjugated carbonyl.

If the acrylonitrile linkage is not through the enolic oxygen then it must be through the 6-position, leading to partial structure Vb for D-I. Of the remaining three oxygens one would need be an alcoholic hydroxyl, another a ketone carbonyl, leaving the third oxygen an ether type. The degenerate pyrone part, therefore, must contain two rings and one carbonyl.

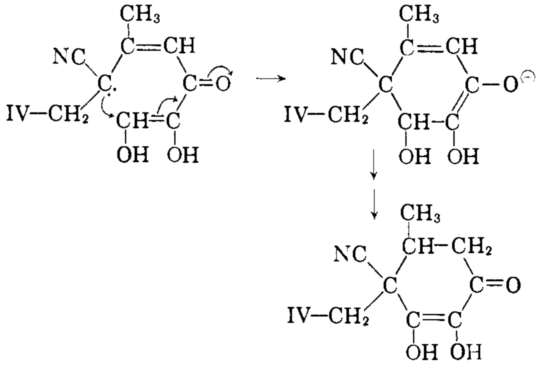
With this evidence and partial structure at hand one may now reconstruct the genesis of D-I from mechanistic considerations. The first step must involve attack of α-deoxykojate anion in its diketo form on acrylonitrile to produce the intermediate nitrile carbanion, IV-$CH_2\bar{C}HCN$. For "normal" cyanoethylations such a carbanion would pick up a proton from a suitable donor to yield the cyanoethylated product. Failure to do so in this abnormal reaction may be rationalized in the following manner. As the carbanion formation is reversible, the equilibrium may be quite unfavorable with respect to the cyanoethyl product, since by β-elimination a resonance-stabilized kojate-type anion is produced. By the following sequence of steps, however, the reaction becomes essentially irreversible and is driven toward the abnormal product. The good yields speak in favor of this assumption, but it should be pointed out that the formation of VI from acrylonitrile and two moles of I may take place in a concerted fashion rather than stepwise as shown above. The fact that maximum solubility of I in methanol is achieved in the presence of 0.5 equivalent of base may indicate the formation of a bimolecular complex of some sort with a spatial relationship between the molecules permitting the concerted step to occur. Also the optimal conditions for synthesis of D-I require presence of 0.5 equivalent of base.



The next stage of the mechanism would involve, directly or indirectly, a proton transfer to give rise to a relatively stable carbanion, activated by a nitrile group and vinylogously by a carbonyl.



The following targets are available for intramolecular attack by this ion: 1. The double bond of the enediol. The reaction would proceed to yield a product which under alkaline conditions would be expected to isomerize to a homolog of reductic acid



Since D-I has none of the properties of a reductic acid, this reaction path may be safely excluded. Alternatively, the second structure of path 1 may channel itself into path 2. 2. The carbonyl of the α-hydroxy aldehyde formed by tautomerization of the enediol, followed by a proton transfer (either concerted, or by mediation of the solvent) and an intramolecular Michael-type attack of the newly created anion.

Several objections can be raised against this structure. First of all, the 1,4-oxide bridge is sufficiently strained that it should be expected to be labile to acids if an analogy to 1,4-cineole is pertinent; but this is contrary to the established stability of D-I. Secondly, the carbonyl group has an α-methylene which should give both a positive Zimmermann test and a piperonylidene derivative, unlike D-I. Consideration of molecular models shows that no appreciable steric crowding exists around this carbonyl so that its lack of reactivity toward 2,4-dinitrophenylhydrazine and similar reagents is hard to rationalize. Finally the hydroxyl present is a secondary one and might be expected to be oxidizable, although its steric inaccessibility could be used to explain this inertness. Path 2, at best, is a dubious one.

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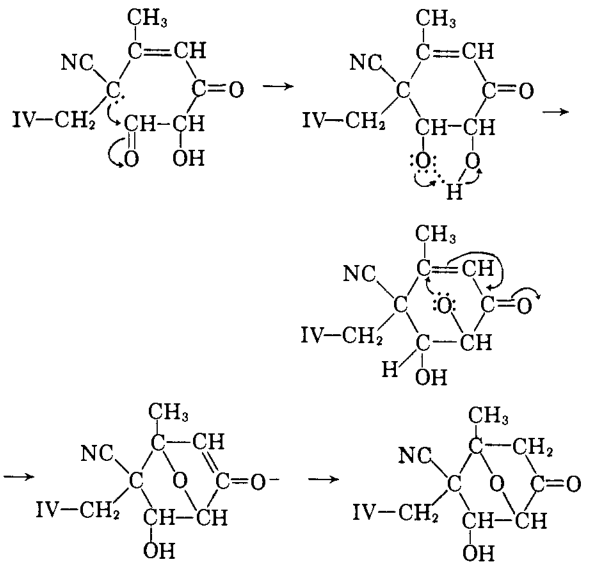
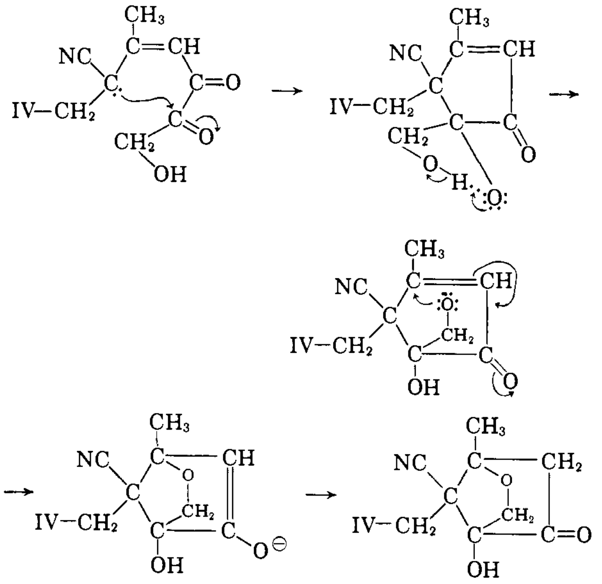
(13) G. Hesse, F. Exner and H. Hertel, *Ann.*, **609**, 57 (1957).

(14) A sample of authentic methylisoreductic acid was kindly supplied by Professor G. Hesse.

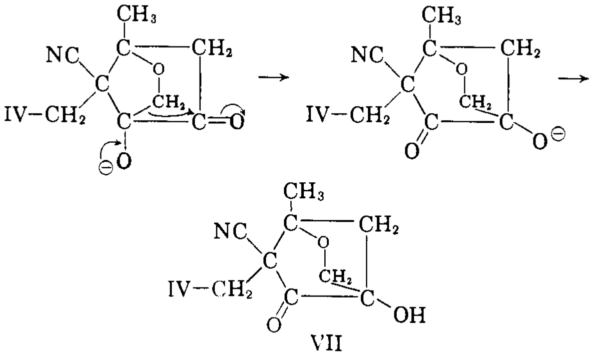


3. The carbonyl of the α-hydroxy ketone formed by tautomerization of the enediol, followed by similar steps as in 2



Here the bicyclic connection involves no 1,4-oxide bridge. The cyclic ether is unstrained and should be quite stable; also the hydroxyl group would be tertiary in agreement with the inertness observed but the objections mentioned earlier against the carbonyl would still remain.

It is possible, however, by postulating a simple base-catalyzed rearrangement to eliminate these objections. The following mechanism would give rise to a carbonyl which is devoid of α-hydrogens and sterically quite crowded, as examination of models will show; this would explain the non-reactivity toward carbonyl reagents, the negative Zimmermann test and non-reaction with piperonal. The rearrangement proposed is analogous to the benzilic acid rearrangement, or to the formation of saccharinic acids in the carbohydrate field. Inspection of molecular models also shows that the molecule is less strained when the methylene bridge is unsubstituted, which would add to the driving force for the rearrangement.



VII

Thus structure VII, which is shown in expanded form as structure II, is offered as the structure of D-I since it satisfies best the experimental findings. Further work on the nature of the other products obtained in the anomalous reaction with acrylic derivatives as well as on their stereochemistry will be reported in a later paper.

Experimental

Titration of D-I.—Samples of D-I were dissolved in 50 cc. of 7:3 pyridine–methanol mixture. One cc. of 1% methanolic solution of brom thymol blue was added to each sample, and the solutions were titrated with potassium methoxide up to the appearance of a dark bluish-green color.

The base was prepared by dissolving about 1.25 g. of potassium in a mixture of 10 cc. of methanol and 25 cc. of benzene. After completion of the reaction, 28 cc. of methanol was added, and mixed, and then diluted to 500 cc. with dry benzene. Standardization against purified kojic acid preceding the titration and against benzoic acid following the titration gave identical molarity.

Three samples of D-I (each about 0.2 g.) titrated for neutralization equivalent of 297, 301 and 303; calculated for $C_{15}H_{15}NO_6$, 305.

Dibenzoate of D-I.—One gram of D-I was left standing with 3 cc. of benzoyl chloride in 40 cc. of dry pyridine for 48 hours. Then excess methanol was added and after 4 more hours all volatile products were removed. The residue was taken up in chloroform, washed with water, bicarbonate, water, dried with sodium sulfate, and decolorized with Norit. Evaporation of the solvent left a sirup which, on boiling with 75 cc. of benzene–toluene mixture, yielded 1.3 g. of crude dibenzoate (78%), m.p. 259–261°. The material was purified by taking it up in chloroform, adding toluene, boiling off the chloroform and cooling. After six recrystallizations in this manner the m.p. rose to 265.5°.

Anal. Calcd. for $C_{29}H_{23}NO_8$: C, 67.83; H, 4.51; N, 2.73. Found: C, 67.46; H, 4.53; N, 2.73. This analysis and all other analyses were performed by Miss H. Beck.

Diacetate of D-I.—One gram of D-I was heated on a hot-plate with 3 cc. of acetic anhydride in pyridine for 5 min. The dark brown solution was evaporated at reduced pressure, the residue was taken up in hot benzene, filtered through a layer of Norit–Celite into a fivefold volume of heptane. The precipitate was filtered off and dried; yield 1 g. (80%), m.p. 120–130°. Repetition of the above procedure did not improve the purity of the material. When the solid was washed on the filter with methanol, however, the brown impurities were leached out, leaving a white solid, m.p. 225–227°. Recrystallization from a mixture of ethyl acetate and pentane afforded white solid, m.p. 230–231.5°.

Anal. Calcd. for $C_{19}H_{19}NO_8$: C, 58.60; H, 4.92; N, 3.60. Found: C, 58.49; H, 5.02; N, 3.76.

Methylation of D-I. Monomethylation.—To a stirred solution of 15.2 g. of D-I in 50 cc. of water containing 3.0 g. of potassium hydroxide 6.3 g. of methyl sulfate was added dropwise over 10 minutes and the solution was stirred for 3 hours at 25°. The yellow color gradually disappeared and solid separated turning the solution into a thick slurry. The solid was collected on a filter, rinsed with water and dried; yield 14 g. or 88%. Recrystallization from methanol gave white crystals, m.p. 229–230°.

Anal. Calcd. for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.37; N, 4.39. Found: C, 59.79; H, 5.46; N, 4.73.

Dimethylation.—Into a solution of 3.05 g. (0.01 mole) of D-I, 15 cc. of water and 2.0 g. of potassium hydroxide (0.035 mole) there was added 2.80 g. (0.022 mole) of methyl sulfate in small portions with rapid stirring at room temperature. After stirring for 6 hours the precipitate that separated was collected, washed with water and dried; yield 0.80 g., m.p. 185–189°. After recrystallization from methanol the m.p. rose to 193–194°.

Anal. Calcd. for $C_{17}H_{19}NO_6$: C, 61.25; H, 5.76; N, 4.21. Found: C, 61.00; H, 5.52; N, 4.30.

The mother liquor was acidified and 1.65 g. of a plastic glob formed which solidified on standing overnight; m.p. after recrystallization from methanol 247°.

Anal. Calcd. for $C_{17}H_{19}NO_6$: C, 61.25; H, 5.76; N, 4.21. Found: C, 61.59; H, 5.66; N, 3.97.

The monomethylation was easy to repeat, although sometimes the yields were lower. The dimethylation was troublesome as the neutral material usually consisted of a mixture of monomethyl and dimethyl ethers which could be separated only with considerable losses in material.

Monoallyl Ether of D-I.—A solution of 6.10 g. of D-I (0.02 mole) in 30 cc. of warm methanol and 25 cc. of water containing 1.1 g. (0.02 mole) of sodium methoxide was refluxed for 4 hours with 2.54 g. (0.021 mole) of allyl bromide. This was allowed to stand overnight, and then was concentrated in a stream of air. The white precipitate was filtered off, washed with water and dried; yield 5.0 g. The material was dissolved in 25 cc. of boiling ethanol, treated with Norit, filtered and cooled. A total of 3.6 g. of material, m.p. 148–150°, was obtained in three crops. The compound could not be sublimed *in vacuo* as decomposition took place. After two recrystallizations from benzene–ligroin white platelets were obtained of m.p. 147°.

Anal. Calcd. for $C_{18}H_{19}NO_6$: C, 62.60; H, 5.54; N, 4.06. Found: C, 62.2; H, 5.52; N, 4.10.

In another run the reaction mixture was completely evaporated and exhaustively extracted with benzene. The extracts, on removal of solvent, deposited a solid which, on recrystallization from benzene and then from ethanol, yielded white crystals of m.p. 162–164°.

Compound D-III by Hydrolysis of D-I.—(A) D-I (1.0 g.) was heated for 30 min. with 20 cc. of 70% sulfuric acid. The dark yellow solution was poured into a small amount of ice and salt. On stirring the mixture and scratching the walls of the beaker 1.2 g. of a white precipitate appeared, but it had no definite m.p. The material was purified by dissolving it in a little 25% sodium hydroxide solution, treating the solution with Norit, filtering and acidifying. On standing for 1 hr. at 5° clusters of needles formed. These were washed with water and 2-propanol to yield 0.65 g. of light creamy needles. The material darkened with some decomposition around 300° and had no well-defined melting point. No improvement of melting point could be effected by recrystallization from acetic acid or by repeated reprecipitation from alkaline solution.

Anal. Calcd. for $C_{15}H_{17}NO_7$: C, 55.71; H, 5.30; N, 4.33. Found: C, 55.84; H, 5.29; N, 4.57.

(B) D-I (3.0 g.) was allowed to stand at room temperature in a stoppered flask with 50 cc. of concentrated hydrochloric acid for two days. The yellow solution was evaporated in a stream of air and the residue was purified through the sodium salt; yield of D-III 2.4 g. The material was identified spectrally.

Direct Synthesis of D-III.—Three grams of α-deoxykojic acid was dissolved in 50 cc. of hot 2-propanol. To the solution 0.7 g. of sodium methoxide was added. The mixture was heated and water was added dropwise until the suspension refluxed smoothly. Then acrylamide (5.0 g.), dissolved in 15 cc. of methanol, was added and the solution was refluxed for three hours, acidified with hydrochloric acid and evaporated in air stream on a steam-bath. The solid residue was extracted twice with ethyl acetate to remove any unreacted deoxykojic acid, then purified as in part A above. The yield was 1.70 g. of creamy powder having an infrared spectrum identical with that of D-III from the reactions above.

Benzoylation and Acetylation of D-III.—Both reactions were performed as described for D-I. In both acylations the only material obtained was the dibenzoate or the diacetate of D-I, identified spectrally and by mixed m.p. determination. The dibenzoate was obtained in 70% yield, the diacetate in about 10% yield, as resin formation occurred in the latter reaction.

Dihydro D-I.—Three grams of D-I was dispersed in 50 cc. of methanol and brought into solution by dropwise addition of base. Excess sodium borohydride was added and the solution was allowed to stand at room temperature for 4 hr. The solution then was acidified with hydrochloric acid and evaporated to dryness. The residue was taken up in 70 cc. of methanol acidified with a small amount of hydrochloric acid. It was boiled at reduced pressure for 30 minutes, then most of the solvent was removed. Fresh methanol was added and the above procedure was repeated thrice. During this operation a white inorganic precipitate separated which was discarded. On addition of 50 cc. of ethyl acetate and partial evaporation of the solution another precipitate came down that gave an intense violet color with ferric chloride; over-all yield about 2 g. (65%), m.p. 228–230°, m.p. 233–234° after recrystallization from ethanol. The methanol distillate gave a positive flame test for boron indicating presence of methyl borate.

Anal. Calcd. for $C_{15}H_{17}NO_6$: C, 58.62; H, 5.58; N, 4.56. Found: C, 57.43; H, 5.49; N, 4.54. Further recrystallization did not change the analysis.

Benzoates of Dihydro D-I.—Three grams of D-I was treated as before, except that after evaporation of the acidified solution the residue was taken up in three 20-cc. portions of warm pyridine. After cooling the solution to room temperature, 10 cc. of benzoyl chloride was added and the solution was left for 8 hr. Then 5 cc. more of benzoyl chloride was added and the solution was evaporated to about 20 cc. in air stream on a steam-bath. This residue was drowned in 150 cc. of 7% sulfuric acid and was extracted with three 50-cc. portions of chloroform. The extracts were washed twice with 10% sodium carbonate, then with water. After removal of solvent at reduced pressure a sirup was obtained. This was boiled with an ether–benzene mixture whereupon 0.5 g. of light-colored precipitate separated, m.p. 227–234 dec. The remainder of the solution was partially decolorized with Norit and concentrated. Addition of heptane caused separation of 0.4 g. of flocculent precipitate. Evaporation of the mother liquor left 0.3 g. of a resin.

The first crop on recrystallization from toluene melted instantaneously when placed on the block at 249.5°; when placed at a lower temperature it decomposed over a range of several degrees. It gave a positive test with ferric chloride. The other precipitate did not.

Anal. Calcd. for $C_{22}H_{21}NO_7$: C, 64.22; H, 5.17; N, 3.41. Found: C, 63.74; H, 5.17; N, 3.33.

The neutral precipitate, on recrystallization from methanol, turned into the enolic one.

Hydrolysis of D-I. Compound D-II.—Four grams of D-I was refluxed for one hour with 30 cc. of constant boiling hydrochloric acid. The solution then was evaporated in air stream at room temperature, the residue taken up in alkali, treated with Norit, filtered and acidified. The product was a yellowish solid, m.p. 249–253° dec., yield 3.2 g. It was purified by recrystallization from acetic acid, and drying over phosphoric anhydride *in vacuo;* m.p. of the pure material, 256°. The same material was obtained by treatment of D-III in the above manner.

Anal. Calcd. for $C_{15}H_{16}O_8$: C, 55.55; H, 4.97. Found: C, 55.26; H, 4.79.

Degradation of D-I and its Monomethyl Ether with Barium Hydroxide.—Two grams of the monomethyl ether of D-I was mixed with 3 g. of anhydrous barium hydroxide and the mixture was steam distilled into 100 cc. of 6 *N* hydrochloric acid that was saturated with 2,4-dinitrophenylhydrazine. The volume of distillate was 150 cc. On standing for a few hours a yellow precipitate formed; yield 170 mg., m.p. 112–117°. Recrystallization from aqueous ethanol and from aqueous dioxane raised the m.p. to 119–121° but not further. Mixed m.p. with authentic acetone 2,4-dinitrophenylhydrazone was 119–121°. The infrared spectra of the two were similar though not quite identical.

The filtrate from the first precipitate, on further standing for a few days, deposited an orange precipitate in small amount. Recrystallization from a mixture of acetic acid and pyridine afforded material of m.p. 300–301°; mixed m.p. with authentic derivative of pyruvaldehyde of m.p. 299°, 298–299°. Their infrared spectra were superimposable. These two products were obtained also from D-I itself, following the same procedure. Processing of the residue from the steam distillation did not yield any well defined products.

Degradation of D-I with Potassium Permanganate.—Compound D-I was suspended either in water buffered with magnesium salt, or acetone. Powdered potassium permanganate was added in small portions until color persisted. After removal of manganese dioxide the volatile materials were removed at reduced pressure and the residue was extracted with chloroform. Evaporation of the solvent left an acidic sirup. This was chromatographed on silica using chloroform–hexane as eluent.

In the course of several runs no well-reproducible results were obtained. The only material obtained in substantial amount from one run was D-I. In two other instances trace amounts of a solid, m.p. 134–139°, were obtained, the infrared spectrum of which showed most peaks of the non-pyrone moiety of the D-I to be intact. Most other fractions from chromatography turned out to be intractable sirups.

Reaction of D-I with Bromine and Alkali.—Compound D-I was treated at 0° with excess bromine in sodium hydroxide solution for 1 hr., then was stirred for 6 hr. at 25°. The mixture was acidified, volatile materials removed, and the residue was extracted with 2-propanol. On evaporation of solvent an amber sirup remained which darkened on exposure to air. The sirup formed a derivative with 2,4-dinitrophenylhydrazine reagent, m.p. 130–140°. Recrystallization from aqueous acetic acid gave material decomposing around 270°.

This derivative could be prepared more conveniently by treatment of the acidified solution after completion of the reaction with 2,4-dinitrophenylhydrazine reagent. The derivative was recrystallized from boiling bromobenzene. It decomposed around 285°.

Ozonolysis of D-I.—Compound D-I in acetic acid was treated with excess ozone (a transient yellow color appeared in the course of the reaction) and the ozonide was decomposed with zinc dust. After filtering off the zinc and removing the acetic acid at reduced pressure a yellow sirup was obtained which gave a weak ferric chloride test.

Attempted chromatography on silica failed to yield any crystalline fractions. Treatment of the sirup with excess 2,4-dinitrophenylhydrazine reagent gave rise to a transient yellow precipitate. Eventually an orange precipitate separated. It was difficult to recrystallize for it was so sparingly soluble in most solvents tried. Orange microcrystals were obtained from boiling bromobenzene, m.p. 290°.

Anal. Calcd. for $C_{23}H_{19}N_9O_{11}$: C, 46.23; H, 3.21; N, 21.10. Found: C, 45.99; H, 3.35; N, 21.10.

Reaction of D-I with Chromic Anhydride.—One gram of D-I was stirred in 25 cc. of acetic acid with 1.0 g. of chromic anhydride at room temperature for 22 hr. The green solution was diluted with 20 cc. of water and evaporated in an air stream. Two grams of a black-green sirup was obtained which crystallized on standing. This was soluble in water, methanol and 2-propanol, the solubility decreasing in that order. It did not melt when heated up to 300°, nor when heated with a bunsen flame at 15 mm. Standing with concentrated hydrochloric acid caused no change, but with concentrated alkali at room temperature chromic hydroxide precipitated. Separation of the hydroxide and acidification of the yellow mother liquor gave no crystalline material on concentration save sodium chloride.

Attempted Hydrogenation and Bromination of D-I.—Shaking of D-I with palladium-on-charcoal under hydrogen in a Parr apparatus for 24 hr. resulted in no uptake of hydrogen and the starting material was recovered unchanged. Similarly, stirring of a solution of D-I in dimethylformamide with excess of bromine for 24 hr. yielded only the starting material on processing.

Evanston, Ill.

[Contribution from Ohio State University]

Reactions of Furan Compounds. XVI.[1] Conversion of Tetrahydro-2-methylenefuran Successively into Dihydromethylfuran, Cyclopropyl Methyl Ketone and Methyl Propenyl Ketone by Heat[2]

By Dorothy M. Aten Armitage and Christopher L. Wilson

Received November 10, 1958

In an extension of Paul's work,[4–6] pure tetrahydro-2-methylenefuran has been prepared in 89% yield by the dehydrobromination of tetrahydrofurfuryl bromide. The olefin isomerizes very easily either by heat or acids to 4,5-dihydro-2-methylfuran. At temperatures between 425 and 525° both compounds rearrange first to cyclopropyl methyl ketone and then to methyl propenyl ketone.

Tetrahydro-2-methylenefuran (I) could have been first made by Kirner[3] who attempted to make methyl tetrahydrofurfuryl ether by the reaction of the chloride and methanol using powdered potassium hydroxide. He described the formation of unsaturated material to which he tentatively gave formula I without, however, any data to support it. Later Paul[4] was somewhat more successful using the reaction of tetrahydrofurfuryl bromide (III) with potassium hydroxide and he proceeded[5] to study the isomerization of the material over alumina at 380°. He obtained a small amount of 2,3-dihydro-1,4-pyran. For reasons which will not be discussed here Paul had expected the pyran as a rearrangement product of tetrahydromethylenefuran, but he showed later[6] that the compound he started with was not I but its isomer II. He demonstrated the easy isomerization of I into II and was able to identify each by ozonolysis.

In the present work using Paul's method but in tetrahydrofurfuryl alcohol as medium, his yield of 50–55% has been raised to 89%.[6] The olefin, tetrahydro-2-methylenefuran (I), b.p. 98–99° (743-mm.), is stable in the presence of bases at ordinary temperature, but on heating or in the presence of

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(1) Part XV, This Journal, **73**, 4803 (1951).

(2) This work was generously supported by the Quaker Oats Co. and the text is taken from a Ph.D. thesis (D.M.A.A.), Ohio State University. 1951.

(3) W. R. Kirner, This Journal, **52**, 3251 (1930).

(4) R. Paul, *Bull. soc. chim.*, [4] **53**, 417 (1933).

(5) R. Paul, *ibid.*, [5] **2**, 745 (1935).

(6) R. Paul and S. Tchelitcheff, *ibid.*, [5] **17**, 520 (1950). Recently M. F. Ansell and D. A. Thomas (*J. Chem. Soc.*, 1163 (1958)) have obtained 68% yield from tetrahydrofurfuryl chloride in diethylene glycol as solvent.