[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF MOUNT HOLYOKE COLLEGE]

The Ultraviolet Absorption Spectra of Some Derivatives of Uracil

BY JANET EVANS AUSTIN

In uracil there are two —NH—CO— groups which are capable of existing in either the lactim or the lactam form. Derivatives of uracil which have been shown definitely to exist in one or the other of these configurations have been known for some time and the compounds recently synthesized by Hilbert[1] in which one group is known to be in the lactim, the other in the lactam form, offer an excellent opportunity for the study of the tautomerism of this series by means of absorption spectra.

The spectra of a number of uracil derivatives in which the 6-position is substituted by a phenyl group have already been determined[2] but as far as the author is aware no series of compounds in which the 6-position does not contain a substituent group has been investigated, and since the phenyl group undoubtedly has some effect on the absorption, a study of the simpler derivatives should be of value in the study of the more complicated ones. Accordingly, the spectra of a number of relatively simple uracil derivatives have been measured in the region 32,000 to 46,000 cm.$^{-1}$. The results indicate that the tautomeric group in the 1,2-position of uracil is in the lactim form, that in the 3,4-position in the lactam form.

Experimental Part

The 3-methyluracil, which was part of a sample prepared by Dr. A. Walti several years ago, was secured through the generosity of Dr. P. A. Levene, and the 3-benzyl-5-methyluracil was supplied by Dr. T. B. Johnson. Since there was enough of each of these compounds to permit further purification, they were recrystallized from the spectroscopically pure ethyl alcohol[3] used as solvent throughout. All the other compounds were prepared by Dr. G. E. Hilbert. The samples used were portions of his analyzed specimens and therefore had the same physical properties as those reported.[1] They were used without further purification since only limited amounts of them were available.

Whenever possible solutions of the solid compounds were made exactly 0.01 *M* and diluted to the degree required by the intensity of their absorption (0.0002, 0.0001, or 0.00002 *M*). The original solutions of hydrouracil and uracil were made 0.002 and 0.001 *M*, respectively, because of their limited solubility, while those of 1,2-dihydro-2-keto-1-tetraacetylglucosido-4-methoxypyrimidine and 1,2-dihydro-2-keto-1-methyl-4-ethoxypyrimidine were made 0.001 and approximately 0.002 *M*, respectively, because of the limited quantities available. Since it is difficult to make solutions of the liquid compounds exactly 0.01 *M*, solutions of approximately this strength whose concentrations were accurately known were used.

The absorption spectra were determined as in previous work[2] by the photographic method of comparison spectra, the only innovation being the use of the copper spark in determining the spectra of 1-methyluracil, 3-methyluracil and hydrouracil.

The extinction coefficients were calculated from the formula

$$\epsilon = \frac{0.9}{cd} \log \frac{T}{T_0}$$

in which 0.9 is a constant depending on the properties of the photographic plate, c is the concentration of the compound in moles per liter of solution, d is the thickness of the absorbing column through which the light passes, and T and T_0 are the times of exposure of the solution and of the pure solvent, respectively. T_0 was 10 seconds throughout; T, 40 or 60 seconds. d was varied from 0.2 to 8 cm.

The curves are based on at least thirty-five experimental points, and for the deepest bands in some cases as many as eighty-five. The points are given for one curve to show their distribution but are omitted from the others to avoid confusion.

Discussion of Results

A few general relationships are quite apparent. As in the case of the closely related substituted hydantoins[4] and 6-phenyluracils,[2] the position of the absorption band depends on the position of the substituent groups in the molecule but is quite independent of the nature of these groups. Thus, all the compounds which have substituents in the 1 and 3 positions: 1,3-dimethyl- (Fig. 1, Curve II), 1,3-diethyl-, 1-methyl-3-ethyl-, 1-methyl-3-benzyl- and 1-benzyl-3-methyluracil (Fig. 3, Curves I, II, III and IV) have a maximum of absorption at 37,800 cm.$^{-1}$; those with 2,4 substitution: 2,4-dimethoxy- (Fig. 1, Curve IV) and 2,4-diethoxypyrimidine (Fig. 2, Curve IV) have a maximum at 38,800 cm.$^{-1}$; and those with 1,4 substitution: 1,2-dihydro-2-keto-1-methyl-4-methoxy- (Fig. 1, Curve III), 1,2-dihydro-2-keto-1-methyl-4-ethoxy- (Fig. 2, Curve III), and 1,2-dihydro-2-keto-1-tetraacetylglucosido-4-methoxypyrimidine (Fig. 4,

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[1] Hilbert, *Science*, **69**, 1796 (1929); THIS JOURNAL, **52**, 2001 (1930).

[2] Evans, *ibid.*, **54**, 641 (1932).

[3] Castille and Henri, *Bull. soc. chim. biol.*, **6**, 301 (1924).

[4] Carr and Dobbrow, THIS JOURNAL, **47**, 2961 (1925); Carr, Report at the Richmond meeting of the American Chemical Society, April, 1927; Hahn and Evans, THIS JOURNAL, **50**, 806 (1928); Hahn and Dyer, *ibid.*, **52**, 2505 (1930).

Curve II) have a maximum at 36,400 cm.$^{-1}$. Even the intensity of the maximum is much the same within a group with the exception of 1,2-dihydro-2-keto-1-tetraacetylglucosido-4-methoxyuracil and 1-benzyl-3-methyluracil whose absorptions are more intense than those of the other compounds having the same type of substitution. In both these cases the substituent in the 1-position is a heavy group containing absorbing groups (—COOR and C_6H_5—) and this may be the cause of the increase in intensity.

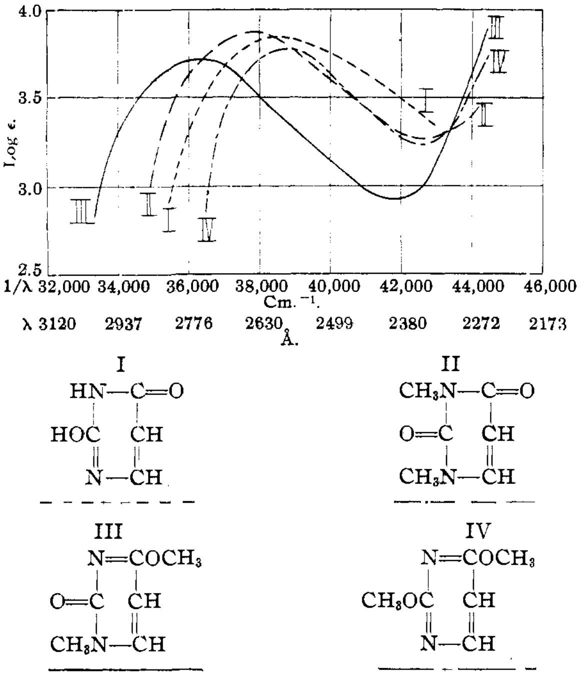

Fig. 1.

The curves of the unsubstituted uracil[5] (Fig. 1, Curve I) and of 3-methyluracil (Fig. 2, Curve I) are practically identical (max. 38,800 cm.$^{-1}$, log ϵ = 3.8). Also, the maximum of the curve of 3-benzylthymine (3-benzyl-5-methyluracil) occurs at the same frequency, 37,800 cm.$^{-1}$, as that found by Heyroth for thymine.[6] That is, substitution of a group in the 3-position produces little if any change in the absorption, and since the absorption is believed to depend on the general structure of the molecule, the structures of uracil and of 3-methyluracil appear to be identical. This means that in uracil the hydrogen of the 3,4 tautomeric group is predominately in the 3-position. Carr, Ho and Wadmond[7] came to the same conclusion from the fact that the absorption of a 6-phenyltetrahydropyrimidine, which has two hydrogen atoms (with no possibility of enolization) in place of the oxygen in the 4-position, is identical with that of 6-phenyluracil, indicating that they must have the same ring structure.

On the other hand, when a substituent is introduced into the 1-position, the absorption curve of the substance is distinctly different from that of uracil. The curves for the five 1,3-disubstituted compounds (Fig. 1, Curve II, and Fig. 3) are all quite similar to that of 1-methyluracil (Fig. 2, Curve II) although the band of the latter is more persistent. This similarity in absorption between the 1,3-disubstituted and the 1-monosubstituted compounds would indicate that the change in absorption from that of uracil and the 3-substituted compounds may be due to some structural change related to substitution in the 1-position.

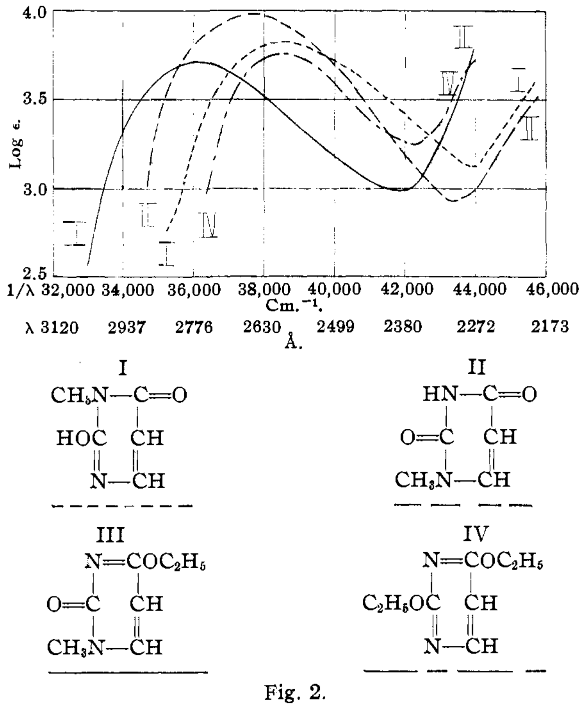

Fig. 2.

The maxima of the curves of 2,4-dimethoxy- (Fig. 1, Curve IV) and 2,4-diethoxypyrimidines (Fig. 2, Curve IV) occur at the same frequency as that of uracil. However, they are considerably

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[5] The position of this curve for uracil is the same as that found by Heyroth and Loofbourow [THIS JOURNAL, **53**, 3441–3453 (1931)] although the extinction coefficient at the maximum is somewhat less. The two determinations were made in different solvents, water and alcohol, and this may account for the difference in the extinction coefficients.

[6] Report at the Washington meeting of the American Chemical Society, March, 1933; Heyroth and Loofbourow, THIS JOURNAL, **56**, 1728 (1934).

[7] Report at the Chicago meeting of the American Chemical Society, September, 1933.

narrower, somewhat less persistent, and the frequencies of the minima are about 2000 cm.$^{-1}$ less than that of uracil. The two types of compounds therefore cannot be considered as having the same ring structure. The two dialkoxypyrimidines must have three double bonds, or their equivalent, in the ring and be similar in structure to pyrimidine itself. Their absorption bands do not coincide with those of pyrimidine, but their maxima are in the same position as those of dichloropyrimidine and dichloromethylpyrimidine, 38,800 cm.$^{-1}$.[6] This effect is apparently due to the weight of the alkoxy groups and is similar to that produced by the substitution of two methoxy groups in benzene since the absorption band of veratrole (o-$C_6H_5(OCH_3)_2$) is shifted about 3000 cm.$^{-1}$ toward the lower frequencies from that of benzene and the extinction coefficients are increased considerably.[8]

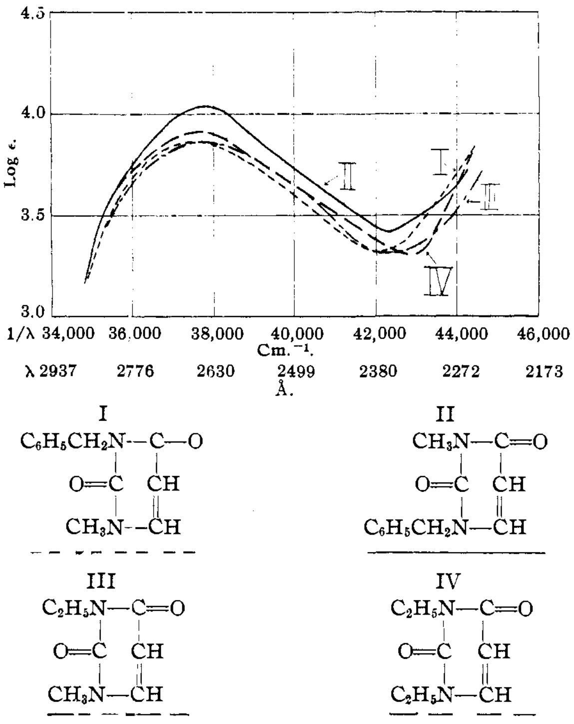

Fig. 3.

That uracil does not exist in the 2-keto-4-hydroxy form may be inferred from the difference in position and form of its curve (Fig. 1, Curve I) from those of the 1-R-4-OR derivatives (Fig. 1, Curve III, and Fig. 2, Curve III). The latter are shifted farther toward the red than any of the other compounds and their bands are very much more persistent.

In the light of these relationships it seems reasonable to conclude that the change in shape of the curves of uracil and 3-methyluracil from those of pyrimidine and the dialkoxypyrimidines is connected with the appearance of a carbonyl group in the 4-position, and that the shift of the position of the curves of the compounds which have substituents in the 1-position toward the visible part of the spectrum from those of uracil and 3-methyluracil is connected with the appearance of a second carbonyl group in the 2-position. If this is true, the tautomeric group in the 1,2-position of uracil itself must exist predominantly in the lactim form, that in the 3,4-position in the lactam form. By analogy, 5- or 6-substituted uracils and 5-substituted hydantoins must have the same configuration.

The frequency at the maximum of the curve of the 5,6-dihydrouracil (Fig. 4, Curve III) is the same as that of uracil and the width of the band is nearly the same although the intensity is much less. Since the reactions involving the tautomeric groups of the 5,6-dihydrouracils are similar to those of uracil, their structure is probably similar to that of uracil.

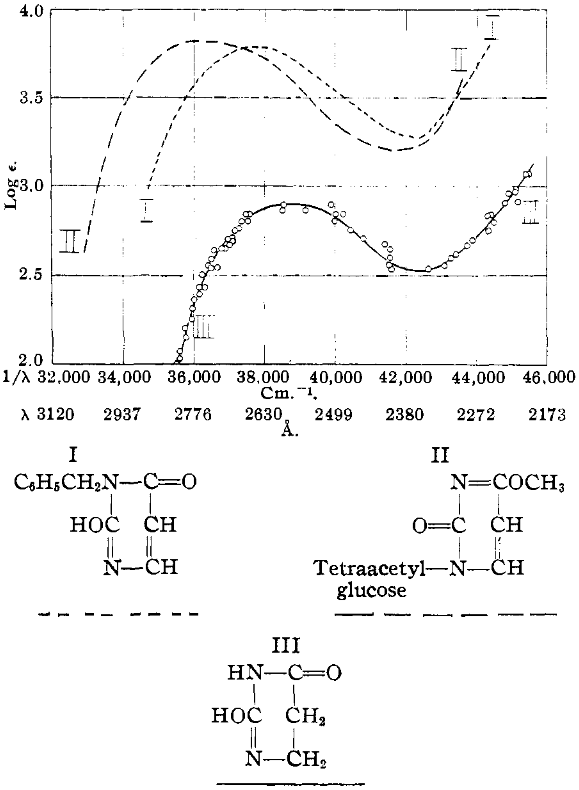

Fig. 4.

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(8) "I. C. T.," Vol. V, p. 372, Fig. 67.

The author is indebted to Dr. G. E. Hilbert, Dr. T. B. Johnson and Dr. P. A. Levene for the samples of the compounds examined, to Dr. F. F. Heyroth for lending the graphs of his absorption curves to facilitate replotting them for comparison, and to Dr. Emma P. Carr for her help throughout the investigation.

Summary

1. The absorption spectra of uracil, 1-methyluracil, 3-methyluracil, 1,3-dimethyluracil, 1,3-diethyluracil, 1-methyl-3-ethyluracil, 1-methyl-3-benzyluracil, 1-benzyl-3-methyluracil, 1,2-dihydro-2-keto-1-methyl-4-methoxypyrimidine, 1,2-dihydro-2-keto-1-methyl-4-ethoxypyrimidine, 1,2-dihydro-2-keto-1-tetraacetylglucosido-4-methoxypyrimidine, 2,4-dimethoxypyrimidine, 2,4-diethoxypyrimidine, 3-benzyl-5-methyluracil and 5,6-dihydrouracil have been determined for the region 32,000 to 46,000 cm.$^{-1}$.

2. The absorption curves for these compounds indicate that the absorption spectra depend upon the position of the substituent in the molecule and are only slightly dependent upon the nature of the substituent.

3. From the spectrographic evidence it appears that the tautomeric group in the 1,2-position of uracil in alcohol solution, and by analogy in hydantoin, exists predominantly in the lactim form, that in the 3,4-position in the lactam form.

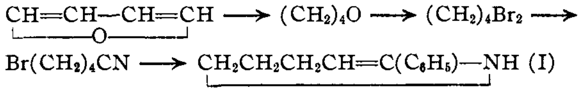
SOUTH HADLEY, MASS. RECEIVED JULY 13, 1934

[CONTRIBUTION FROM THE WALKER LABORATORY OF THE RENSSELAER POLYTECHNIC INSTITUTE]

The Formation of Alpha-Phenyltetrahydropyridine by the Action of Phenylmagnesium Bromide on Delta-Bromovaleronitrile[1]

BY JOHN B. CLOKE AND OSBORN AYERS

Some time ago a method was described for the synthesis of α-substituted pyrrolines by the action of Grignard reagents on γ-chlorobutyronitrile.[2] The present communication describes a method for the formation of α-substituted tetrahydropyridines by an extension of the same general reaction. Our α-phenyltetrahydropyridine (I) was obtained by means of the following transformations



$$\underbrace{\mathrm{CH{=}CH{-}CH{=}CH}}_{\mathrm{O}} \longrightarrow (\mathrm{CH_2})_4\mathrm{O} \longrightarrow (\mathrm{CH_2})_4\mathrm{Br_2} \longrightarrow$$
$$\mathrm{Br(CH_2)_4CN} \longrightarrow \underbrace{\mathrm{CH_2CH_2CH_2CH{=}C(C_6H_5){-}NH}} \text{ (I)}$$

Experimental Part

Reduction of Furan with the Raney Catalyst.—A mixture of 10 g. of nickel catalyst,[3] 100 g. of *n*-butyl alcohol and 100 g. of furan[4] was heated to 50° in an electrically heated bottle of a Burgess-Parr outfit and shaken with hydrogen until the pressure became practically constant. Distillation of the filtered solution gave, as a rule, 80% yields of the tetrahydrofuran of b. p. 63–67°.

1,4-Dibromobutane.—A part of the tetramethylene dibromide was obtained by the method of Smyth and Walls[5] and part as follows. A weight of 39 g. of red phosphorus was placed in a flask, which was immersed in ice water, and provided with a stirrer, condenser and dropping funnel; 400 g. of bromine was then added slowly to the well-stirred mixture, and this was followed by 54 g. of tetrahydrofuran, when the mixture was heated on a water-bath for half an hour. The separation and purification of the dibromide in the usual way gave a 53% yield.

δ-Bromovaleronitrile was prepared by the addition of 39 g. of potassium cyanide in 40 cc. of water to a boiling and well-stirred solution of 108 g. of 1,4-dibromobutane in 175 cc. of alcohol. The mixture was refluxed for about three hours, when the nitrile was purified by a procedure similar to that described by Allen[6] for γ-chlorobutyronitrile. The δ-bromovaleronitrile, which was obtained in a 33% yield, boiled at 110–111° at 11 mm. It possessed a density d_4^{20} of 1.3989 and a refractive index n_D^{20} of 1.47811, which correspond to a molecular refractivity (n^2) of 32.83 as compared with the calculated value of 32.75.

Anal. Calcd. for C_5H_8NBr: N, 8.64. Found: N, 8.72, 8.68.

α-Phenyltetrahydropyridine.—A Grignard reagent was prepared from 4.8 g. of magnesium, 100 cc. of ether and 31 g. of bromobenzene. To this reagent 16.1 g. of the δ-bromovaleronitrile in ether was added during the course of a half hour. The stirring and refluxing were then continued for a two and a half hour period, when the cooled solution was added slowly from a separatory funnel to 250 cc. of liquid ammonia, which was contained in a Dewar flask. When the ammonia had evaporated, the residue was extracted with ether. The extract was evaporated to 50 cc. and treated with a slight excess of aqueous hydro-

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(1) From a thesis presented by Osborn Ayers to the Rensselaer Polytechnic Institute in partial fulfilment of the requirements for the degree of Chemical Engineer.

(2) Cloke, THIS JOURNAL, **51**, 1174 (1929).

(3) Covert and Adkins, *ibid.*, **54**, 4116 (1932).

(4) Wilson, "Organic Syntheses," Vol. VII, 1927, p 40.

(5) Smyth and Walls, THIS JOURNAL, **54**, 2262 (1932).

(6) Allen, "Organic Syntheses," Vol. VIII, 1928, p. 52.