

64. *The Absorption Spectra of Organic Compounds containing Nitrogen. Part I. Derivatives of Hydantoin.*

By R. E. STUCKEY.

The absorption spectra of hydantoin and of 5:5'-dimethyl-, 1:5:5'-trimethyl-, and 3-methyl-hydantoin in acid and alkaline solution are given. Evidence from this source indicates that hydantoin in aqueous and alcoholic alkaline solution undergoes amido-imidol tautomerism involving the hydrogen of the 3-position. Substitution in the 3-position is therefore easily detected. The spectra of the analogous open-chain compounds, acetylurea and hydantoic acid, are compared with that of hydantoin and the effect of the introduction of nitro- and phenyl groups into the parent ring is reported.

THE interpretation of the broad bands present in the ultra-violet absorption spectra of many organic compounds in solution is still difficult, and the underlying doubt as to whether or not data relating to such bands are of fundamental significance detracts from the value of any conclusions drawn (cf. Morton and Stubbs, *J.*, 1940, 1347). Recently attempts have been made (Chako, *J. Chem. Physics*, 1934, 2644; Förster, *Z. Elektrochem.*, 1939, 45, 551) at mathematical treatment of such bands, and Bowen (*Ann. Reports*, 1943, 40, 12—29) has summarised evidence relating the absorption wave-length to electronic orbital changes. The treatments are somewhat complex even for simple molecules and perhaps of greater practical value at the present are semi-empirical studies of various chromophoric groupings in attempts to arrive at generalisations (cf., e.g., Booker, Evans, and Gillam, *J.*, 1940, 1453, and subsequent papers). The present paper is the first of a series in which the absorption spectra of a number of organic compounds containing nitrogen, and especially those derived from or containing the urea molecule, are to be studied.

In practically all such work the possibility of amido-imidol tautomerism, $\cdot\text{NH}\cdot\text{CO}\cdot \rightleftharpoons \cdot\text{N}\cdot\text{C}(\text{OH})\cdot$, has to be considered, and of particular interest is the effect of molecular environment on any changes in light absorption which may be associated with the tautomerism. Doubts have been expressed concerning the value of absorption spectra in assessing the molecular changes in such a system. For instance, although earlier work by Hartley and Dobbie (*J.*, 1899, 75, 640) gave definite indications that isatin had the pseudo-isatin or lactam structure, a re-examination of the spectra by Morton and Rogers (*J.*, 1925, 127, 2698; cf. Dabrowski and Marchlewski, *Bull. Soc. chim.*, 1933, 53, 946; Ault, Hirst, and Morton, *J.*, 1935, 1653) showed

that the curves were too close for any reliable conclusions to be drawn. Again, although Hantzsch (*Ber.*, 1931, **64**, 664; *Z. anorg. Chem.*, 1932, **209**, 213) held that all alkali salts of such compounds were in the imidol form $\cdot\text{C}(\text{OR})\cdot\text{N}\cdot$, yet views have been expressed, *e.g.*, by Ramart-Lucas and Grunfeld for benzamides (*Bull. Soc. chim.*, 1937, **4**, 478), and by Ley and Specker (*Ber.*, 1939, **72**, 192), doubting the validity of conclusions drawn from the absorption spectra of substances containing the $\cdot\text{CO}\cdot\text{NH}\cdot$ grouping, although the latter authors give values illustrating a shift towards longer wave-lengths on formation of a metal enol-salt in ordinary keto-enol tautomerism.

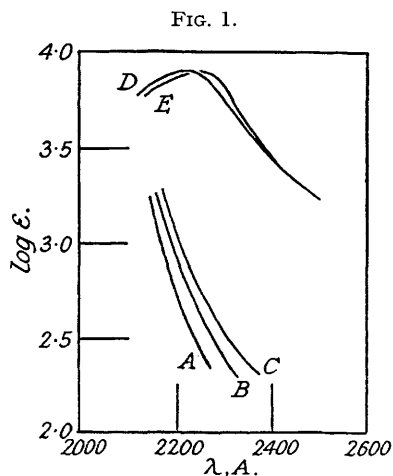
Nevertheless, if a further activating group is present, *e.g.*, in the case of the grouping $\cdot\text{CO}\cdot\text{NH}\cdot\text{CO}\cdot$, fairly clear cut changes in the absorption spectrum can be obtained as shown for uracil (Heyroth and Loofbourrow, *J. Amer. Chem. Soc.*, 1931, **53**, 3441) and other purines and pyrimidines, and for 5:5'-disubstituted barbituric acids (Fredholm, Thesis, Uppsala, 1939; Stuckey, *Quart. J. Pharm.*, 1941, **14**, 217; 1942, **15**, 377). Most of the hydantoin derivatives studied in the present paper contain this grouping.

The absorption spectrum of hydantoin was measured by Asahina (*J. Chem. Soc. Japan*, 1929, **4**, 202), using an old method, although the effect of pH was not noted and no numerical results were given. The results for the hydantoin derivatives studied are shown in Figs. 1—3 and in the table.

Absorption maxima and wave-lengths.

	$\lambda_{\text{max.}}$, A.	$\log \epsilon_{\text{max.}}$		$\lambda_{\text{max.}}$, A.	$\log \epsilon_{\text{max.}}$
Hydantoin			5:5'-Dimethylhydantoin		
In N/100-aqueous NaOH	2230	3.90	In N/100-aqueous NaOH	2230	3.88
In N/100-alcoholic NaOEt ...	2210	3.90	1:5:5'-Trimethylhydantoin		
1-Nitrohydantoin			In N/100-aqueous NaOH ...	2310	3.91
In water and N/100-aqueous			Acetylurea		
HCl	2310	3.95	In N/10-aqueous NaOH	2220	3.11
In N/100-NaOH	2450	4.00			

The end absorption shown by hydantoin (Fig. 1) is little different either in alcohol or in N/100-hydrochloric acid and under both conditions Beer's law is obeyed. In N/100-aqueous alkaline solution increased absorption is shown and a broad band develops having a peak at 2230 A. A similar band develops in solutions in alcoholic sodium ethoxide. It is to be expected, in accordance with modern theory, that tautomerism would follow ionisation (*e.g.*, on dilution) and therefore that the intensity of absorption in water would increase on dilution as with barbituric acid (Stuckey, *Quart. J. Pharm.*, 1942, **15**, 370). However, the small dissociation constant of hydantoin, $K_a = 7.59 \times 10^{-10}$ (Wood, *J.*, 1906, **89**, 1833), coupled with difficulties of measurements at wave-lengths less than 2200 A. and low extinction coefficient, made it difficult to realise any significant increase in absorption. The spectrum in M/400-aqueous solution therefore represents almost completely the un-ionised form.



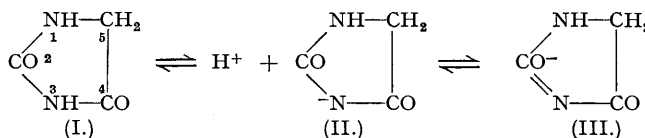
A, Hydantoin in alcohol. B, Hydantoin in N/100 hydrochloric acid. C, Hydantoin, M/400 in water. D, Hydantoin in N/100 alcoholic sodium ethoxide. E, Hydantoin in N/100 aqueous sodium hydroxide.

5:5'-Dimethylhydantoin (Fig. 2) exhibits absorption which is in general very similar to that of the parent hydantoin, with the appearance of a peak in alkaline solution. This rules out the possibility of tautomerism: $\cdot\text{CH}_2\cdot\text{CO}\cdot \rightleftharpoons \cdot\text{CH}\cdot\text{C}(\text{OH})\cdot$ involving groups in positions 4 and 5 since it can be fairly assumed that the characteristic absorption associated with such a change would differ from that due to amido-imidol tautomerism involving positions 1 or 3.

In a similar manner the close comparison of the absorption of 1:5:5'-trimethylhydantoin (Fig. 2) with that of hydantoin and 5:5'-dimethylhydantoin eliminates position 1 from the tautomerism and indicates that the only remaining $\cdot\text{NH}\cdot$ group, *i.e.*, in the 3-position, must be the one involved, producing structures (II) and (III) from the parent hydantoin.

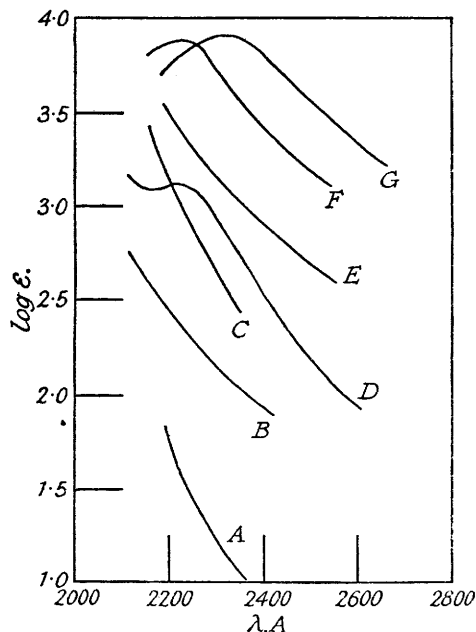
Confirmation was obtained by the preparation and examination of 3-methylhydantoin which did *not* show the increase in absorption on changing from ordinary aqueous to alkaline solution

common to the other hydantoin derivatives studied. This conclusion is in agreement with the electrometric titration results of Zief and Edsall (*J. Amer. Chem. Soc.*, 1937, **59**, 2245; cf.



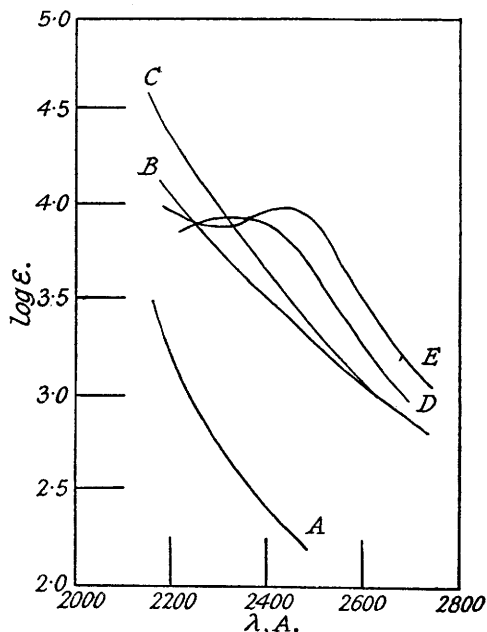
Pickett and McLean, *ibid.*, 1939, **61**, 423), who found that only the hydrogen in position 3 undergoes dissociation. The determination of absorption spectra thus affords a means of detecting substitution in the 3-position in the hydantoin ring.

FIG. 2.



- A, Hydantoinic acid in water, N/100-hydrochloric acid, and N/100-sodium hydroxide. B, Acetylurea in water and N/10-hydrochloric acid. C, 5:5'-Dimethylhydantoin in water and N/100-hydrochloric acid. D, Acetylurea in N/10-sodium hydroxide. E, 1:5:5'-Trimethylhydantoin in water and N/100-hydrochloric acid. F, 5:5'-Dimethylhydantoin in N/100-sodium hydroxide. G, 1:5:5'-Trimethylhydantoin in N/100-sodium hydroxide.

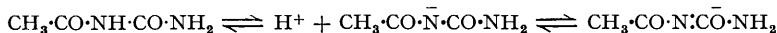
FIG. 3.



- A, 3-Methylhydantoin in water, N/100-hydrochloric acid, and N/100-sodium hydroxide. B, 5:5'-Diphenylhydantoin in water and alcohol. C, 5:5'-Diphenylhydantoin in water and alcohol. D, Nitrohydantoin in water and N/100-hydrochloric acid. E, Nitrohydantoin in N/100-sodium hydroxide.

The peak absorption of hydantoin in alkaline solution is comparable to that developing in alkaline solutions of 5:5'-disubstituted barbituric acids, where the urea group amido-imidol tautomerism also occurs. Thus diethylbarbituric acid showed $\log \epsilon_{\text{max.}} = 3.94$ at 2460 Å. (Stuckey, *Quart. J. Pharm.*, 1942, **15**, 381). The end absorptions of both hydantoin and diethylbarbituric acid indicate the possibility of a peak absorption, similar to that in alkali, occurring in acid solution at wave-lengths *ca.* 2000 Å. and thus not realisable under the experimental conditions used. This indicates the possibility that the effect of the tautomeric amido-imidol change on absorption spectrum is merely to shift the peak to longer wave-lengths.

Open-chain compounds analogous to hydantoin include acetylurea and hydantoinic acid. The spectrum of acetylurea (Fig. 2) shows an increased and selective absorption in aqueous alkaline solution together with a shift to longer wave-lengths, and by analogy with hydantoin a urea-type amido-imidol tautomerism is indicated:



Both acid and alkaline spectra for this substance are at a lower level than in those for hydantoin and evidently ring formation in the latter compound is responsible for a big increase in absorption ca. 2200 Å.

Hydantoic acid, $\text{NH}_2\cdot\text{CO}\cdot\text{NH}\cdot\text{CH}_2\cdot\text{COOH}$ (see Fig. 2), shows the end absorption characteristic of amino-acids and has the same spectrum in alkaline as in acid solution, indicating the absence of tautomerism in aqueous solution. In this compound there is no $\cdot\text{CO}\cdot\text{NH}\cdot\text{CO}\cdot$ grouping, and it is evident that in the type of compounds studied the group $\cdot\text{CO}\cdot\text{NH}\cdot$ needs a further activating influence before amido-imidol tautomerism occurs in aqueous solution.

The introduction of two phenyl groups in the hydantoin ring, producing 5 : 5'-diphenyl-hydantoin, causes a general increase in absorption both in water and in acid and alkaline aqueous solution, although a characteristic acid-alkaline shift indicating tautomerism is still shown (Fig. 3).

Franchimont and Klobbie (*Rec. Trav. chim.*, 1888, **7**, 12) first prepared nitrohydantoin by the action of nitric acid on hydantoin and assigned to it the structure of 1-nitrohydantoin on the general rule that nitration occurred at the $\cdot\text{NH}\cdot$ group adjacent to CH_2 , verification being obtained from ring-splitting experiments. A study of the absorption spectrum (Fig. 3) yields further confirmation of this structure in that 1-nitrohydantoin shows a shift towards the red on passing to alkaline solution, thus indicating tautomerism. Since tautomerism still occurs, the nitro-group cannot have entered the 3-position. The action of nitric acid on 5 : 5'-dimethyl-hydantoin produced a nitro-derivative, 1-nitro-5 : 5'-dimethylhydantoin, but 1-methylhydantoin failed to nitrate under the same conditions. The nitro-group must therefore have entered the 1-position. Further spectroscopic evidence of this may be adduced from the fact that a 5-nitrohydantoin would possess the grouping $\cdot\text{CH}\cdot\text{NO}_2$ and might be expected to show tautomerism producing $\cdot\text{C}\cdot\text{NO}\cdot\text{OH}$ accompanied by a radical difference in the spectrum change. The introduction of the nitro-group into hydantoin causes in general a shift of absorption to longer wave-lengths, so that a peak can now be realised in acid solution. This strengthens to some extent the possibility mentioned above that tautomeric amido-imidol change in this type of compound is accompanied merely by a shift of the absorption spectrum to longer wave-lengths without significant change in the value of ϵ_{max} .

EXPERIMENTAL.

Absorption Spectra.—Determinations of absorption spectra were made with a Hilger medium quartz spectrograph and Spekker photometer using a condensed spark between tungsten-steel electrodes as the normal light source. Difficulty was experienced in getting satisfactory blackening of the photographic plate below 2300 Å. unless an inconveniently long exposure was used. To some extent the use of Ilford Q Plates with uranium-copper electrodes helped to solve this problem. The molecular extinction coefficient ϵ is defined by the relation $\log_{10} I_0/I = \epsilon cl$, where c is the molar concentration, l the length of tube in cm., and I_0 and I are the intensities of incident and transmitted light.

Preparation of Compounds.—Owing to the possibility of tautomerism, unequivocal methods of preparation were essential for the methylated hydantoin. Compounds not specifically mentioned were purified by recrystallisation from alcohol before determination of their light absorption.

1 : 5 : 5'-Trimethylhydantoin. Biltz and Slotta (*J. pr. Chem.*, 1926, **113**, 240) prepared this substance from α -methylaminoisobutyronitrile via *N*-methyl-*N*-(α -cyanoisopropyl)urea and record it as difficult to crystallise, giving no m. p. It was found that, after removal of water by several evaporations with absolute alcohol, the substance crystallised from this solvent and had m. p. 160° (corr.) (Found : C, 50.7; H, 7.0. Calc. for $\text{C}_8\text{H}_{10}\text{O}_2\text{N}_2$: C, 50.1; H, 7.0%).

5 : 5'-Dimethylhydantoin was prepared similarly from α -aminoisobutyronitrile and crystallised from absolute alcohol. Methylation of hydantoin in sodium hydroxide solution with methyl sulphate was used for the preparation of 3-methylhydantoin, the constitution of the product having previously been established (Biltz and Slotta, *loc. cit.*; Harries and Weiss, *Annalen*, 1903, **327**, 355).

1-Nitro-5 : 5'-dimethylhydantoin. 5 : 5'-Dimethylhydantoin (1.0 g.) and concentrated nitric acid (10 c.c.) were evaporated to a syrup on a water-bath. After cooling, absolute alcohol (20 c.c.) was added, the mixture boiled and filtered, and the filtrate evaporated to crystallisation. Recrystallisation from absolute alcohol gave white crystals, m. p. 143–144° (not sharp) (Found : C, 33.9; H, 4.2. $\text{C}_8\text{H}_9\text{O}_4\text{N}_3$ requires C, 34.7; H, 4.1%). At temperatures above the m. p. decomposition occurred with the evolution of bubbles of gas. The compound is sparingly soluble in alcohol, but soluble in water.

1-Nitrohydantoin was prepared following the method of Franchimont and Klobbie (*loc. cit.*).