265–270°.[10] The aniline salt of phenylcarbamic acid, $C_6H_5NHCOOH \cdot H_2NC_6H_5$, might be stable even in the presence of water under carbon dioxide pressure. This salt might be capable of rearranging under the combined agencies of heat and carbon dioxide pressure to give the aniline salt of anthranilic acid in analogy to the reported results with the potassium salt. This mechanism appears consistent with the observed lower conversions in the presence of aluminum chloride and aniline hydrochloride. Other possible intermediates in the transformation to the quinazolinedione are indicated in the diagram.

(10) N. W. Hofmann, *Ber.*, **18**, 764 (1885). Triphenyl isocyanurate, m.p. 275°, was prepared by heating phenyl isocyanate (5 moles) with potassium acetate (1 mole) at 100°.

Acknowledgments.—The authors are pleased to acknowledge the assistance given by Dr. N. E. Searle who supplied known samples of *sym*-di-*o*-tolyl- and di-*p*-tolylurea. We would like to thank Drs. W. W. Prichard, E. L. Jenner, J. R. Roland and A. L. Barney, and Messrs. A. W. Larchar, H. S. Young and P. J. Rennolds for stimulating discussions and helpful suggestions.

WILMINGTON, DELAWARE

[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

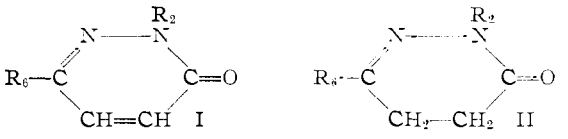
Absorption Spectra of Heterocyclic Compounds. VII.[1] Some 3(2H)-Pyridazones

BY EDGAR A. STECK AND FREDERICK C. NACHOD

RECEIVED MARCH 2, 1957

The absorption spectra of a series of 3-pyridazones have been reported and interpreted.

Pyridazine derivatives may be considered to contain a potential hydrazine unit in the 1,2-diazine ring and hence are not readily obtainable from biochemical transformations involving nitrogen. In fact, this ring system has not been found to occur in natural products, a sharp distinction from the other diazines. This heterocyclic type has not been investigated as thoroughly as the pyrimidines and pyrazines, and relatively few reports of physicochemical studies on pyridazines have appeared in the literature.[2-14] Some work has been done[3,9,13] on the absorption spectra of 3(2H)-pyridazones, which are cyclic hydrazones. Our interest in the 6-substituted 3(2H)-pyridazones as chemotherapeutic agents[15,16] and intermediates for the preparation of other potential pharmaceuticals has led us to study the absorption spectra of this type (I) and also the related 4,5-dihydro compounds II.



The range of structures which may be chosen for 3(2H)-pyridazones and related dihydro compounds is limited sharply by the non-equivalence of the two formulas possible for pyridazine.[5,7] Thus, comparison of the absorption spectra of 6-phenyl-3(2H)-pyridazone (I, R_2 = H, R_6 = C_6H_5) with those of 2-methyl-6-phenyl-3-pyridazone (I, R_2 = CH_3; R_6 = C_6H_5) and 3-methoxy-6-phenylpyridazine (III) clearly substantiates the formulation of the first-mentioned compound as (I). The spectra of the three compounds in 95% ethanol are shown in Fig. 1.

III

Absorption spectra of 6-(2-thienyl)-3(2H)-pyridazone and the related 4,5-dihydro compound in 95% ethanol, 0.01 *N* sodium hydroxide and 0.01 *N* hydrochloride are presented in Fig. 2. 4,5-Dihydro-6-(2-thienyl)-3(2H)-pyridazone shows little difference in pattern of spectra in the three solvents. While the spectra of 6-(2-thienyl)-3(2H)-pyridazone in ethanol and acid are identical, the absorption in basic solutions is more closely related in effect to those obtained with the dihydro compound. This indicates that the sodium enolate, which may be formed through keto-enol tautomerism in this type of the pyridazone, is more or less closely related to the dihydropyridazone (*cf.* ref. 13). However, the behavior in neutral or acid solution shows that 6-(2-thienyl)-3(2H)-pyridazone may not exist in keto form (in those solvents) as evident by comparison of Fig. 2 with Fig. 1.

In Table I, the comparison of spectral absorption of 6-substituted 3(2H)-pyridazones in neutral, alkali and acid solutions is presented. A chlorine in the *p*-position of the phenyl group produced a slight batho- and hyperchromic effect, this being more pronounced when ethanol was the solvent. This behavior is not unexpected, nor was a similar one in the case of the 6-(2-thienyl)-3(2)-pyridazone

(1) Previous contribution: E. A. Steck, F. C. Nachod and G. W. Ewing, THIS JOURNAL, **71**, 2334 (1949).

(2) M. G. Korshun and C. Roll, *Bull. soc. chim.*, [4] **39**, 1223 (1926).

(3) D. Biquard and P. Grammaticakis, *ibid.*, [5] **7**, 766 (1940).

(4) W. Hückel and W. Jahnentz, *Ber.*, **74**, 652 (1941); **75**, 1438 (1942).

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(15) E. A. Steck, U. S. Patent 2,624,730.

(16) E. A. Steck, R. P. Brundage and L. T. Fletcher, THIS JOURNAL, **75**, 1117 (1953); (b) to be published.

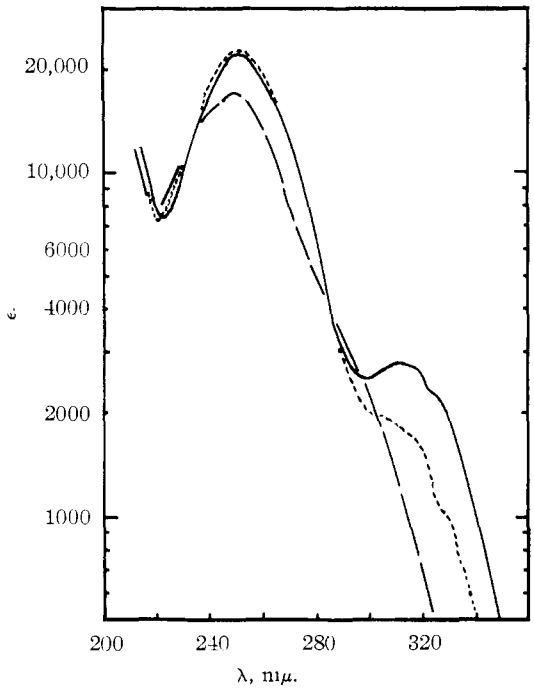


Fig. 1.—Absorption spectra in 95% ethanol of: - - - - -, 6-phenyl-3(2H)-pyridazone; — —, 3-methoxy-6-phenylpyridazine; ——, 2-methyl-6-phenyl-3(2H)-pyridazone.

and its bromo derivative (*cf.* ref. 17). In the substitution of the nucleophilic nitro group in the *m*-position, there is less effect than noted with the *p*-halogen type, and a slight hypochromic shift results (*cf.* ref. 17).

Table II summarizes significant aspects of the absorption spectra of 6-substituted 4,5-dihydro-3(2H)-pyridazones obtained in ethanolic, basic and acidic solutions. The general interrelationships in these cases were of the same character as observed for the 6-substituted 3(2H)-pyridazones.

(17) E. A. Steck, G. W. Ewing and F. C. Nachod, THIS JOURNAL, 71, 238 (1949).

TABLE I

ABSORPTION SPECTRA OF 6-SUBSTITUTED-3(2H)-PYRIDAZONES

6-Substituted-3-(2H)-pyridazone	Solvent[a]	Maxima[b] λ	Maxima[b] ε × 10³	Minima[b] λ	Minima[b] ε × 10³	Inflection[b] λ	Inflection[b] ε × 10³
6-Phenyl	E	253	22.0	220	8.3	300	2.0
	B	265	17.0	225	11.3	300	4.3
	A	249	23.0	221	7.2	295	2.2
6-(4-Chloro-phenyl)	E	257	27.5	226	8.7	300	2.5
	B	265	20.0	232	9.9	305	5.7
	A	255	27.1	224	7.5	295	3.0
6-(3-Nitro-phenyl)	E	250	23.5	217	13.2		
	B	265	22.5	241	12.3		
	A	245	24.5	217	13.6		
6-(2-Thienyl)	E	270	16.0	232	3.9		
	B	293	13.5	235	5.1	270	10.0
	A	268	15.8	230	4.1		
6-(5-Bromo-2-thienyl)	E	318	16.9	235	3.7		
	B	318	17.6	238	4.0		
	A	319	16.2	235	3.5		

[a] Legend: E, ethanol; B, 0.01 *N* NaOH; A, 0.01 *N* HCl. [b] Wave length in mμ; ε × 10³, extinction values.

It may be noted that the dihydro compounds exhibit bathochromic and hypsochromic displacement with respect to the related 3(2H)-pyridazones. This is a consequence of the fact that a greater number of contributors may be formulated for the dihydro type which contain conjugation permissible for such a system having non-equivalence of structural forms.

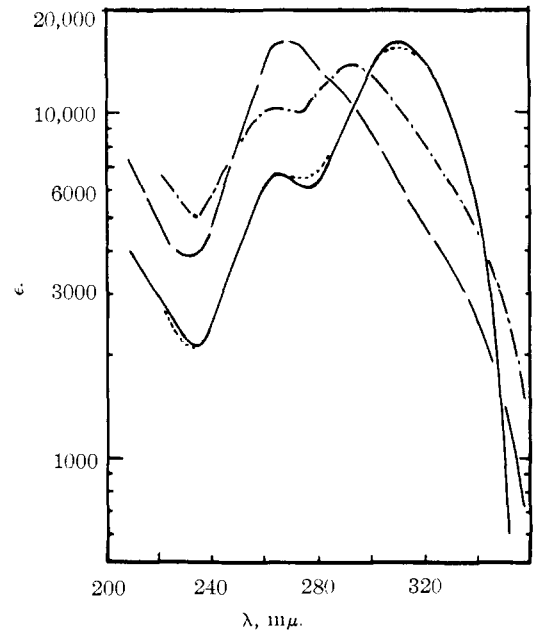


Fig. 2.—Absorption spectra of 6-(2-thienyl)-4,5-dihydro-3-(2H)-pyridazone: —, in 95% ethanol; - - - -, in 0.01 *N* NCl and 0.01 *N* NaOH; 6-(2-thienyl)-3(2H)-pyridazone; — —, in 95% ethanol and 0.01 *N* NCl; —·—·—, in 0.01 *N* NaOH.

TABLE II

ABSORPTION SPECTRA OF 6-SUBSTITUTED-4,5-DIHYDRO-3-(2H)-PYRIDAZONES

6 Substituted-4,5-dihydro-3(2H)-pyridazone	Solvent[a]	Maxima[b] λ	Maxima[b] ε × 10³	Minima[b] λ	Minima[b] ε × 10³
6-Phenyl	E	285	16.1	236	2.2
	B	280	16.8	232	2.3
	A	280	16.0	232	2.3
6-(4-Chlorophenyl)	E	290	19.0	240	2.6
	B	285	19.2	235	2.7
	A	285	19.2	235	2.9
6-(3-Nitrophenyl)	E	274	18.8	236	7.3
	B	274	20.4	232	6.4
	A	274	20.6	234	6.6
6-(2-Thienyl)	E	310	15.5	235	2.2
	B	311	15.1	235	2.3
	A	311	15.4	235	2.1

[a,b] Legend as in Table I.

Table III contains information on the salient features of the absorption spectra of certain 2,6-disubstituted 3-pyridazones. Among the simpler representatives of the group, *viz.*, 2-methyl-6-phenyl-3-pyridazone and the related 2-(4-chlorophenyl) compound, the spectra in ethanol (in particular) show the expected patterns resulting from increased conjugation. A maximum was found in the short-wave range when alcoholic

TABLE III

ABSORPTION SPECTRA OF VARIOUS 6-SUBSTITUTED POLYHYDRO-3(2H)-PYRIDAZONES

6-Substituent	Polyhydro	Other substituent	Solvent[a]	Maxima[b] λ	Maxima[b] ε × 10³	Minima[b] λ	Minima[b] ε × 10³
Phenyl		2-Methyl	E	250	22.4	222	7.5
				309	2.8	298	2.5
			B	250	22.1	222	8.1
			A	250	22.0	222	7.9[f]
Phenyl		2-(4-Chlorophenyl)	E	240	23.8	297	2.9
				335	5.6		
			A[c,d]	240	23.2	220	11.6
				333	5.4	297	2.6
Phenyl	4,5-H_2	2-(4-Chlorophenyl)	E	260	15.6	233	8.7
				300	13.0	287	12.4
			B	236	12.5	269	5.5
				315	15.4	319	15.0
				333	16.1		
			A	255[e]	19.0	231	6.9
				287	11.0	260	9.8
			A[c]	260	14.7	233	7.2
				295	12.8	285	12.2
4-Chlorophenyl	4,5-H_2	2-(4-Chlorophenyl)	E	259	16.4	235	11.0
				303	15.8	282	13.5
			B	242	16.0	272	5.8[g]
				338	18.0		
			A	259	15.5	237	10.4
				303	15.5	280	13.2
2-Thienyl	4,5-H_2	2-(4-Chlorophenyl)	E	260	14.7	232	6.1
				322	15.0	290	7.6
			B	254	16.2	283	5.2[h]
				352	17.5		
			A	259	11.4	233	6.0
				317	15.3	284	7.1

[a,b] Legend as in Table I. [c] Alcoholic acid. [d] Not soluble in aqueous or alcoholic alkali. [e] Flat maximum. [f] Inflection at 300 mμ (3.0). [g] Inflection at 313 mμ (15.4). [h] Inflection at 310 mμ (9.7).

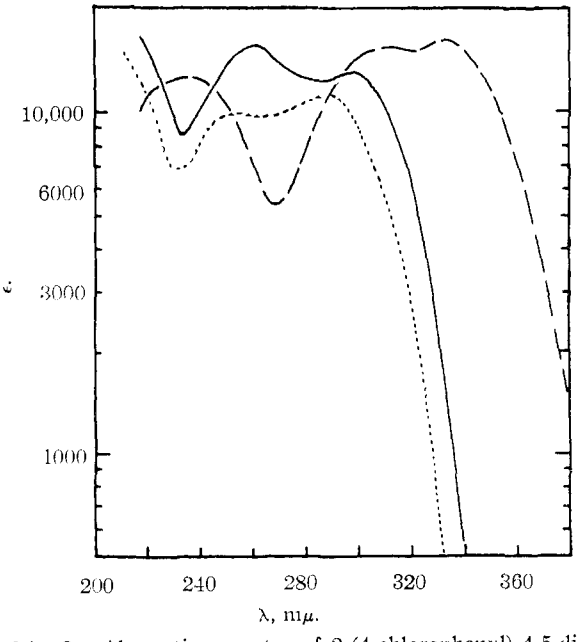
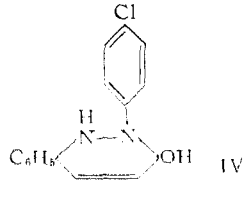


Fig. 3.—Absorption spectra of 2-(4-chlorophenyl)-4,5-dihydro-6-phenyl-3(2)-pyridazone; ——, in 95% ethanol; - - - -, 0.01 *N* HCl; — —, 0.01 *N* NaOH.

hydrochloric acid was used to dissolve 2-(4-chlorophenyl)-6-phenyl-3-pyridazone. The effect of varying the 6-substituent of 2-(4-chlorophenyl)-4,5-dihydro-3-pyridazones also was studied, with the substituent involved being a phenyl, a 4-chlorophenyl or a 2-thienyl group. Figure 3 gives detailed information on 2-(4-chlorophenyl)-4,5-dihydro-6-phenyl-3-pyridazone, with the spectra run in ethanol, base and acid. In the case of the 6-phenyl compound, it is to be noted that a marked bathochromic shift occurred when 0.01 *N* sodium hydroxide was used as solvent rather than ethanol or 0.01 *N* hydrochloric acid. This alteration is obviously a result of an increase in conjugation, possibly through formation of IV (as sodium salt). The presence of a 4-chlorophenyl or a 2-thienyl group in position 6 of the 2-(4-chlorophenyl)-4,5-dihydro-3-pyridazones did not lead to such definite spectral evidence. In each of these latter cases, there is an inflection in the region in which a bifurcation was found for the 6-phenyl compound (*cf.* Fig. 3). It is to be noted that the dihydro-3-pyridazones bearing a substituent in position 2 follow the general aspects found in 3(2H)-pyridazones, with the additional expected complexity.



IV

Experimental

The preparative aspects of the compounds studied have been reported in detail.[15,16] The ultraviolet absorption spectra were determined with a Beckman DU spectrophotometer using the technique described previously.[18]

Acknowledgment.—The assistance of Mrs. M. Becker is gratefully acknowledged.

(18) G. W. Ewing and E. A. Steck, THIS JOURNAL, **68**, 3181 (1946).

RENSSELAER, NEW YORK

[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

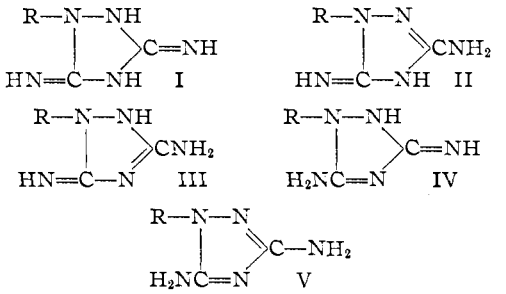
Absorption Spectra of Heterocycles. VIII.[1] Some Guanazole Derivatives

BY EDGAR A. STECK AND FREDERICK C. NACHOD

RECEIVED MARCH 9, 1957

The ultraviolet absorption spectra of several 1-arylguanazoles have been determined and their relation with structure treated. As a result of chemical and physical considerations, it has been suggested that 1-arylguanazoles be formulated as 3(5)-amino-1-aryl-5(3)-imino-1,2,4-triazolones (III) or (IV) rather than as 1-aryl-3,5-diimino-1,2,4-triazolidines (I).

The investigation of guanazole derivatives as potential pharmaceuticals[2] led to the preparation of certain 1-aryl-, 1-aryl-2-substituted and 1-aryl-3-substituted guanazoles which showed interesting structural aspects. Stollé and Dietrich[3] have noted that five structures (I-V) may be assigned to 1-substituted guanazoles, but no further treatment of this matter has been reported. The present discussion is based upon the ultraviolet absorption spectra of the 1-arylguanazoles and derivatives.



The reaction of arylhydrazines with cyanoguanidine might result in the formation of 1-arylguanazoles having several possible structures, as indicated by formulas I-V. These types represent the relationship of these 1,2,4-triazoles with guanidines and biguanides where arrangement of the atoms may be considered as being formed of two amidine groups. In these electrically neutral structures it is seen readily that the greatest degree of conjugation is present in V; forms III and IV show less conjugation, and no conjugation occurs in I and II. A study was made of the various proton donor and acceptor forms possible for those 1,2,4-triazole derivatives known as guanazoles; a summary of these considerations is shown in Table I. The contribution of the non-conjugated forms exceeds those of either conjugated type; this is in harmony with the experimental findings.

In Fig. 1 are shown the spectra of 1-phenylguanazole in acid, base and ethanol. For purposes of comparison, the spectrum of biphenyl in hexane[4] is also included since, as will be seen later in the case of 1-(4-xenyl)-guanazole (Fig. 3), there is a typical super-position of the component spectra in the solvent studied. It may be noted that the highest maximum in the spectrum of 1-phenylguanazole is attained in alcoholic solution. There is a related shift in the spectrum to longer wave lengths in neutral solution, whereas the spectra in solutions of both high and low *p*H are found to

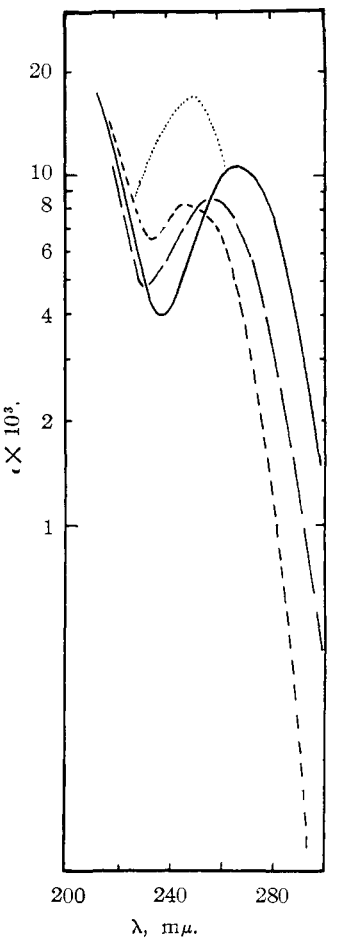


Fig. 1.—Absorption spectra of 5(3)-amino-3(5)-imino-1-phenyl-1,2,4-triazolone in: —, 95% ethanol; - - -, 0.01 *N* HCl; — —, 0.01 *N* NaOH; and . . . .biphenyl in *n*-hexane.

(1) Previous contributions, E. A. Steck and F. C. Nachod, THIS JOURNAL, **79**, 4408 (1957).

(2) E. A. Steck, R. P. Brundage and L. T. Fletcher, to be published.

(3) R. Stollé and W. Dietrich, *J. prakt. Chem.*, [2] **139**, 193 (1934).

(4) M. T. O'Shaughnessy and W. H. Rodebush, THIS JOURNAL, **62**, 2096 (1940).