to their butyl esters by the method of Gurin and Clarke.[5,20] After evaporation of the butyl alcohol as directed by these authors, the oil remaining was taken up in ether and precipitated by petroleum ether. The precipitate, on standing in the refrigerator, crystallized and was recrystallized from petroleum ether with alcohol added. The derivatives of glutamic and aspartic acids crystallized as silky needles (yield nearly quantitative), lysine also as silky needles (yield 20%), and proline as clear prisms (yield 50%). The arginine derivative was soluble in alcohol but insoluble in ether or petroleum ether. It has not been possible to cause this derivative to crystallize. The characteristics of these compounds are shown in Table II.

TABLE II

Amino acid	M. p. of de.iv., °C.	Analyses, % Calcd.	Found	Calcd.	Found
d-Glutamic acid[21]	61–62	N 3.39	3.19	S 7.76	7.89
l-Aspartic acid[22]	64–65	N 3.51	3.35	S 8.03	8.17
d,l-Lysine[23,24]	111–113	C 56.42	56.28[25]	H 6.71	6.50[25]
l-Proline[26]	53–55	C 59.03	58.85[25]	H 7.13	6.90[25]
d-Arginine	Oil				

(20) *Cf.* also Gurin, THIS JOURNAL, **58**, 2104 (1936).

(21) That is, di-*n*-butyl [N-*p*-toluenesulfonyl]-*d*-glutamate.

(22) That is, di-*n*-butyl [N-*p*-toluenesulfonyl]-*l*-aspartate.

(23) That is, *n*-butyl [α,ϵ-di-*p*-toluenesulfonylamino]-*n*-caproate.

(24) Product contained a trace of ash; analytical data corrected for this.

(25) Analysis made under the direction of Dr. O. P. Wintersteiner.

(26) That is, *n*-butyl [N-*p*-toluenesulfonyl]-*l*-pyrrolidine-α-carboxylate.

Acknowledgment.—One of us (E. W. M.) acknowledges with pleasure his indebtedness to: (1) Dr. H. B. Lewis, for the privilege of working in his laboratories at the University of Michigan, and for the gift of samples of several of the amino acids; (2) The Rockefeller Fund, an appropriation from which partly supported this investigation; (3) Dr. Wm. de B. MacNider, for the gift of a part of his research funds; (4) Dr. O. P. Wintersteiner, through whose courtesy certain of the analyses reported in Table II were made.

Summary

The *p*-toluenesulfonyl derivatives of nineteen amino acids have been prepared of which six have not been described previously. The *p*-toluenesulfonyl derivatives of aspartic acid, *d*-glutamic acid, *d,l*-lysine and *l*-proline did not crystallize. The non-crystalline derivatives, except tryptophane, were converted to their butyl esters and these crystallized, with the exception of arginine. The butyl esters of the derivatives of the four remaining amino acids are described for the first time in this paper.

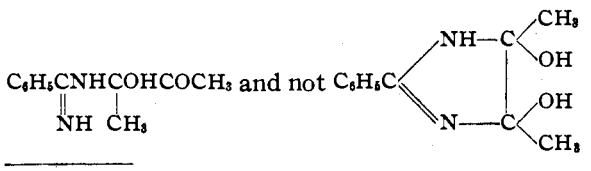
CHAPEL HILL, N. C. RECEIVED JANUARY 28, 1937

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF COLORADO]

The Structure of Benzamidine-glyoxal and of its Compounds with Aromatic Aldehydes

BY JOHN B. EKELEY AND ANTHONY R. RONZIO

In former papers[1] it has been shown that in alkaline solution aromatic amidines form addition products with glyoxal which can be isolated as the free bases or as their hydrochloride salts. In water solution the addition products are dissociated into amidine and glyoxal since from the solutions the osazone and dioxime of glyoxal can be obtained. We now have absorption spectra evidence which confirms this conclusion. We have exactly the same kind of evidence that the addition product from benzamidine and diacetyl



obtained by Diels and Schleich[2] is, like that of benzamidine-glyoxal, an open chain compound as they assumed.

Inspection of the absorption spectra curves for benzamidine hydrochloride, benzamidine-glyoxal and benzamidine-diacetyl confirms the above statements.

There has been described[1] a long series of compounds which were obtained by the action of aromatic aldehydes upon aromatic amidines and glyoxal in alkaline solution. From the evidence then at hand we assumed them to contain either a pyrimidine or a glyoxaline ring. Ruhemann and Cunnington[3] prepared derivatives from benzamidine and phenylpropiolic ester, one of which, diphenylglyoxalidone, a yellow compound, pos-

(1) Ekeley and Ronzio, THIS JOURNAL, **57**, 1353 (1935); Ekeley and Elliott, *ibid.*, **58**, 163 (1936).

(2) Diels and Schleich, *Ber.*, **49**, 1713 (1916).

(3) Ruhemann and Cunnington, *J. Chem. Soc.*, **75**, 954 (1899).

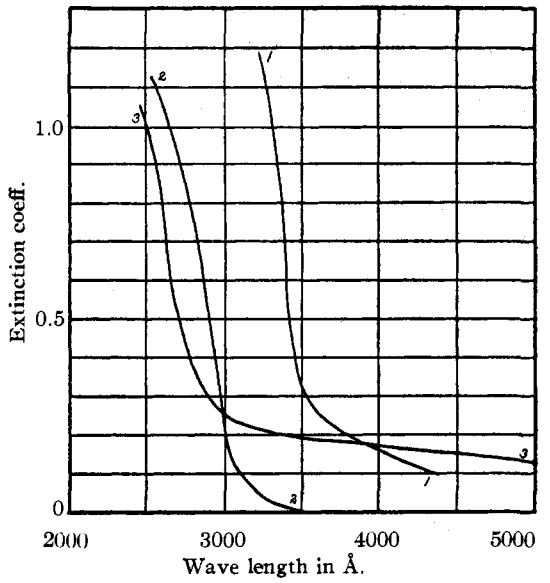


Fig. 1.—Curve 1, benzamidine·HCl·$2H_2O$, 0.0328 g./100 ml. of H_2O, 1-cm.cell; curve 2, benzamidine–glyoxal addition product, 0.00375 g./50 ml. of dioxane, 1-cm, cell; curve 3, benzamidine–diacetyl addition product, hydrochloride 0.00205 g./50 ml. of H_2O, 1-cm. cell.

sesses properties similar to the one obtained by us from benzaldehyde, benzamidine and glyoxal

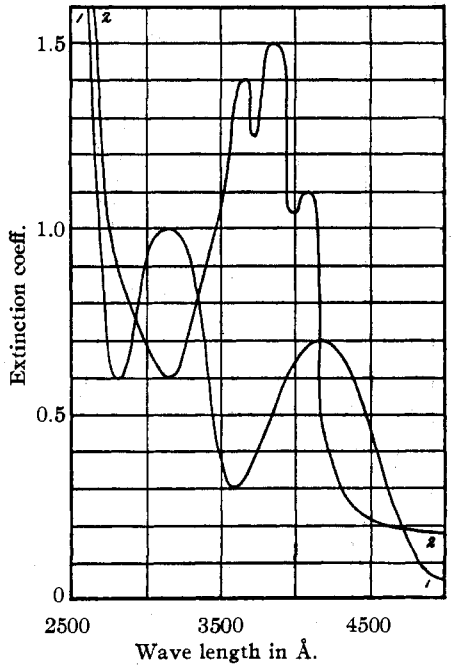


Fig. 2.—Curve 1, Ruhemann and Cunnington's glyoxalidone, 0.00090/50 ml. of KOH–95% E + OH soln., 1-cm. cell; curve 2, same, 0.00100 g./50 cc. of dioxane, 1-cm. cell.

The second compound they proved to be identical with Pinner's[4] diphenylhydroxypyrimidine. We have prepared these compounds and compared the absorption spectra curves obtained from them both in dioxane[5] and in dilute potassium hydroxide solution with the curves obtained from our benzaldehyde, benzamidine, glyoxal compound in the same solvents. The similarities between the curves from R. and C.'s glyoxalidone and those from our benzaldehyde-benzamidine–glyoxal compound are so very pronounced that we are forced to the conclusion that their structures are similar and that both have a glyoxaline ring in acid,

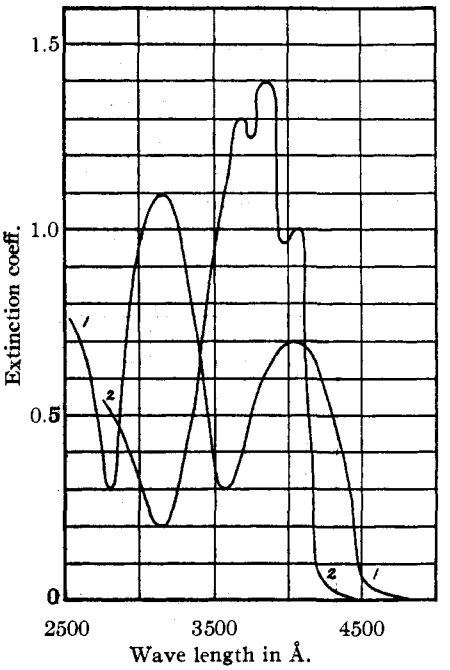


Fig. 3.—Curve 1, benzamidine–benzaldehyde–glyoxal compound, 0.00215 g./100 ml. of KOH–H_2O solutions, 1-cm. cell; curve 2, same, 0.00135 g./100 ml. of dioxane, 1-cm. cell.

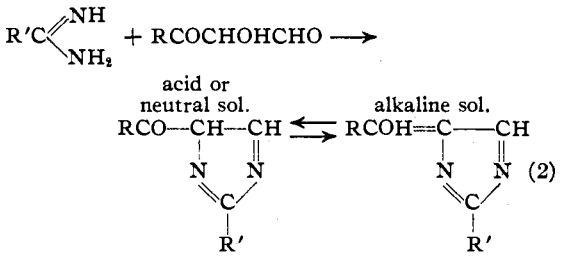
basic, or neutral solution, the change from acid to alkaline solution bringing about a corresponding change in the two compounds, namely, to that of a tautomeric form.

The reactions involved in the formation of the condensation product between aromatic aldehydes, aromatic amidines and glyoxal are

$$RCHO + OCHCHO \longrightarrow RCOCHOHCHO \quad (1)$$

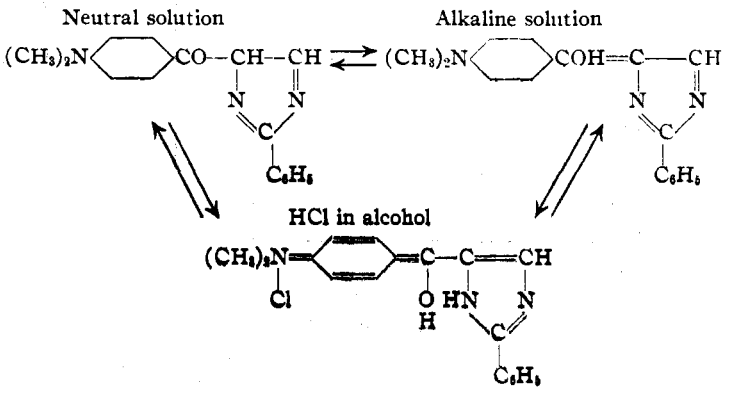
(4) Pinner, *Ber.*, **22**, 1612 (1889).

(5) Technical dioxane purified by the method of Oxford [*Biochem. J.*, **28**, 1325 (1934)] gives very faint narrow absorption bands at 2610, 2550, 2500 Å. These bands are too weak and narrow to interfere in absorption spectra work.



In one case out of forty-five compounds obtained from aromatic aldehydes, namely, that from *p*-dimethylaminobenzaldehyde, does the solution change color when made acid, especially in alcohol solution. In this case the color becomes deep red. The absorption spectrum curves show that the presence of the *p*-dimethylamino group in the original aromatic nucleus causes the loss of the characteristic triplet in dioxane solution, while in acid the curve suffers a further change and is shifted toward the red end of the spectrum. The changes in acid solution may be explained by the assumption of the formation of a quinonoid structure, while in alkaline solution the color is due to the presence of the fulvenoid chromophore alone.

From the mother liquor of the benzamidine-glyoxal addition product we obtained a small



amount of an acid[1] which from the empirical formula we assumed to be a condensation product of glyoxylic acid, benzamidine and glyoxal, since

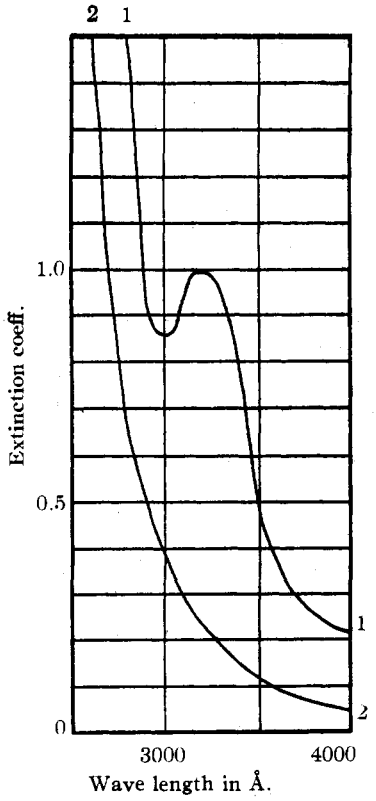


Fig. 4.—Curve 1, diphenylhydroxypyrimidine, 0.00170 g./50 ml. of dioxane, 1-cm. cell; curve 2, same, 0.00085 g./50 ml. of KOH-H_2O solution, 1-cm. cell.

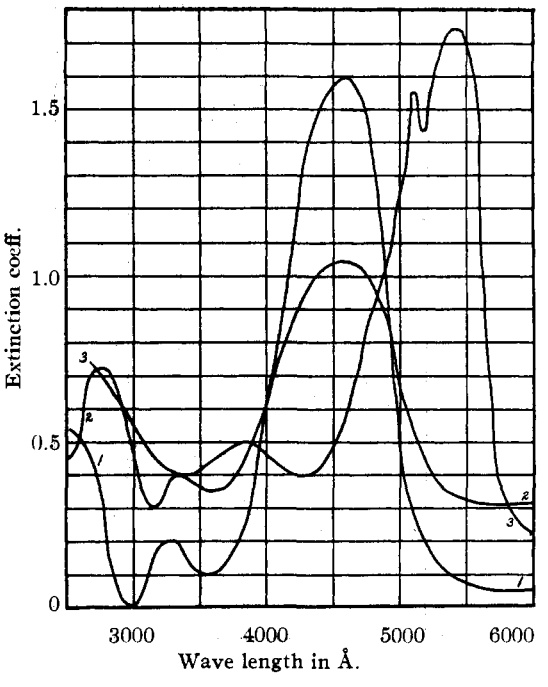
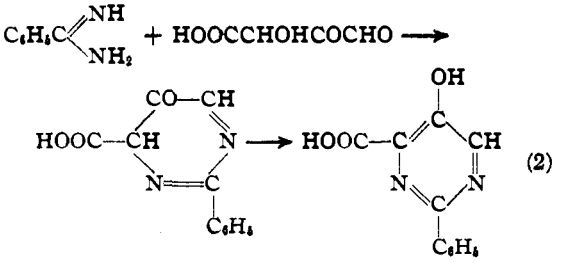


Fig. 5.—Curve 1, benzamidine–glyoxal–*p*-dimethylaminobenzaldehyde compound, 0.00056 g./50 ml. of dioxane, 1-cm. cell; curve 2, same, 0.00060 g./50 ml. of KOH-H_2O solution, 1-cm. cell; curve 3, same, 0.00067 g./50 ml. of 95% ethyl alcohol containing 1 cc. of concd. HCl, 1-cm. cell.

the glyoxal used contained glyoxylic acid together with oxalic acid. The same compound in a 75% yield was then prepared from glyoxylic acid (prepared by the method of Tafel and Friedrichs[6]) and benzamidine-glyoxal. They were both recrystallized from alcohol–water solution, m. p. 255°. *Analyses.* Calcd. for $C_{11}H_8N_2O_3$, compound from mother liquor: C, 61.11; H, 3.70; N, 12.95. Found: C, 61.50; H, 3.90; N, 12.82. Compound from glyoxylic acid and benzamidineglyoxal, found: C, 61.00; H, 3.90; N, 13.08.

Comparison of the absorption spectrum curve of this compound with that of Pinner's diphenylhydroxypyrimidine reveals such striking similarities that we must assign to this acid the pyrimidine structure, so that in this case the compound is phenylhydroxypyrimidine carboxylic acid. The formation of the acid would seem to be according to the following reactions

$$HOOCCHO + OHCCHO = HOOCCHOHCOCHO \quad (1)$$



The absorption spectra curves herein given were obtained using a Hilger E3 quartz spectrograph, a Hilger sectorphotometer and a high frequency under-water spark. Eastman panchromatic plates were used. In plotting the curves we used wave lengths as abscissas and "extinction coefficients" as ordinates.

Summary

1. Absorption spectra data are in accord with chemical data pointing to an open chain formula for the addition products of aromatic amidine and glyoxal and for those of benzamidine with diacetyl.

(6) Tafel and Friedrichs, *Ber.*, **37**, 3187 (1904).

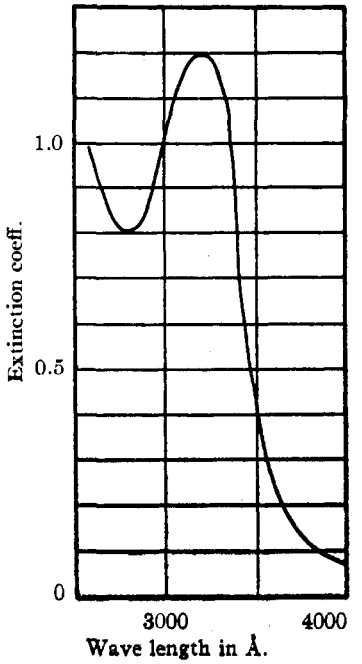


Fig. 6.—Glyoxylic acid-benzamidine-glyoxal compound, 0.00170 g./50 ml. of dioxane, 1-cm. cell.

2. The structures of the compounds formed from aromatic aldehydes, aromatic amidines and glyoxal are generally phenylbenzoylglyoxalines in acid or neutral solution and existing in a tautomeric form in alkali solutions.

3. The compound derived from *p*-dimethylaminobenzaldehyde, benzamidine and glyoxal gives absorption spectra curves in dioxane in which the characteristic triplet has become a single band, in alkaline solution it suffers a further change and in hydrochloric acid solution is shifted toward the red probably due to the formation of a quinonoid ring.

4. The compound derived from glyoxylic acid gives absorption spectra similar to diphenylhydroxypyrimidine, hence is assumed to be a phenylhydroxypyrimidine carboxylic acid.

BOULDER, COLORADO RECEIVED MARCH 18, 1937