Summary

1. 1-Phenyl-3-hydroxy-5-pyrazolone imide was prepared by ring closure of β-cyanoacetylphenylhydrazine obtained from phenylhydrazine and cyanoacetyl chloride or cyanoacetazide.

2. The relation of 1-phenyl-3-hydroxy-5-pyrazolone imide and 1-phenyl-3-amino-5-pyrazolone is shown by acid hydrolysis of both compounds to 1-phenyl-3-hydroxy-5-pyrazolone.

3. Color reactions of β-cyanoacetylphenylhydrazine and of the pyrazolone derivatives are described.

ROCHESTER, NEW YORK RECEIVED OCTOBER 14, 1942

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF YALE UNIVERSITY]

The Acidic Ionization Constant of Glycine in Dioxane–Water Solutions

BY HERBERT S. HARNED AND CLAIR M. BIRDSALL[1]

The ionization constants of acetic, formic, propionic acids and water[2] have been determined from 0 to 50° in water and in dioxane–water solutions from cells without liquid junction. In order to extend these results to include an ionization of another type of weak electrolyte, cells of the type

$$H_2/Z^{\pm}(m_1),\ HZCl\ (m_2),\ X\%D,\ Y\%H_2O/AgCl\text{-}Ag$$

have been employed to evaluate the acidic ionization constant of glycine as a function of the composition of a medium of varying dielectric constant and of the temperature. In this cell, $Z^{\pm}$ represents the amphion, $^{+}NH_3CH_2COO^{-}$, HZCl, glycine hydrochloride and X the percentage by weight of dioxane in the solvent. From these ionization data, the entropy, heat content and heat capacity of the ionization reaction may be evaluated with a fair degree of accuracy.

Cells of this type have been employed frequently[3] in recent years to determine the acidic ionization constant of amino acids in water, and without modification may be adapted to the investigation of ionization equilibrium in water–organic solvent mixtures. The ionization under consideration is given by the expression

$$^{+}HZ \rightleftarrows Z^{\pm} + H^{+}$$

and the corresponding equation for the thermodynamic ionization constant is

$$K_A = \frac{m_Z m_H}{m_{ZH}} \frac{\gamma_Z \gamma_H}{\gamma_{ZH}} \qquad (1)$$

where m represents molality, γ activity coefficient and the ionic species are designated by the subscripts, Z, ZH and H.

The thermodynamic equation for the cell is

$$E = E^{0*} - RT/NF \ln \gamma_H \gamma_{Cl}\, m_H m_{Cl} \qquad (2)$$

where E^{0*} is the standard potential in a given solvent. Since $\gamma_H \gamma_{Cl}$ in a solution containing glycine is not exactly known but can only be approximated by employing values for hydrochloric acid at the appropriate ionic strength in a solvent which does not contain glycine, it is necessary to define the quantities M_H' and K_A' by the equations

$$K_A' \equiv \frac{m_Z' m_H'}{m_{ZH}'} = \frac{(m_1 + m_H')m_H'}{(m_2 - m_H')} \qquad (3)$$

$$\log m_H' \equiv \frac{(E - E^{0*})}{k} + 2 \log \gamma_{HCl} + \log m_2 \qquad (4)$$

since $m_{Cl} = m_2 = m_{HZ}$. As the ionic strength decreases, the apparent hydrogen ion concentration m_H' approaches the actual hydrogen ion concentration m_H so that at infinite dilution K_A' equals K_A. E^{0*} and γ_{HCl} have been determined by Harned and Morrison,[4] m_2 is known, so that measurement of E yields all the data necessary for the computation of m_H'. From these values of m_H' determined at a number of suitable concentrations, K_A' is determined by equation (3) and extrapolated to zero ionic strength where it equals the thermodynamic ionization constant K_A.

Experimental Procedure and Observed Electromotive Forces.—The experimental technique described in detail by Harned and Morrison[5]

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[1] This contribution contains material from a dissertation presented by Clair M. Birdsall to the Graduate School of Yale University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1942.

[2] Harned and Kazanjian, THIS JOURNAL, **58**, 1912 (1936); Harned and Fallon, *ibid.*, **61**, 2374 (1939); Harned and Done, *ibid.*, **63**, 2579 (1941); Harned and Dedell, *ibid.*, **63**, 3308 (1941).

[3] Harned and Owen, *ibid.*, **52**, 5091 (1930); Harned and Owen, *Chem. Rev.*, **25**, 31 (1939); Owen, THIS JOURNAL, **56**, 24 (1934); Nims and Smith, *J. Biol. Chem.*, **101**, 401 (1933); P. K. Smith, A. C. Taylor and E. R. B. Smith, *ibid.*, **122**, 109 (1937).

[4] Harned and Morrison, THIS JOURNAL, **58**, 1908 (1936).

[5] Harned and Morrison, *Am. J. Sci.*, **33**, 161 (1937).

was employed. Two stock solutions of glycine hydrochloride and glycine were prepared by weighing glycine and standard hydrochloric acid into a large flask and diluting with conductivity water. These had the compositions, $m_1 = m_Z = 0.65472$, $m_2 = m_{HZCl} = 0.53104$ whence $m_1/m_2 = 1.2329$, and $m_1 = m_Z = 0.55792$, $m_2 = 0.45075$, whence $m_1/m_2 = 1.2378$, respectively. The concentrations are expressed in molalities, moles per 1000 g. of solvent. The cell solutions were made by diluting weighed portions of these stock solutions with known weights of water and dioxane.

The difficulty in preparing pure glycine causes the largest error in the final composition of the cell solutions. The material employed was obtained by crystallizing the highest grade glycine available three times from conductivity water. The crystals were dried over potassium hydroxide sticks in a vacuum desiccator. A sample of this material heated in an Abderhalden drier was found to lose 0.16% of its weight in ninety-six hours. The loss in weight during the last twenty-four hours was only one per cent. of the total loss while the loss during the first nine hours was over 50%. The preparation was assumed therefore to contain 0.16% of water.

TABLE I

ELECTROMOTIVE FORCES OF THE CELLS $H_2/Z^{\pm}$ (m_1), HZCl (m_2), $X\%$D, $Y\%H_2O$/AgCl–Ag, CONSTANTS OF EQUATION $E = E_{25} + a(t - 25) + b(t - 25)^2$; VALID FROM 0 TO 50°

D = dioxane. X = % dioxane by weight. $\Delta_{av.}$ = average deviation between observed electromotive forces and those computed by equation.

I. $X = 20$

$m_1 = 1.2329\ m_2$ m_2	E_{25}	$a \times 10^6$	$-b \times 10^8$	$\Delta_{av.}$(mv.)
0.009277	0.49879	118	148	0.03
.010644	.49490	103	142	.03
.012540	.49039	87	145	.04
.014919	.48584	68	136	.07
.015691	.48450	62	140	.02
.021981	.47591	27	140	.05

II. $X = 45$

$m_1 = 1.2378\ m_2$ m_2	E_{25}	$-a \times 10^6$	$-b \times 10^8$	$\Delta_{av.}$(mv.)
0.010916	0.48638	114	117	0.09
.012380	.48369	125	110	.03
.013999[a]	.48180	131	110	.09
.016631	.47752	142	104	.05
.017435[a]	.47641	145	90	.08
.018605	.47498	150	106	.05
.019043	.47461	107	153	.08
.023395	.47067	108	162	.05

[a] $m_1 = 1.2329\ m_2$

III. $X = 70$

$m_1 = 1.2378\ m_2$ m_2	E_{25}	$-a \times 10^6$	$-b \times 10^9$	$\Delta_{av.}$(mv.)
0.009163	0.46840	395	600	0.08
.011962	.46509	396	610	.08
.012624	.46463	392	610	.10
.013117	.46435	389	580	.04
.015897	.46215	394	600	.08
.019606	.45972	397	610	.08
.022249	.45845	391	590	.04

Measurements of each cell at a given concentration were made in triplicate. The electromotive force was first read at 25°, then at 0 or 50° and then at 5° intervals until 25° was reached. The agreement at 25° at the beginning and end of the experiment was used as a criterion of the cell behavior.

Table I contains the parameters of the quadratic equation

$$E = E_{25} + a(t - 25) + b(t - 25)^2 \qquad (5)$$

used to express the experimental electromotive force as a function of the temperature. The last column contains the average deviation of the observed from the calculated results. These deviations show that the equation represents the electromotive force to within ±0.1 mv. The overall reproducibility of the measurements is not as accurate. This will appear later from the plots of the extrapolation functions.

Ionization Constants.—The ionization constants were determined by graphical extrapolation of the values of K_A' obtained by equations (3) and (4). The standard potentials required for this computation were computed by the equations[6]

$$\begin{aligned} X = 20;\ E^{0*} &= 0.20303 - 760.5 \times 10^{-6}\,(t - 25) - 3.70 \times 10^{-6}\,(t - 25)^2 \\ X = 45;\ E^{0*} &= 0.16352 - 1135 \times 10^{-6}\,(t - 25) - 3.70 \times 10^{-6}\,(t - 25)^2 \qquad (6) \\ X = 70;\ E^{0*} &= 0.06395 - 1767 \times 10^{-6}\,(t - 25) - 3.70 \times 10^{-6}\,(t - 25)^2 \end{aligned}$$

derived from the data of Harned and Morrison.[7] The values of γ_{HCl} necessary for the calculation were read from graphs of the data of Harned and Morrison.[8]

Extrapolations of the results for the three solvent mixtures at 25° are shown by the plots in Fig. 1. These are satisfactory although not as consistent as extrapolations of similar nature in water. Obviously, the best result was obtained

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[6] Harned, Morrison, *et al.*, THIS JOURNAL, **61**, 49 (1939).

[7] Harned and Morrison, *ibid.*, **58**, 1908 (1936).

[8] Revised values of this activity coefficient, recalculated from the data of Harned and Morrison, are tabulated by Harned and Donelson, *ibid.*, **60**, 339 (1938), (20% dioxane); *ibid.*, **60**, 2128 (1938), (45% dioxane); Harned, Donelson and Calmon, *ibid.*, **60**, 2133 (1938), (70% dioxane).

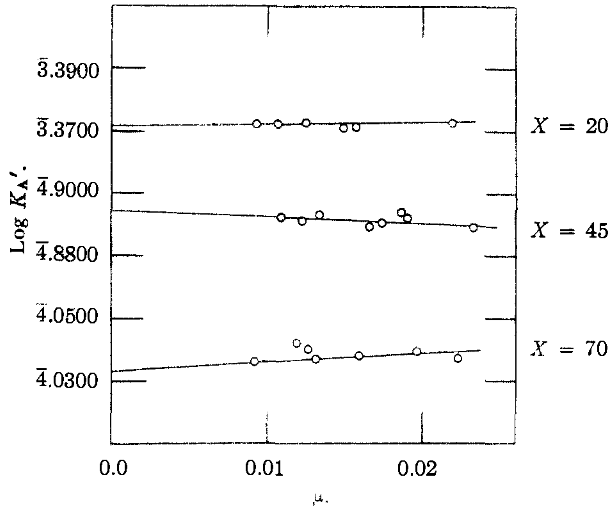

Fig. 1.—Extrapolations at 25°: log K_A' *versus* μ; diameters of circles = 0.2 mv.

TABLE II

THE ACIDIC IONIZATION CONSTANT OF GLYCINE IN DIOXANE-WATER SOLUTIONS $-\log K_A = pK_A$; X = % DIOXANE BY WEIGHT

	$X = 20$		$X = 45$		$X = 70$	
t	pK_A	$\Delta \times 10^{-3}$	pK_A	$\Delta \times 10^{-2}$	pK_A	$\Delta \times 10^{-3}$
0	2.7370	0.0	3.1980	−0.2	4.0490	−1.1
5	2.7093	− .1	3.1735	− .2	4.0292	+0.6
10	2.6846	− .3	3.1528	+ .5	4.0106	+ .8
15	2.6638	+ .3	3.1338	+ .1	3.9945	+ .9
20	2.6464	+1.5	3.1177	.0	3.9818	+1.9
25	2.6285	−0.5	3.1053	+1.0	3.9650	−3.6
30	2.6148	− .9	3.0920	−1.2	3.9593	−0.2
35	2.6054	+ .5	3.0845	0.0	3.9528	+ .3
40	2.5964	.0	3.0783	+ .4	3.9485	+ .9
45	2.5896	− .5	3.0728	− .6	3.9447	+ .1
50	2.5866	+ .6	3.0714	+ .6	3.9434	− .1

with the 20% dioxane mixture. Values of $-\log K_A$ or pK_A are given at all temperatures in Table II.

Derived Thermodynamic Quantities.—For the computation of the ionization constant as a function of the temperature, the equation

$$\log K = -A^*/T + D^* - C^*T \quad (7)$$

employed by Harned and Robinson[9] was used. This is consistent with equations

$$\Delta F_i^0 = -A' - D'T + C'T^2 \quad (8)$$
$$\Delta H_i^0 = A' - C'T^2 \quad (9)$$
$$\Delta C_{p_i}^0 = -2C'T \quad (10)$$
$$\Delta S_i^0 = D' - 2C'T \quad (11)$$

which may be used to calculate the standard free energy, heat content, specific heat and entropy of the ionization reaction. Here

$$A' = 2.3026\,RA^*$$
$$D' = 2.3026\,RD^*$$
$$C' = 2.3026\,RC^*$$

The temperature of the maximum value of the ionization constant, T_θ and the value of the ionization constant at this temperature may be obtained by

$$T_\Theta = \sqrt{A^*/C^*} \quad (12)$$
$$\log K_\Theta = D^* - 2\sqrt{C^*A^*} \quad (13)$$

Table III contains values of these constants.

The accuracy with which equation (7) represents the observed results as a function of temperature is shown in third and seventh columns of Table II where the differences between observed and calculated results are recorded. This agreement indicates excellent consistency of the results with temperature which is very advantageous for computing the heat content and capacity, but must not be construed to represent the over-all accuracy in determining the ionization constant.

Thermodynamic Quantities.—The thermodynamic quantities for the acidic ionization of glycine at 25° calculated by use of equations (8) to (11) are given in Table IV.

TABLE III

CONSTANTS OF EQUATIONS (7) TO (13)

X = per cent. dioxane by weight

X	A^*	D^*	C^*	A'	D'	C'	T_Θ	$-\log K_\Theta$
0[10]	1300.53	5.5277	0.011792	5949.98	25.2894	0.053949	332.1	**2.3043**
20	1368.9361	5.6875	.012493	6263.1564	26.0216	.057161	331.0	**2.5806**
45	1273.4896	4.7113	.011887	5826.4691	21.5553	.054386	327.3	**3.0702**
70	1187.2975	3.3894	.011322	5432.1235	15.5073	.051801	323.8	**3.9435**

TABLE IV

THERMODYNAMIC QUANTITIES AT 25°

X	ΔF_i^0, cal./mole	ΔH_i^0, cal./mole	$\Delta C_{p_i}^0$, cal./deg./mole	ΔS_i^0, cal./deg./mole
0[11]	3205	1156	−32.2	− 6.9
20	3586	1183	−34.1	− 8.1
45	4233	993	−32.4	−10.9
70	5412	829	−30.9	−15.4

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[9] Harned and Robinson, *Trans. Faraday Soc.*, **36**, 973 (1940).

[10] Calculated by Dr. R. A. Robinson from the data of Owen, THIS JOURNAL, **56**, 24 (1934).

[11] Owen, *ibid.*, **56**, 24 (1934). Calculated from least squared equation by Dr. R. A. Robinson.

Summary

The acidic ionization constant of the ampholyte glycine has been determined by measurement of the electromotive forces of the cell $H_2/Z^{\pm}$ (m_1), HZCl (m_2), X%D, Y%H_2O/AgCl–Ag and subsequent calculations.

The measurements were carried out in media containing 20, 45 and 70% dioxane by weight, and over a temperature range from 0 to 50° inclusive.

The thermodynamic ionization constants may be expressed by equation (7) the constants of which were determined by the method of least squares. By use of equations (8) through (11) and the constants in Table III the numerical evaluation of the thermodynamic functions is possible. These values at 25° have been given for the ionization in solutions containing 0, 20, 45 and 70% dioxane.

NEW HAVEN, CONN. RECEIVED NOVEMBER 7, 1942

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

A Synthesis of Cinnamic Acids from Methyl Acrylate or Acrylonitrile and Diazonium Salts

BY C. F. KOELSCH

From a study of a number of examples, Meerwein and his co-workers[1] concluded that the coupling of diazonium salts with α,β-unsaturated compounds led to the attachment of an aryl group to an α-carbon atom. But the only products whose structures were rigorously proved were those derived from α,β-unsaturated compounds already arylated in the β-position.

Because such coupling reactions of diazonium salts probably involve free aryl radicals[2] and because nitrobenzene reacts readily and leads to *o*- and *p*-nitrobiphenyls,[3] it appeared possible that steric factors might be more important than the direction of polarization of the α,β-unsaturation in determining the carbon atom to which the aryl group became attached. For this reason the behaviors of acrylonitrile and of methyl acrylate toward diazonium salts have been studied.

It has been found that these substances couple readily, and that in every case the product is formed through the union of an aryl group with the β-carbon.

$$ArN_2Cl + CH_2{=}CHCN \longrightarrow ArCH_2CHClCN$$

Since the products are formed in fairly good yields, and since they can be transformed into derivatives of cinnamic acid, the reaction has some promise as a preparative method.

Further studies are being carried out to determine the effect of various substituents in the unsaturated component on the proportion of α- to β-arylation which it undergoes.

Experimental

In a large number of orienting runs it was established that certain conditions, already noted by Meerwein and his collaborators, were almost essential for a successful coupling. These were the presence of acetone, the presence of cupric salt, and the maintenance of the proper *p*H. It was found, however, that this latter condition could be fulfilled as well by using a sodium acetate buffer as by using the chloroacetate of Meerwein.

The following procedure gave generally satisfactory results. A mixture of 0.5 mole of amine with 50 ml. of water was treated with 100 ml. of concd. hydrochloric acid, warmed if necessary to effect solution, then cooled by adding ice, and finally diazotized by adding a concentrated solution of 35 g. of sodium nitrite. This diazonium salt was added dropwise to a stirred mixture kept at 25° prepared by neutralizing 30 g. of acetic acid in 100 ml. of water with 40% sodium hydroxide, adding 15 g. of cupric chloride, 250 ml. of acetone, and 25 g. of acrylonitrile (or 43 g. of methyl acrylate). After the diazonium solution had been added, the mixture was warmed slowly to 35–40°, and stirring was continued for two hours or until no more nitrogen was evolved. The *p*H was then about 6; it was changed to *p*H 2 by adding hydrochloric acid, the oil was separated and the aqueous part was washed once with ether.

In the cases where a nitrodiazonium salt was used, the combined oil and extract was diluted with 250 ml. of ether, causing the separation of a dark red tar. This was extracted five times with 50-ml. portions of ether, and the combined ether solutions were then concentrated. The residue crystallized and was fairly pure α-chloronitrohydrocinnamonitrile; for complete purification this substance was distilled in small quantities under reduced

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[1] Meerwein, Buchner and van Emster, *J. prakt. Chem.*, **152**, 237 (1939); *cf.* British Patent 480,617; Bergmann and Weinberg, *J. Org. Chem.*, **6**, 134 (1941).

[2] Haworth, Heilbron and Hey, *J. Chem. Soc.*, 372 (1940).

[3] France, Heilbron and Hey, *ibid.*, 369 (1940); Elks, Haworth and Hey, *ibid.*, 1284 (1940).