[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

Reduction of Nitroguanidine. XII. Oxidation Potentials of the Nitro-nitrosoguanidine and the Nitroso-aminoguanidine Systems[1]

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Introduction

Systems in organic chemistry capable of forming thermodynamically reversible voltaic cells are relatively few in number. Not more than fourteen of such classes of systems have been shown to be completely thermodynamically reversible.[2] Accordingly, the evaluation of new systems, which can be demonstrated to fall in this category, is of fundamental importance to our extension of knowledge in the sphere of physico-organic chemistry. For such systems, free energy changes and heats of reactions may be calculated readily from the electrochemical data obtained. Of far greater importance, the evaluation of such physical data enables the investigator to gain an insight into the "fine" mechanism of his reactions as so ably demonstrated by Clark,[2a] Conant,[3] Fieser[4] and more recently Michaelis.[5] Smith and Sabetta[6] found that the nitro-nitrosoguanidine oxidation system was reversible and the E_0 was +0.88 volt in the acid region but it changed at about *p*H 7 and was +0.85 volt at *p*H 8. This paper will present results of further measurements of the oxidation potential of the nitro-nitrosoguanidine system and also the results obtained in the measurements of the oxidation potential of the nitroso-aminoguanidine system. On the basis of these values, the probable true mechanisms for the several reactions are postulated in terms of the molecular and ionic forms of nitroguanidine, nitrosoguanidine and aminoguanidine.

Experimental

Apparatus.—In measuring the e. m. f. of the nitro-nitrosoguanidine system a Leeds and Northrup Type K-2 potentiometer was used with a Leeds and Northrup box galvanometer with lamp and scale (No. 2500-C). The measurements were made at 25.0 ± 0.1° but it was found that temperature control did not increase the precision of the measurements. In measuring the e. m. f. of the nitroso-aminoguanidine system the equipment was the same as that used by Smith and Sabetta.[6] It is probably not possible to obtain nitrosoguanidine in extremely high purity and, also, it is not possible to control the purity of this substance exactly.

Materials.—Nitrosoguanidine was prepared by the method described by Sabetta, Himmelfarb and Smith[7] and solutions of weighed amounts of this compound in distilled water were prepared as needed. Nitroguanidine of high purity was prepared as described by Smith, Sabetta and Steinbach.[8] Aminoguanidonium chloride was prepared in solution by treating pure aminoguanidonium bicarbonate with hydrochloric acid and adjusting to *p*H 6.8. Buffer solutions were prepared as recommended by Clark[9] except that they were twice the concentrations given by Clark. The solutions were checked by diluting with equal volumes of water and measuring with the hydrogen electrode. Electrodes were prepared as described by Smith and Sabetta,[6] which is essentially Popoff's procedure.[10]

Method.—Measured volumes of standard solutions of nitrosoguanidine and of aminoguanidine were added to 50 ml. of standard buffer solution and then diluted to 100 ml. This solution was transferred to the cell which was fitted with a rubber stopper. Three electrodes, a nitrogen delivery tube, and a saturated calomel electrode were fitted through the rubber stopper. The contents of the cell were agitated by a stream of nitrogen which had been purified by passing through a solution of potassium hydroxide, a solution of pyrogallic acid, and finally through distilled water. The e. m. f. of the nitrosoaminoguanidine system and of the nitro-nitrosoguanidine system was determined by measuring the e. m. f. of the primary cell

$$\mathrm{Hg} \mid \mathrm{Hg_2Cl_2\ (satd.\ KCl)} \parallel \begin{matrix}\mathrm{RNO}\\ \mathrm{RNH_2}\\ (\mathrm{H^+})\end{matrix} \mid \mathrm{Pt} \qquad \text{or}$$

$$\mathrm{Hg} \mid \mathrm{Hg_2Cl_2\ (satd.\ KCl)} \parallel \begin{matrix}\mathrm{RNO_2}\\ \mathrm{RNO}\\ (\mathrm{H^+})\end{matrix} \mid \mathrm{Pt}$$

The symbol RNO_2 represents nitroguanidine, RNO, nitrosoguanidine, and RNH_2, aminoguanidine. A summary of the results of the measurements of the nitro-nitrosoguanidine system is tabulated in Table I and presented graphically in Fig. 1. The results of the measurements of the nitroso-aminoguanidine system are tabulated in Table II and presented graphically in Fig. 2.

Discussion of Results

Molecular and Ionic Forms of Nitroguanidine, Nitrosoguanidine and Aminoguanidine.—The properties of nitroguanidine[11] and nitrosoguanidine[7,12] indicate the amphoteric character of these substances. In considering mechanisms of reactions of these compounds we must know what molecular and ionic forms are probably present. In guanidonium salts the guanidonium ion may best be written as $[C(NH_2)_3]^+$ and the carbon atom has its "usual" covalency of 3, as it has in the carbonate ion.[13] It should be considered also

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(2) A. E. Remick, "Electronic Interpretations of Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1943, p. 233.

(2a) Clark, *Chem. Rev.*, **2**, 127 (1925).

(3) Conant, Small and Taylor, THIS JOURNAL, **47**, 1959 (1925).

(4) Fieser, *ibid.*, **52**, 4915 (1930).

(5) Michaelis, *Chem. Rev.*, **16**, 243 (1935); **22**, 437 (1938).

(6) Smith and Sabetta, THIS JOURNAL, **54**, 1034 (1932).

(7) Sabetta, Himmelfarb and Smith, *ibid.*, **57**, 1478 (1935).

(8) Smith, Sabetta and Steinbach, *Ind. Eng. Chem.*, **23**, 1124 (1931).

(9) Clark, "The Determination of Hydrogen Ions," Williams and Wilkins Co., Baltimore, Md., 1929, pp. 200–201.

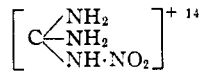
(10) Popoff, Kunz and Snow, *J. Phys. Chem.*, **32**, 1056 (1928).

(11) Thiele, *Ann.*, **270**, 1 (1892).

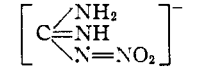
(12) Thiele, *ibid.*, **273**, 133 (1893).

(13) Davis, Yelland and Ma, THIS JOURNAL, **59**, 1993 (1937); Thielacker, *Z. Krist.*, **90**, 51 (1937).

that substituted guanidonium ions are similar and that the carbon has a covalency of 3. The neutral molecule of nitroguanidine is a weak base which in an acidic solution accepts a proton and becomes a cation, $[C(NH_2)_2(NHNO_2)]^+$, which may be written as



In an alkaline solution the neutral molecule is a weak acid and donates a proton and the resulting anion may be represented as



and in very strongly alkaline solution the monovalent anion may donate a second proton and become a divalent anion. For instance, Franklin has prepared secondary metallic salts of guanidine in liquid ammonia and guanidine is a much weaker acid (and stronger base) than nitroguanidine and nitrosoguanidine. The analogous ions of nitrosoguanidine are present in solutions of this compound.

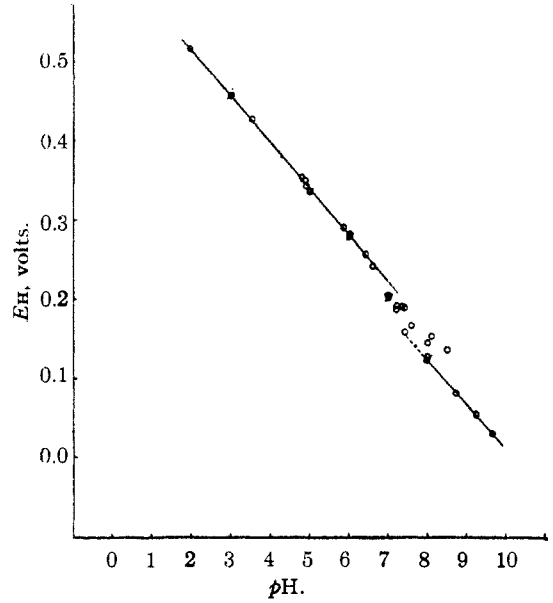
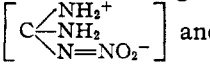
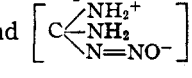
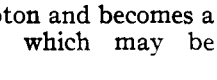


Fig. 1.—E_H—pH Functional relationships in the oxidation system nitro-nitrosoguanidine: ⊖, Sabetta; O, Pribyl.

The values of K_B, K_{A_1} and K_{A_2} for nitroguanidine and nitrosoguanidine are not known. However, K_B is of the same order of magnitude as K_{A_1} for both nitroguanidine and nitrosoguanidine since the isoelectric point for each substance is very near pH 7.[7] In the region of pH 7 the "zwitter ions"  and  predominate.

(14) In this formula a single line indicates one covalent binding.

Aminoguanidine in acid–base properties is more like guanidine because it is a strong base. The monovalent cation



exists in acidic solutions but it is such a weak acid that it exists also in basic solutions. However, if the reaction of the solution is strongly basic, the cation will donate a proton and leave the neutral molecule. In the interpretation of the results of the measurements of the nitro-nitrosoguanidine and the nitroso-aminoguanidine oxidation systems the validity of the above postulations regarding the ions of nitroguanidine, nitrosoguanidine and aminoguanidine has been verified because these postulations have made possible a logical explanation of the facts presented in this paper.

The Nitro-nitrosoguanidine Oxidation System.—It can be observed from an examination of Table I and Fig. 1 that for the acid region pH 2–7, the E_H of the nitro-nitrosoguanidine oxidation system is a linear function of pH and that E_0 has an average value of 0.88 volt. Between pH 7 and pH 8 the E_H values are not in good agreement, and E_0 values as calculated on the basis of the normal hydrogen electrode vary from 0.85 to 0.88 volt.

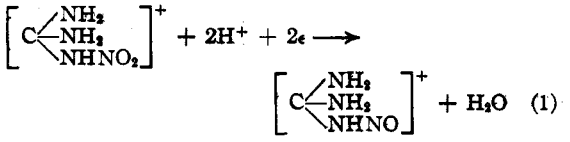
TABLE I

MEASUREMENT OF THE E. M. F. OF THE NITRO-NITROSOGUANIDINE OXIDATION SYSTEM

pH	Av. observed e. m. f. at 25°	Calculated E_0, H_2 Electrode = 0
1.97	0.515	0.882
3.53	.425	.881
4.78	.359	.883
4.87	.357	.882
4.90	.345	.878
5.85	.291	.883
6.00	.281	.884
6.41	.256	.821
6.60	.255	.878
6.97	.201	.861
7.20	.188	.863
7.34	.180	.862
7.42	.157	.848
7.60	.165	.863
8.00	.135	.858
8.10	.163	.880
8.50	.124	.875
8.73	.082	.847
9.26	.053	.850
9.68	.024	.846

However, from pH 9 to pH 10, E_H values are again a linear function of pH but the intercept E_0 is 0.85 volt. The slope of both lines is 0.06.

These facts may now be explained as follows: in acidic solutions the nitroguanidonium ion is reduced to the nitrosoguanidonium ion in accordance with the equation



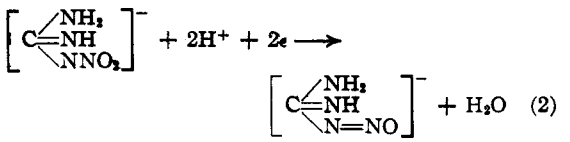
and the e. m. f. of the system follows the Peters equation

$$\text{e. m. f.} = 0.88 - \frac{0.06}{2}\log\frac{(\text{RNO})}{(\text{RNO}_2)(\text{H}^+)^2} \qquad \text{(I)}$$

Therefore when (RNO) = (RNO_2) the equation reduces to

$$\text{e. m. f.} = 0.88 - 0.06p\text{H} \qquad \text{(II)}$$

In basic solution, on the other hand, both nitroguanidine and nitrosoguanidine react as acids, and, accordingly, yield monovalent anions. In this basic region the reduction of nitroguanidine to nitrosoguanidine may be formulated as



Equations I and II are valid for this region *p*H 8 to *p*H 10 except E_0 has changed from 0.88 to 0.85 volt. This is to be expected because a new oxidation system is in reality present.

From *p*H 7 to *p*H 8 both forms of ions and "zwitter ions" all are present and slight changes in conditions probably alter concentrations of the several forms so that equilibrium is not readily established. In this region the mechanism of the reaction is changing from that represented by equation (1) to that of equation (2). The difference in diminution of free energy in the two regions may be regarded as the diminution of the free energy of the reaction involved in passing from cations to anions. The conclusions of Smith and Sabetta[6] are confirmed and supplemented by these further measurements of the oxidation potentials of the nitro-nitrosoguanidine system.

TABLE II

MEASUREMENT OF THE E. M. F. OF THE NITROSO-AMINOGUANIDINE OXIDATION SYSTEM

*p*H	E_H, average observed e. m. f. at 25°	Calculated average E_0, H electrode = 0
1.0	0.352	0.655
1.9	.296	.652
2.5	.273	.661
3.0	.247	.666
4.0	.184	.666
4.87	.148	.683
6.0	.114	.894
6.3	.128	.929
6.5	.120	.942
7.0	.138	1.001
8.0	.079	1.035
8.2	.060	1.034
8.5	.048	1.038
8.78	.012	1.014
9.0	− .015	1.029
9.3	− .080	0.997
9.82	− .114	.997
10.00	− .170	.962
10.3	− .174	.983
11.0	− .255	.968
12.1	− .351	.968

The Nitroso-aminoguanidine Oxidation System.—An examination of the data in Table II and of Fig. 2 indicates that the nitroso-aminoguanidine oxidation system is complicated. The E_H–*p*H relationship is linear in the region *p*H 1 to *p*H 5 and the slope is 0.06 for this "strong" acidic region. Near the neutral zone of *p*H 6 to *p*H 8 there is no consistency in the relationship between E_H and *p*H, but from *p*H 8 to *p*H 10, E_H again is a linear function of *p*H but the slope is 0.09. From *p*H 10 to *p*H 12 a new linear relationship is followed with a slope 0.09 but a different intercept. The three intercepts are *p*H 1 to *p*H 7, E_0 = 0.66 volt (normal hydrogen electrode 0) *p*H 8 to *p*H 10, E_0 = 1.03 volts, and finally *p*H 10 to *p*H 12, E_0 = 0.97 volt.

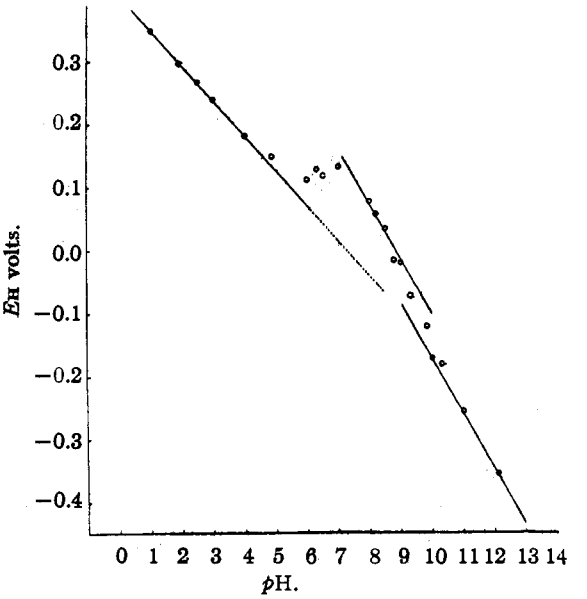
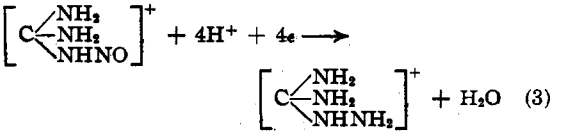


Fig. 2.—E_H—*p*H Functional relationship in the oxidation system nitroso-aminoguanidine.

If we treat the nitroso-aminoguanidine system in a manner analogous to that presented above for the nitro-nitrosoguanidine system, a logical explanation of the facts is offered. In acidic solutions nitrosoguanidonium ion is reduced to aminoguanidonium ion as follows



and the Peters equation written as

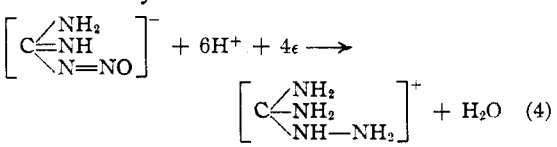
$$\text{e. m. f.} = 0.66 - \frac{0.06}{4}\log\frac{\text{RNH}_2}{\text{RNO}(\text{H}^+)^4} \qquad \text{(III)}$$

holds. When $(RNH_2) = (RNO)$ the equation may be simplified to

$$\text{e. m. f.} = 0.66 - 0.06\ p\text{H} \qquad \text{(IV)}$$

The first or acid portion of the system therefore follows the mechanism formulated in (3).

The anomalous behavior of the system in the region pH 6 to pH 8 may be attributed to a condition of change from the mechanism of equation (3) to a new mechanism. From pH 8 to pH 10 this new mechanism is followed. As in the case of the nitro-nitrosoguanidine system in this region nitrosoguanidine is in the form of the monovalent nitrosoguanidine anion which is reduced to the aminoguanidonium ion and the equation for the reaction may be formulated as



$$+ 6H^+ + 4\epsilon \longrightarrow$$

$$+ H_2O \qquad (4)$$

and the Peters equation takes the form

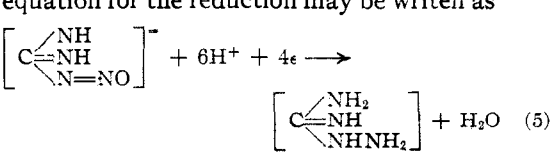
$$\text{e. m. f.} = 1.03 - \frac{0.06}{4} \log \frac{RNH_2}{(RNO)(H^+)^6} \qquad \text{(V)}$$

So in this case when $(RNH_2) = (RNO)$ the equation becomes

$$\text{e. m. f.} = 1.03 - 0.09p\text{H} \qquad \text{(VI)}$$

These postulations agree with all the known facts of the chemistry of nitrosoguanidine and of aminoguanidine and are entirely consistent with the behavior of the nitro-nitrosoguanidine system. In fact the general behavior of the nitroso-aminoguanidine system was predicted to this point.

From pH 10 to pH 12 the intercept has changed by 60 millivolts. This is certainly beyond the precision of the measurements or outside the possible error of the standard buffer solutions and accordingly must be accounted for. If we assume that nitrosoguanidine exists as a divalent anion in this "strong" alkaline region and that aminoguanidine exists as the neutral molecule the equation for the reduction may be writen as



$$+ 6H^+ + 4\epsilon \longrightarrow$$

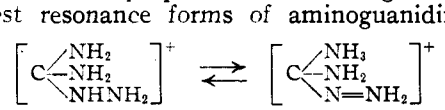
$$+ H_2O \qquad (5)$$

and when $(RNH_2) = (RNO)$ the Peters equation becomes similar to (V)

$$\text{e. m. f.} = 0.97 - 0.09p\text{H} \qquad \text{(VII)}$$

Admittedly this last postulation is tentative but it accounts for all facts known at present.

The possibility of chemical reactions taking place in the "strong" basic region has been considered. Thiele[11] found that nitrosoguanidine reacted with aminoguanidine in alkaline solution to form hydrazodicarbamidine, and Ponzio and Gastaldi[15] showed that under alkaline conditions aminoguanidine may be converted to *sym*-diaminotetrazine with the liberation of ammonia. However, it is not easy to see how these admittedly possible chemical reactions would account for the constancy of slope of the curve in the alkaline region. It is of interest to point out that some of the chemical properties of aminoguanidine[16] suggest resonance forms of aminoguanidine as



Such resonating forms might have an effect on the oxidation potential.

Thermodynamic Constants.—Since the normal oxidation potential is referred to the normal hydrogen electrode as 0, we may compute the change in free energy, $-\Delta F$, for these reactions if carried out in a solution of hydrogen ion activity of unity. Table III gives a summary of the several thermodynamic constants which have been calculated from these data and also the equilibrium constants for the several reactions.

TABLE III

THERMODYNAMIC CONSTANTS

pH	E_0	$-\Delta F$	log K
A. Nitro-nitrosoguanidine System			
2 to 6	0.88	40.6	29.8
7.5 to 10	0.85	39.2	28.8
B. Nitroso-aminoguanidine System			
1 to 4	0.66	61	45
8 to 9	1.03	143	70
10 to 12	0.97	134	65

Summary

1. The normal oxidation potentials of the nitro-nitrosoguanidine system have been determined. Mechanisms, in terms of probable ionic forms of the reactant, for these reduction reactions have been suggested which are based on E_H–pH functional relationships.

2. The normal oxidation potentials of the nitroso-aminoguanidine system have been determined. Mechanisms, in terms of the probable ionic and molecular forms of the reactants, have been suggested which are based on E_H–pH functional relationships.

3. The probable ionic and molecular forms of nitroguanidine, nitrosoguanidine and aminoguanidine have been discussed in some detail. The facts and theoretical considerations which have been presented in this paper give a better understanding of the reactions involved in the reduction of nitroguanidine and of nitrosoguanidine.

4. The free energies and the equilibrium constants of the reactions involved in the reduction of nitroguanidine and of nitrosoguanidine have been calculated from the normal oxidation potentials of the several oxidation systems.

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(15) Ponzio and Gastaldi, *Gazz. chim. ital.*, **43**, II, 43 (1913).

(16) Lieber and Smith, *Chem. Rev.*, **25**, 258 (1939).