Analysis of most probable reactions among products in Miller's experiment

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Abiogenesis is a term used to describe the initial biochemical origin of life as having been initiated within the proverbial "primordial soup". The contention is that the entire biochemistry essential for life was derived from chemical reactions between simple molecules, producing essential amino acids and their peptides, plus nucleotides required for forming RNA and DNA. Presumably, all the initial chemical substances needed for these processes were contained within the waters on the primordial earth; hence, the term "primordial soup". During the 1950s various investigators having notable names such as Urey, Miller, Fox and others, initiated a series of laboratory controlled simulations under presumed environmental conditions conducive to the formation of amino acids and their subsequent production of polypeptides and on to proteins. Even though several amino acids were indeed produced from these reactions, a variety of other products were also produced as well. The results of these findings have since been hailed as a triumph toward the biochemical evolution of life. This study demonstrates in detail what prospects for chemical reactions would have existed in the products of Miller's reactions.

The data provided by Stanley Miller's classic modeling of the "prebiotic earth", relevant to the chemistry presumed essential to the origin of life[1,2] are presented in table 1. In reporting acid concentrations consideration has been given to the presence of ammonia and the effect it has on the acidity of the mix (see Appendix). Note that the amount of ammonia (NH_3) present is insufficient to alter the acidity of the system.

Table 1 gives the moles of the most abundant reaction products produced from electronic spark and heat activation of CH_4, NH_3, H_2 and H_2O, simulating a reducing atmosphere. Of course we are aware of the fact that current thinking is that the earth's primordial atmosphere was not reducing, but contained primarily water, carbon dioxide, lesser amounts of nitrogen, some hydrochloric acid (from volcanic out gassing), some oxygen and little or no ozone. The primary reason for this alternate atmospheric model is the realization that Miller's model is both thermodynamically and kinetically unfavorable toward the formation of peptide bonds. Hence, the requirements for production of amino acids and subsequent peptide bond formation would be different from what Miller and his colleagues presumed. We will address this further in the conclusion section of this report. None the less, it is the primary purpose of this work to focus upon Miller's system *per se*.

If the primitive earth had an ocean volume of some 10^{19}L, as proposed,[3] (although it is now known to be 10^{21} L), the proportional total moles of H_3O^+ from all the acids in the Miller's sample mix (see table 1) would be about 3.42×10^{16} in the 10^{19} L of ocean. If the ocean p^H were about 9, as inferred in some studies[3,4], then the $p^{OH} = 5$ and the molar concentration of OH^- would be $[OH] = 1 \times 10^{-5}$ M, which would be 10^{14} moles of OH^- in 10^{19} L of water. Upon addition of 3.42×10^{16} moles of acid, 10^{14} moles of OH^- are neutralized according to the following reaction:

$$\underset{(1.7 \times 10^{16}\ \text{moles})}{H_3O^+} + \underset{(10^{14}\ \text{moles})}{OH^-} \leftrightarrow \underset{(3.42 \times 10^{16}\ \text{moles})}{2HOH} \quad (1)$$

and which still leaves 3.41×10^{16} moles of excess H_3O^+ of nearly 1.6×10^{16} moles in the 10^{19} L volume. At this acid concentration the $p^H = 2.47$, a rather highly acidic environment in which reactions must take place.

Under these conditions all amino acid components would be in the cationic form: $H_3^+N(—)CO_2H$, and not in the form: $H_2N(—)CO_2$, which is conducive for reactions in an alkaline p^H environment. Thus any reactions involving amino acids must be occur with the amine end in the cationic form.

Most probable reactions

The most abundant reported constituent, other than HCN, among Miller's products is formic acid, present in a concentration of 2.33×10^{-3} moles (see table 1). While, according to Miller's data, the amount of ammonia is about equivalent to the amount of formic acid (FA) reported in the reaction products, there is no report of ammonium formate or any ammonium carboxylates in the products. Naturally, one would expect that such ammonium salts would have formed and thus annihilated all carboxylic acids. But apparently the reaction conditions did not allow enough gaseous ammonia to be dissolved in the aqueous environment to form any measurable amounts of ammonium carboxylates, which if why Miller made no mention of them (table1). The next most abundant components are glycine and alanine, 6.3×10^{-4} moles and 4.9×10^{-4} moles (total) respectively.

Based on these reported data, this aspect of the study will be confined only to the prospects of reactions involving formic acid, glycine and alanine. The point in focus is,

if the formic acid can react with the glycine and/or alanine at a rate faster than any reactions between glycine/glycine (Gly/Gly), glycine/alanine and alanine/alanine, then there would be no amino acids available to form even a single peptide bond.

The approach of this work is to evaluate relative magnitudes of reaction rates via the theory of activated complexes and their energies of activation. Only the initiation of a reaction in the forward direction is considered as the barometer for a probable reaction. It says nothing about the propagation of a reaction so as to obtain an observable product. This is a matter of the equilibrium constant. This study is confined specifically to FA/Gly *vs* Gly/Gly reactions, under the reaction conditions appropriate to the solution environment, as described above. Only if the reaction kinetics of the amino acid pair Gly/Gly are more favorable than that of the FA/Gly pair, would it be conceivable to consider the probability of peptide bond formation.

Table 1. Chemical product's in Miller's experiment.

Compound Name	Chemical Formula	Symbol	Moles[a] (x 10^{-4})	Molarity[b] (x 10^{-4})	P^{Ka}	$[H_3O^+]^c$ (x 10^{-4})
Formic acid	HCO_2H	FA	23.3	47	3.75	8.3
Glycine	$NH_2CH_2O_2H$	Gly	6.3	13	2.34	11*
Glycolic acid	$HOCH_2CO_2H$	GlA	5.6	10	3.83	3.2
d,l Alanine	$NH_2(CH_3)CHCO_2H$	d,l,Ala	3.4	6.8	2.33	6.0*
Lactic acid	$H_3CCH(OH)CO_2H$	LcA	3.1	6.2	3.86	2.3
B. Alanine	$NH_2(CH_3)CHCO_2H$	β,Ala	1.5	3.0	3.51	1.9*
Acetic acid	H_3CCO_2H	AcA	1.5	3.0	4.36	0.95
Propionic acid	$H_3CCH_2CO_2H$	PrA	1.3	2.6	4.87	0.53
						Total = 34.2
(Imino di acetic acid)[d]	–	–	(0.9)	–	–	–
						P^H=2.47

a) Reported by Miller, ref. 2.
b) Based on 0.5 L volume, as reported.
c) Calculated at equilibrium. No reactions between components accounted for.
d) This and all subsequent products in amounts too small to be significant.
e) Net P^H of all H_3O^+ in solution.
* Prior to any reactions occurring.

Specific considerations

The work of Sherwood, Flores and Ponnamperuma[4] indicates that glycine forms a dipeptide when it is reacted with the tetramer 1,2 diamino,1,2 dicyano ethylene formed from HCN under basic p^H (8–10) conditions. However, as has already been shown, the conditions pertinent to Miller's products are not basic, but are on the contrary highly acidic. Thus, this reaction mechanism is not likely for the case in point. In fact, the investigators of the glycine/tetramer reaction explicitedly state, "*At low p^H no diglycine is detectable.*"[4] Consequently, it is apparent that in the absence of alkaline conditions no peptide bonding will be catalyzed by HCN.

Conversely, Stienman *et al.* have reported coupling of amino acids at low p^H with the addition of sodium di-cyanamide.[5] However, the presence of any di-cyanamide is not indicated in any of Miller's reaction products.

Formic acid / Glycine formylation reaction

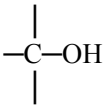
As has already been discussed, there are a number of reported studies involving formic acid formylation reactions. But in this specific case the reaction in question is:

$$HCO_2H + {}^+H_3NCH_2CO_2H \rightarrow HCONHCH_2CO_2H + H_3O^+ \quad (2)$$

The thermo chemistry of this reaction will be considered first.

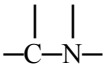
Thermochemistry

The thermo chemistry of the FA/Gly reaction in equation (2) entails the following energy changes:

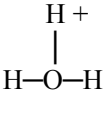


bond breaking = 498 kJ/mol

2(H—N)+ bonds breaking = 2 (636 kJ/mol)
= 1,272 kJ/mol



bond formation = 414 kJ/mol



2 bonds forming 2 (699kJ/mol)
= 1,397 kJ/mol

Ignoring kinetic energy contributions, which for these molecules are not only relatively much smaller than the bond dissociation energies, but are all roughly the same orders of magnitude, the net energy changes for one mole of each reactant and product in (2) are:

(498 + 1,272) kJ *vs* (414 + 1,397) kJ

1,770 kJ ‹ *1,811* kJ

$\Delta H^{\circ}_{rxn} = \sum$ BDE (bonds broken) - $\sum$ BDE (bonds formed)

ΔH°_{rxn} = (1,770–1,811) kJ = **- 41** kJ

Hence the enthalpy of this reaction in the standard state is exothermic by 41 kJ and is thus thermodynamically favorable, but only by a few kilojoules of energy.

Reaction kinetics

The energy of forming an activated complex, E_a, in the transition state of a reaction mechanism is key to the reaction rate. The magnitude of E_a will govern the over all rate of the reaction expressed in terms of the reaction rate constant, k_{rxn}.

It is to be noted that the computation of k_{rxn} in terms of E_a, may not actually match an experimental determination of k_{rxn}. In the latter instance, there are solvent and concentration factors involved in the reaction mechanism, which are not accounted for in the computation of E_a initially or the subsequent calculation of k_{rxn}.

Transition state theory of reaction rate mechanisms is normally approached through quantum mechanical procedures; however, this methodology will not be invoked in this study. A classical approach, wherein electrostatic interactions are evaluated via standard relations, will be used to evaluate the most pertinent interactions between molecules of this complexity. It is anticipated that this will be as reliable as an accurate as any quantum mechanical computation, if such were indeed possible, without substantial approximations. In fact, many such calculations are conducted on molecules of this complexity, over varying degrees of sophistication, yielding computed results deviating by at least some twenty to thirty percent from experimental data, in the best cases. Hence, it is expected that the approach taken here will be at least as good as the quantum mechanical level of reliability.

A "hydrogen bonded" type of interaction in the transition state is a most likely mechanism in the FA/Gly reaction presented in equation (2), in which water (H_3O^+ in acid)

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is split off during the **-C—N-** bond formation in the N-formylation reaction.

However, there are other competing interactions which must also be addressed.

Formic acid molecules can unite as dimers via hydrogen bonding. The bond energy is reported to be 59–63 kJ/mole experimentally and 50–63 kcJ/mole via computations.[6] Also, formic acid can hydrogen bond to H_3O^+, for which an energy has not been reported. But hydrogen bonding between formaldehyde and H_3O^+ has been reported to have an energy of 8 kcal/mole.[7] Thus it is expected that the formic acid / H_3O^+ hydrogen bond would be some 59–63 kJ/mole.

Formic acid hydrogen bonded with formamide has also been studied theoretically and found to have energies in a range of 17 to slightly above 50 kJ/mole.[8]

As it will be shown subsequently, the E_a calculated for the transition state pertinent to the reaction of interest is a somewhat higher energy than any of those cited above.

The "hydrogen bonded" type of interaction model for the transition state activated complex in the FA/Gly reaction,

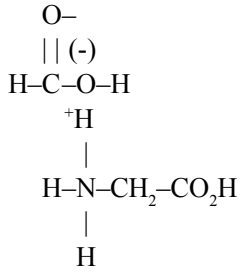
Table 2. Critical data for charge and dipole interactions.

Compound	Atom site	Relative charge	Bond	Bond distance (x 10^{-12}m)	Bond angle (degrees)	BDE[a] (kcal/mole)	BIC[b]	BDM[c] (x 10^{-30} C m)
Formic acid								
HCO_2H	**O**(OH)	-0.390	**O**—H	97	—	498	0.13	—
	H(OH)	0.210	O—**H**	97	—	498	0.13	—
Glycine								
$H_3^+NCH_2CO_2H$	**H**(H_3^+N)	0.650	$H^{+\delta}$—N	122[d]	108 $(HNH)^+$	~ 636[e]	0.45	8.14
	N	-0.246						
	C(CH_2)	-0.001						
	H(CH_2)	0.002						
	C(CO_2H)	0.004	**C**—OH	136	103 (COH)	≈ 418	0.19	—
	O(CO)	-0.378						
	O(COH)	-0.361	**O**—H	97	—	498	0.23	5.00
	H(COH)	0.028	O—**H**	97		498	0.21	3.26

a) Bond dissociation energy
b) Bond ionic character BIC = [BDE – EC] / [EI – EC] ; EC = covalent bond energy; EI = ionic bond energy.
c) Bond dipole moment
d) Based on data for NH_4^+
e) Interpolated from reported data for H_2O/H_3O^+ *vs* NH_3/NH_4^+

is a classical electrostatic charge-dipole. According to literature references, the optimal interaction distance should be about 1.96 Å.[9]

All required atomic charges and adjusted inter atomic distances, were determined according to Sanderson electro negativity concepts which have been shown to be highly reliable in evaluating bond energies and partial charges where applicable.[10] The interaction will entail the carboxylic end of formic acid and the dipole on the H_3^+N—end of glycine, according to the following representation



(3)

The energy of this charge-dipole is given by

$$E_{q,\mu} = -\frac{|q|\mu}{4\pi\varepsilon R^2}\cos\theta \qquad (4)$$

where q = the charge on the OH oxygen of formic acid; μ = the $(H_3N)^+$–dipole moment on glycine; ε = the electrical permittivity (8.854 x 10^{-12} C^2 $m^{-1}J^{-1}$); R = charge-dipole distance; and θ = angle between charge and dipole moment vector. All critical data are provided in table 2.

Bond dipole moments (BDM) are evaluated from the relation:

BDM = (fractional ionic character)
x (magnitude of electron charge)
x (charge-dipole distance)

From the data in table 2, the $(H_3N)^+$–dipole moment is calculated as follows:

BDM (H^+–N) = 0.45 x (1.6 x 10^{-19} C) x (122 x 10^{-12} m)
= 8.78 x 10^{-30} Cm

total dipole moment = 3 BDM x Cos (H–N–H angle
= 3 (8.787 x 10^{-30} Cm) | Cos 108° |
= 8.14 x 10^{-30} Cm

Returning to equation (4), the pertinent data are: q = -0.39 x (1.6 x 10^{-19} C); μ = 8.14 x 10^{-30} Cm; R = 196 x 10^{-12} m; θ ~ 17° (interpolated from the C–O–H bond angle in formic acid; the H–N–H bond angle in the $(H_3N)^+$–group of glycine; and the–N–H^+–O hydrogen bond distance). The charge–dipole interaction energy is

$$E_{q,\mu} = \frac{-0.39(1.6\ x\ 10^{-19}\ C)(8.14\ x\ 10^{-30}\ Cm)}{4\pi(8.854\ x\ 10^{-12}\ C^2m^{-1}J^{-1})(1.96\ x\ 10^{-12}m)} \mid Cos17^\circ \mid$$

$$= \frac{-5.07\ x\ 10^{-49}}{4.28\ x\ 10^{-30}}(0.956)\ J/molecule$$

= -1.13 x 10^{-19} J/molecule

Converting to kJ/mole: (-1.13 x 10^{-19} J/molecule) x (6.11 x 10^{20} kJ $mole^{-1}$/J $molecule^{-1}$) = -69 kJ/mole, or E_a = **- 69** kJ/mole.

Reaction rate constants may be computed from the Absolute Reaction Rate theory by the expression:

$$k_{rxm} = \frac{RT}{Nh}e^{-E^*/RT} \qquad (5)$$

R = 8.314 J K^{-1} mol^{-1}; T = 298K; N = 6.022 x 10^{23} molecules/mole; h = 6.626 x 10^{-34} Js, E* = E_a = -69 x 10^3 J/mole, k_{rxn} = *7.7 x 10^{24} s^{-1}*, which is kinetically highly favorable in the forward direction.

It is to be remembered that this is an estimate of the reaction *being initiated* in the forward direction. The likelihood of a product being isolated is dependent upon the equilibrium constant for the process.

If the equilibrium were to be evaluated then the rate constant for the reverse reaction is required. In considering the reverse reaction, it is to be noted that the C–N bond in the FA/Gly formylated product will be hydrolyzed by the H_3O^+. Let us consider the interaction for this process as governed by hydrogen bonding and reflect on the following.

Hydrogen bonding between two neutral H_2O molecules is some 25 kJ/mole, while quantum mechanical calculation yield a best value of 21 ±1.0*kcal/mole*.[11] The H_3O^+–H_2O hydrogen bond is calculated to be 138 kJ/mole,[12] which is a magnitude of 6.6 times greater than the neutral water dimer. The H_2O–NH_3 hydrogen bond is calculated to be 23 kJ/mole.[13] Thus the NH–O and HO–H hydrogen bonds in neutral systems are about the same energy (~21 kJ/mole) while in H_3O^+–O and H_3O^+–N systems the energy is increased to some 138 kJ/mole.

Keeping in mind that the reverse FA/Gly reaction (see equation (2)) should entail a transition state in which the H_3O^+ hydrogen bonds to the N site of the C–NH– formylated product, the energy of the activated complex should be about 138 kJ/mole. If $E_a \approx 13 \times 10^4$ J, then according to equation (5) the magnitude of the rate constant for the reverse reaction should be $k \approx 7 \times 10^{34}$. This is a clear indication that although the rate constant for initiating the forward reaction is favorable, the rate constant of the reverse reaction is far more favorable and the equilibrium will lie far to the left. Consequently, no Gly formylated product would be observed unless the H_3O^+ in the reaction products is neutralized. This is in complete agreement with what is reported in the literature as cited earlier.

Glycine / Glycine peptide bond formation

This reaction involves two positively charged dipoles ($H^+_3NCH_2CO_2H$), thus the only reasonable interaction of any significance is dipole-dipole. It is the strongly positive (H^+_3N) dipole end of one molecule will interact with the rather weakly negative (CO_2H) dipole end of a second molecule. The overall reaction is

$$HCO_2CH_2NH_3^+ + HCO_2CH_2NH_3^+ \rightarrow HCO_2CH_2N(H)-C(=O)-CH_2NH_3^+ + H_3O^+ \quad (6)$$

Thermochemistry

The same procedures which were applied to the formic acid / glycine reaction are also utilized in this reaction. All bond energies are essentially the same as given previously, with the exception of the glycine–glycine peptide bond. The energy of this bond is calculated to be **326 kJ/***mole*, as compared to the 597 kJ/mole for the formic acid / glycine formylation bond.

Consequently, the enthalpy for the Gly/Gly peptide bond formation in the standard state is: $\Delta H^\circ_{rxn} = (1{,}770–1{,}724)$ kJ = +46 kJ. This reaction is endothermic and will not occur spontaneously without the input of additional energy.

Reaction kinetics

The E_a for the dipole-dipole activated complex in the transition state is computed in the same manner as was done for the formic acid / glycine reaction. Using appropriate data in table 2, the negative dipole end of glycine is found to have a net dipole moment of 1.86×10^{-30} C m for the $–CO_2H$ group. Recall, the H_3^+N–group has a net dipole moment of 8.13×10^{-30} C m. The energy for this interaction is given by:

$$E_{\mu 1 \mu 2} = -\frac{2\mu^1\mu^2}{4\pi\varepsilon R^3} Cos\theta \quad (7)$$

where $\mu_1 = 8.13 \times 10^{-30}$ C m; $\mu_2 = 1.86 \times 10^{-30}$ C m; $\theta \approx 17^\circ$ (since this is still a hydrogen bonded type of interaction between dipoles of the same chemical make up as in the FA/Gly case presented earlier); and $R = 196 \times 10^{-12}$ m. Substitution into equation (7) gives the result

$$E_{\mu 1 \mu 2} = -\frac{3.52 \times 10^{-59}}{8.38 \times 10^{-40}} (0.956)$$

$$= -1.72 \times 10^{-20} \text{ J/molecule}$$

$$= \mathbf{-21\ kJ\ mole^{-1}}$$

which is in very good agreement with the enthalpy change for forming peptide bonds from amino acids as reported by Hutchens.[15]

Thus $E_a = -21 \times 10^3$ J/mole, $k_{rxn} = 3.0 \times 10^{16}$ s^{-1} and substitution into equation (5) provides $k_{rxn} = 2.8 \times 10^{16}$ s^{-1}. So this reaction is initially also kinetically favorable in the forward direction, provided the required energy of activation is realized once the thermodynamic requirements are satisfied. However, it is noted that this initial reaction will be some *nine orders of magnitude slower* than the FA/Gly reaction. Undoubtedly, the FA/Gly reaction will dominate all competitive reactions among Miller's reaction products, based on initial reaction kinetics in the absence of equilibrium considerations.

Conclusion

Recall from table 1 that the relative concentrations of formic acid and glycine are 4.7×10^{-4} M and 1.3×10^{-4} M respectively. Since the formylation reaction between these two components is decidedly favorable both by thermodynamic and kinetic criteria, this will be the dominant reaction to be initiated among all other possible reactions within the system. The formylation reaction rate relative to the initial concentrations is: $Rate_{rxn} = (1.8 \times 10^{25}\ s^{-1})(4.7 \times 10^{-4}\ M)(1.3 \times 10^{-4}\ M) = 1.1 \times 10^{18}\ M^2\ s^{-1}$. Based on initial conditions alone, at this rate all of the glycine available would have been used up almost instantly and all of the 9.5×10^{-5} M alanine would have been reacted, while still leaving a sizable excess of 2.5×10^{-4} moles of formic acid.

Consequently, it appears that there would be *no chance of forming even one peptide bond*, since no amino acids would remain which would not be initially subject to reacting with formic acid. But even if it were possible for the peptide bond to form somehow, it would be hydrolyzed by the highly acidic environment.

In conclusion, if the products resulting from Miller's experiment are indeed representative of what is anticipated in a realistic prebiotic soup (as Miller and most others are inclined to believe), then there would be no possibility of forming any peptides, much less proteins, etc., from such a mixture of chemical components.

Researchers have continued to seek plausible pre-biotic peptide bond forming conditions. A most recent method reportedly produced dipeptides from pure amino acids exposed to high salt concentrations and selected transition metals.[15] While the conditions appear to be quite plausible considering the ancient envionment of the earth, the products fall woefully short of a functioning polypeptide. In fact, after some 56 years of empirical exploration, intelligent design continues to be the most successful explanation to account for the production of cellular components (such as functioning polypeptides and the like) and all the more for a living cell. Evolutionary abiogenesis is a poor substitute for intelligence, organization and selectivity required to arrange chemical substances into the complex ensembles found in even the most "primitive" organisms. The bottom line is "it is a *God thing*", not evolutionary abiogenesis.

Appendix: Question of Nh_3 effects on the P^h of Miller's reaction mixture

According to Miller[2] the initial gas pressures were: NH_3 = 20 cm, CH_4 = 20 cm and H_2 =10 cm in a 5.5-L vessel. As the 5 L of water were introduced into the vessel and heated to boiling, the total pressure varied from 60–80 cm. Thus water vapor between 10–30 cm pressure was also present in the gas mixture.

From the general gas equation: PV = nRT, the number of moles of NH_3 = 0.057 in V = 5.5 L and T = 35°C = 308K. This amounts to 0.011 moles/L. But the NH_3 is subjected to sparking prior to its dissolution in the water which is introduced subsequently. Thus the following reaction occurs initially: $2NH_3 \leftrightarrow N_2 + 3H_2$. At the 900K spark discharge temperature[16] the approximate value of the equilibrium constant for this reaction is K_{eq} = 750, so the dissociation of ammonia if very favorable.

According to Miller,[17] NH_3 provides 10% of the (NH_3 + N_2 + H_2) mix; hence, the NH_3 partial pressure when the cooled (35°C) gases attain a pressure of 50 cm, is (0.1 x 500 mm) = 50 mm or 0.066 atm. From the general gas equation, the number of moles is n = 0.0144 moles in 5.5 L = 0.0026 moles/L. At temperatures approaching the boiling point of water (90–100°C) the maximum solubility of ammonia is about 7%; thus, (0.07 x 0.0026 moles/L) = 1.8×10^{-4} moles/L after the reaction.

Considering the aqueous solution dissociation equilibrium: NH_3 (aq) $\leftrightarrow NH_4^+ + OH^-$, the molar concentrations are: $[NH_3] = (1.8\times10^{-4} - x)$, $[NH_4^+] = [OH^-] = x$ and $K_b = 1.8\times10^{-5}$. Solving the equilibrium for $x = 4.9 \times 10^{-5}$ M = $[OH^-]$. The total sum of all acids in millers mix of products yields 3.42×10^{-3} M = $[H^+]$ (see table 1). Hence, 3.42×10^{-3} M $[H^+] + 4.9 \times 10^{-5}$ M $[OH^-] = 4.9 \times 10^{-5}$M {HOH} and the remaining $[H^+] = 3.4 \times 10^{-3} - 4.9 \times 10^{-5} = 3.35 \times 10^{-3}$ M, for which the p^H = **2.47**.

Consequently, the amount of ammonia dissolved in Miller's aqueous solution portion of his apparatus in insufficient to cause any change in the overwhelming acidity of the solution.

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16. Miller, ref. 2, p. 2354.
17. Miller, ref. 2, table 1, p. 2354.

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