

Determination of the Solubility of Nitrous Oxide in Water By Gas Chromatography

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The solubility of nitrous oxide in water was investigated with a gas chromatographic method using direct injection of liquid samples. This method avoids problems associated with manometric methods. The Bunsen coefficients were found to be: At 30° C., 0.485; 32.5° C., 0.469; 37° C., 0.429; 40° C., 0.403; 45° C., 0.365; 50° C., 0.338. The average standard error of the mean of these data was ± 0.57 per cent. The differential heat of solution of nitrous oxide (ΔH) was found to be -3.35 kcal. degree⁻¹·mole⁻¹ and constant over the investigated range of temperatures.

DIFFICULTIES of manometric techniques in measuring the solubility of nitrous oxide in water have been overcome by a gas chromatographic technique which is adaptable to the accurate and reasonably rapid assay of dissolved gases in water, and also in solutions containing appreciable amounts of solids, such as whole blood. To gain data about the solubility of nitrous oxide in pure water and to prove the accuracy and reliability of this method, we have investigated the solubility coefficients for nitrous oxide in water over the range of temperatures from 30° to 50° C. This range covers most physiological conditions including hypothermia and hyperthermia.

Methods

Water was equilibrated with nitrous oxide under controlled conditions. A known amount of the saturated solution was analyzed by means of gas chromatography. The inter-

grated detector output was compared with that resulting from the analysis of known amounts of pure gas. The Bunsen coefficients were then calculated from the resultant data.

Equilibration. Pure water was equilibrated with nitrous oxide in absorption bottles of the inverted stopper type. The bottles were modified by providing an additional port in their side near the bottom over which a small serum bottle cap was tightly fitted. Samples could thus be withdrawn from the bottle without opening it. To assure the absence of temperature differentials between the water bath and the equilibrated solutions, several of the bottles were also equipped with a thermistor bead cemented into an additional small porthole so that it was in contact with the solution contained in the bottle. These thermistors, in conjunction with appropriate circuitry permitted monitoring of the temperature within the solution. Up to 10 absorption vessels were filled with 75 ml. of water and simultaneously equilibrated with nitrous oxide. Gentle mechanical agitation was supplied in addition to that caused by the gas bubbling through the solution. The temperature of the water bath was controlled to within 0.1° C. with a thermistor sensor and a bridge controller. The solutions were equilibrated with nitrous oxide for at least thirty minutes and only one sample was withdrawn from each absorption vessel for subsequent analysis.

Sample Handling. The liquid samples were withdrawn from the bottle with gas-tight Hamilton microsyringes. A slight excess of volume, but never more than 40 μ l., was withdrawn and rapidly adjusted to the preset volume of 20 μ l. which was injected into the gas chromatograph immediately.

Gas standards were also injected with gas-tight microsyringes.

Contamination of the gas standards with air was kept to a negligible minimum. Figure 1 shows that the small amount of air which was

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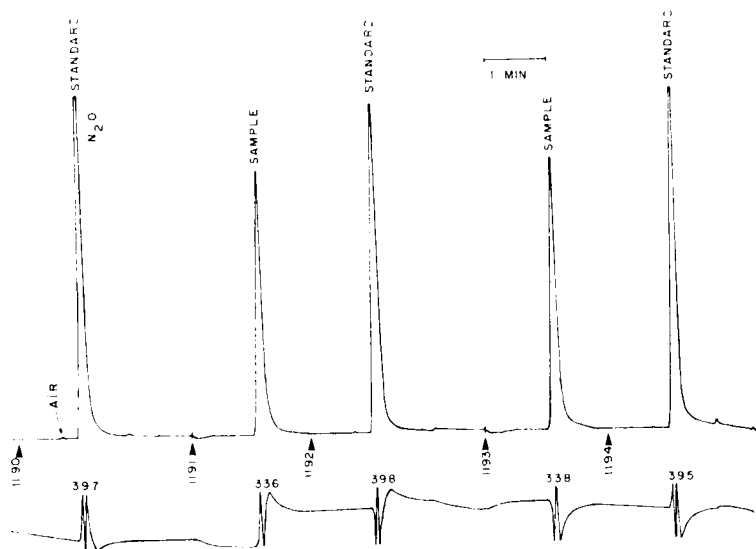


FIG. 1. Analysis of liquid samples alternating with gas standards. Top trace: recorder output (attenuation $32\times$ for gas samples, $8\times$ for liquid samples). Bottom trace: Disc integrator output, the figures directly above the tracing indicate the counts. Introduction of gas or liquid at arrows. Numbers 1190, 1192 and 1194 represent gas standards ($40\ \mu\text{l}$. uncorrected); numbers 1191 and 1193 liquid samples ($20\ \mu\text{l}$). The air peaks are so small that they do not cause an integrator response, they are caused by unavoidable contamination of the gas standard during introduction into the injection port.

introduced caused only a minute recorder deflection which was too small to cause a response of the Disc integrator. The use of sampling valves was avoided because of the solubility of gases in gaskets and O-rings.

Gas Chromatographic Assay. Sample vaporization was performed in a specially designed injection port with a disposable Vycor glass liner operated at 150°C .

Absorption of the water and separation of nitrous oxide from a mixture of oxygen and nitrogen can be achieved with a single column. We used a 6 mm. diameter copper column of 3 m. length packed with 30/60 mesh molecular sieve type 3A.* Using helium as the carrier gas, the column was operated at an inlet pressure of 2.8 at., a flow rate of 75 ml. per minute and a temperature of 75°C . At this temperature the peaks are adequately separated and the time for each analysis is reasonably short. Water is retained completely for many hours. This is a special characteristic of molecular sieve type 3A. The mixture of oxygen and nitrogen has a mean retention time of 47.3 ± 0.16 sec. (S.E.M.); nitrous oxide has a mean retention time of 65.3 ± 0.23 sec. (S.E.M.). Figure 1 shows the separation of the peaks.

The gases were detected with a full-bridge hot wire thermal conductivity detector operated at a temperature of 150°C . and a constant bridge current of 640 mA. The detector

output was displayed on a potentiometer recorder with a span of 1 mV. and a full-scale response of 1 sec. The recorder output was simultaneously integrated by means of a Disc integrator (bottom trace in figure 1).

Calculations. Assays of samples of gas solution (liquid samples) were performed alternately with assays of known amounts of gas (gas standards). The first assay of a gas standard preceded the first assay of a liquid sample, the last assay of a gas standard followed the last assay of a liquid sample in any given series of experiments. Thus two gas standards bracketed each sample (fig. 1). This procedure eliminated possible errors due to long-term drift and randomized the influence of short-term drift in the sensitivity of the detector or the recorder. The mean number of counts from the two bracketing standards was used as the basis for calculations of the amounts of gas contained in the bracketed sample.

The gas volumes were reduced to STP conditions, thus yielding the decimal fraction of gas in solution in the liquid sample. Taking into account the barometric pressure at which the experiment was performed and the water vapor pressure at the temperature of the experiment, the decimal fraction was converted to the Bunsen coefficient with a correction factor derived from Henry's Law.

Results

The results over the range of temperatures from 30°C . to 50°C . are presented in table 1.

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TABLE 1. Solubility of Nitrous Oxide in Water

°C	°K	$\frac{1}{\text{°K}} \times 1,000$	*U	Bunsen coefficient	S.E.M.	N
30	303	3.300	0.450	0.485	±0.0026	20
32.5	305.5	3.328	0.436	0.469	±0.0024	20
37	310	3.226	0.392	0.429	±0.0028	40
40	313	3.195	0.364	0.403	±0.0025	20
45	318	3.145	0.324	0.365	±0.0017	20
50	323	3.096	0.288	0.338	±0.0026	20

* U = Decimal fraction (corrected to STP) in solution.

S.E.M. = Standard error of mean.

The reciprocal of absolute temperature was multiplied by 1,000 to eliminate ciphers.

In general, gas solubility varies inversely with temperature, but there are exceptions to this general rule and the relationship between temperatures and solubility is not necessarily linear. Also, the slope of the function of temperature versus solubility has to be determined experimentally for each individual gas in each individual solvent. A measure of this slope is the differential heat of solution, or partial molal heat of solution (ΔH). This can be calculated by means of the van't Hoff solubility equation if one substitutes the Bunsen coefficient for K.

$$\frac{d \ln \alpha}{dT} = \frac{\Delta H}{RT^2} \quad (1)$$

If ΔH is assumed to be constant and this formula is integrated between the limits of T_1 and T_2

$$\log \frac{\alpha_2}{\alpha_1} = \frac{\Delta H}{2.303R} \left(\frac{T_2 - T_1}{T_1 T_2} \right) \quad (2)$$

Using equation (2) ΔH can be calculated using the following units and definitions:

α = Bunsen absorption coefficient.

T = Absolute temperature in degrees K.

R = 1.987 cal. degree⁻¹·mole⁻¹. The ideal gas constant expressed in terms of calories.

ΔH = The differential heat of solution of the gas in saturated solution.

When calculated according to formula (2) between the limits of $T_1 = 303^\circ \text{K}$. (30°C .) and $T_2 = 323^\circ \text{K}$. (50°C .) ΔH was found to be $-3.35 \text{ kcal. degree}^{-1} \cdot \text{mole}^{-1}$ for nitrous oxide in water.

If ΔH were, indeed, constant over the investigated range of temperatures, a plot of the logarithms of the Bunsen coefficients against the reciprocals of absolute temperature should give a straight line relation. That this linear relation does indeed exist is shown in figure 2.

Discussion

A review of the literature on the solubility of nitrous oxide since 1900 has revealed considerable differences in the solubility figures for nitrous oxide, a gas for which more figures are available than for many others (Markham and Kobe¹). Table 1 illustrates some typical figures which were obtained in or near the physiological range of temperatures and at atmospheric pressure using pure water as the solvent.

The investigators quoted in table 2 used manometric methods for the estimation of nitrous oxide; until recently these were the only reliable and sufficiently accurate methods available. Sy and Hasbrouck,² working in this

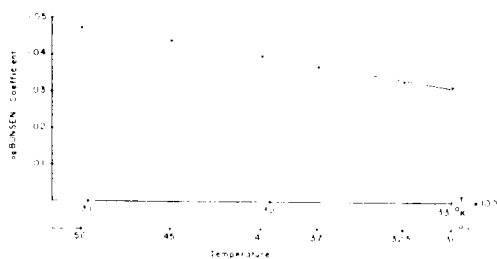


FIG. 2. The relation between the solubility of nitrous oxide in water (expressed as the Bunsen coefficient) and temperature. See text for the mathematical expression of this relation. Straight line fitted visually. The nonlinear centigrade scale at the bottom was added for convenience.

TABLE 2. Solubility of Nitrous Oxide in Water

Author	Year	Temperature °C.	Bunsen Coefficient
McIntosh ³	1958	20	0.68
Nunn ⁴	1956	20	0.63
Orcutt and Seevers ⁵	1937	25	0.549
Seidell ⁶	1928	25	0.545
Harris ⁷	1951	37	0.395
Sy and Hasbrouck ²	1964	37	0.367

laboratory, pointed out the problems of manometric methods. The unextractable fraction and the reabsorbed fraction of gas can be minimized by repeated extractions and rapid and consistent work, but they cannot be completely eliminated. Correction factors are usually applied to the data to compensate for these factors, but the magnitude of these factors is often determined by a certain degree of speculation and therefore open to criticism. Manometric methods do not distinguish between nitrous oxide and other gases, particularly nitrogen, which cannot be absorbed chemically in the reaction chamber. This may not be a great problem when one studies solutions of nitrous oxide in water or other liquids *in vitro*, but it becomes serious when one attempts to study solutions of nitrous oxide in blood prepared by equilibration *in vivo*.

The technique presented here would appear to have several advantages over previous methods. The liquid sample is directly vaporized in an inlet system which permits the repeated injection of gases and vaporizable liquids without damage to the gas chromatograph and which also permits the injection of nonvaporizable solids. Direct vaporization is preferable to vacuum extraction or purging because it results in the immediate and complete release of all volatile or gaseous components.

The use of molecular sieve type 3A which separates nitrous oxide from oxygen and nitrogen and has a very high affinity for water obviates the need for multiple columns with their complicated, time-consuming and potentially troublesome switching mechanisms.

The procedure of injecting standard amounts of pure gas bracketing each sample and relating their average measurements to the measurements of the sample appears to eliminate effectively the influence of long-term and short-

term changes in the sensitivity of the amplifier and recording system. We believe that nothing less than this relatively time-consuming procedure which requires the assay of more standards than samples will assure accurate data, although for less critical, especially clinical investigations, simpler methods might suffice at a sacrifice in accuracy. The data presented show an average accuracy of ± 0.57 per cent, S.E.M., probably better than that obtained with manometric methods so far.

Summary

A gas chromatographic method is presented which appears to obviate certain difficulties inherent in previous methods employed for the assay of gases in liquids, especially manometric methods. The samples are vaporized directly in a special injection port with disposable liner. Nitrous oxide is separated from the air gases and from water vapor by means of a single column. The sensitivity of the whole system is continually calibrated with gas standards eliminating the influence of short-term and long-term changes in sensitivity.

Bunsen absorption coefficients are presented for nitrous oxide in water over the range of temperatures from 30° C. to 50° C. with an average standard error of the mean of ± 0.57 per cent.

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