wave length of 285.5 mμ may therefore be corrected for the scattering contribution at every *p*H. The values of $\Delta D_{285.5}$ arising solely from absorption may then be plotted as a function of *p*H, as shown in Fig. 3. The points fit reasonably well to the curve representing the experimental titration curve for insulin in the acid *p*H range.[9] It is important to use the experimental rather than a theoretical titration curve for acid groups since the calculation of the electrostatic factor wZ is subject to considerable uncertainty.[9] On the other hand, the use of the insulin titration curve is not entirely satisfactory since the curve represents ionizations of 6 carboxyl groups of intrinsic *pK* 3.6 and 4.7, while the spectral data probably refer, as pointed out in a previous paper,[2] to only one or possibly two ionizing groups. Having demonstrated the effect of light scattering on the ultraviolet difference spectrum, the anomalies near the insolubility region previously reported[2] disappear, and the significance of the titration curve of Fig. 3 remains as discussed previously, *i.e.*, the data are compatible with the presence of a tyrosyl-carboxylate ion hydrogen bond in which the carboxylate acceptor has an observed *pK* of 3.5 to 3.6.

In conclusion, whereas ultraviolet difference spectra may provide information on internal hydrogen bonding in non-aggregating systems, a possible contribution from light scattering must be taken into account if the state of aggregation of the protein is *p*H-dependent.

---

[9] C. Tanford and J. Epstein, THIS JOURNAL, **76**, 2170 (1954).

[CONTRIBUTION FROM THE BALLISTIC RESEARCH LABORATORIES, ABERDEEN PROVING GROUND, MARYLAND]

The Reaction of Nitric Oxide with Triethyl Phosphite

BY LESTER P. KUHN, J. OMAR DOALI AND CARL WELLMAN

RECEIVED FEBRUARY 12, 1960

The liquid phase reaction, $2NO + (EtO)_3P \rightarrow N_2O + (EtO)_3PO$, is described. The reaction is first order in nitric oxide and first order in phosphite and the reaction rate is quite insensitive to the nature of the solvent. A mechanism is proposed for the reaction which involves the intermediate $(EtO)_3PNO$.

A reaction which does not appear to have been previously reported in the literature has been found to occur between nitric oxide and triethyl phosphite to yield nitrous oxide and triethyl phosphate

$$2NO + (C_2H_5O)_3P \longrightarrow N_2O + (C_2H_5O)_3PO$$

The reaction goes cleanly and quickly in the liquid phase at room temperature. When the reaction is run in the presence of excess phosphite, the nitrous oxide that is formed shows no tendency to be further reduced to nitrogen. In the succeeding paragraphs, we present a study of the kinetics of the reaction and a mechanism which is consistent with the kinetic data. After the completion of the experimental portion of this work, a paper appeared by Cox and Westheimer,[1] which describes a reaction between nitrogen dioxide and phosphite esters to give the corresponding phosphate ester and nitrous oxide and nitrogen. This reaction is said to proceed rapidly, even at −80°, and has proved useful[2] for the preparation of phosphate esters, particularly in instances where the phosphate ester is sensitive to acid or base. Since nitric oxide is much less reactive than nitrogen dioxide, it would appear that the reaction described here is also of preparative value. It also constitutes a convenient method of preparing very pure nitrous oxide.[3]

The products and stoichiometry of the reaction were determined by stirring triethyl phosphite (0.1 mole) at room temperature in a system containing nitric oxide at 300 mm. (0.036 mole). The final pressure at the end of the reaction was 144 mm. (slightly less than the theoretical 150 mm. due to the greater solubility of nitrous oxide in the liquid as compared with nitric oxide). The gas was found by both infrared and mass spectrometric analysis to be nitrous oxide of purity greater than 99%. Gas chromatography of the liquid after reaction showed that it consisted of triethyl phosphite and triethyl phosphate, the yield of the latter being 0.018 mole (100%).

For the kinetic studies the reaction was carried out by rapidly stirring a solution of triethyl phosphite in the desired solvent in an atmosphere of nitric oxide. The rates were followed manometrically. Because the reaction is quite rapid, very vigorous stirring is required to obtain conditions such that the reaction rate is independent of stirring speed. By using a high-speed motor and a stirrer of the proper shape (see Experimental), it was possible to make the reaction rate independent of stirring speed as shown by the fact that in a series of experiments in which the initial concentration of reactants was kept constant but the stirring speed was varied, the observed reaction rate was constant. The phosphite was generally present in considerable excess, the initial molar ratio of phosphite to nitric oxide being about 4, so that the concentration of phosphite did not change by more than 10% during the first 60% of the reaction. Under these conditions good first order rate curves were obtained, as shown in Fig. 1.

The results from a number of runs at 0° using different initial concentrations of phosphite, different initial pressures of nitric oxide and different solvents are given in Table I. When the initial

---

[1] J. R. Cox, Jr., and F. H. Westheimer, THIS JOURNAL, **80**, 5441 (1958).

[2] J. R. Cox, Jr., Robert Wall and F. H. Westheimer, *Chem. and Ind.* (*London*), 929 (1959).

[3] In the paper by Cox and Westheimer (ref. 1), the statement is made that phosphite esters do not react with nitric oxide. In response to private communication with Professor Westheimer, further experiments by Cox and Westheimer have, however, fully confirmed the results here reported.

concentration of triethyl phosphite is kept constant and the initial pressure of nitric oxide is varied from 200 to 500 mm. the first order rate constant remains unchanged, indicating that the reaction is first order in nitric oxide. Using different initial concentrations of phosphite it was found that the first order rate constant is proportional to the triethyl phosphite concentration indicating that the reaction is also first order in phosphite. The total order of the reaction is therefore two, and the second order rate constants are given in the last column of Table I. It can be seen from the table that the reaction rate is not very sensitive to the nature of the solvent, the rate increasing by a factor of about two in going from the slowest solvent, hexane, to the fastest solvent, toluene. There is also no correlation between the polarity or dielectric constant of the solvent and the reaction rate.

TABLE I

SECOND ORDER RATE CONSTANT FOR THE REACTION BETWEEN NITRIC OXIDE AND TRIETHYL PHOSPHITE AT 0°

NO[a]	TEP[b]	Solvent	k_2[c]
393	1.2	Benzene	0.079
195	1.2	Benzene	.078
500	1.2	Benzene	.080
400	1.2	Toluene	.080
201	1.2	Toluene	.078
501	1.2	Toluene	.076
400	1.7	Toluene	.071
401	0.6	Toluene	.0800
397	0.6	Butyl ether	.0470
404	1.2	Butyl ether	.043
398	1.2	Butyl ether	.043
397	1.8	Butyl ether	.048
395	1.2	*n*-Hexane	.040
396	1.2	Ethanol	.061
396	1.2	Cyclohexene	.040
406	1.2	Amyl acetate	.066

[a] Pressure in mm. [b] Moles per liter of triethyl phosphite. [c] Second order rate constant in Sec.$^{-1}$ moles^{-1} liters. The method of calculation is given in the Experimental portion.

The mechanism proposed, which is compatible with the experimental data, is

$$NO\cdot + (EtO)_3 \xrightarrow{\text{slow}} (EtO)_3P\text{-}N = O$$

$$(EtO)_3P\text{-}N = O + NO\cdot \xrightarrow{\text{fast}} (EtO)_3PO + N_2O$$

If the first step is slow and rate-determining, followed by a rapid second step, then the kinetics of the reaction will be $r = 2k[NO][(EtO)_3P]$ which is in agreement with experiment. The structure of the intermediate formed in step 1 was arbitrarily chosen. If it is correct then the second step is a four center reaction in which the oxygen of the second nitric oxide molecule becomes bound to phosphorous. Alternatively, the structure of the intermediate may be pictured as $(RO)_3\dot{P}ON$, in which case the oxygen of the second nitric oxide molecule would appear as nitrous oxide. The kinetic data do not enable one to chose between these two alternatives. The fact that the reaction rate is relatively insensitive to the nature of the solvent indicates that the intermediate formed in the first step is not ionic in character but is a radical with little charge separation. Other examples of the facile participation of phosphite esters in free radical reactions have appeared in the literature.[4] In these reactions, triethyl phosphite is believed to react with a radical to form a new radical with odd electron on phosphorus. For example, the light and peroxide catalyzed reaction of triethyl phosphite with CCl_4 is believed to involve the step $CCl_3\cdot + (EtO)_3P \rightarrow (EtO)_3\dot{P}CCl_3$ which is analogous to the first step shown above.

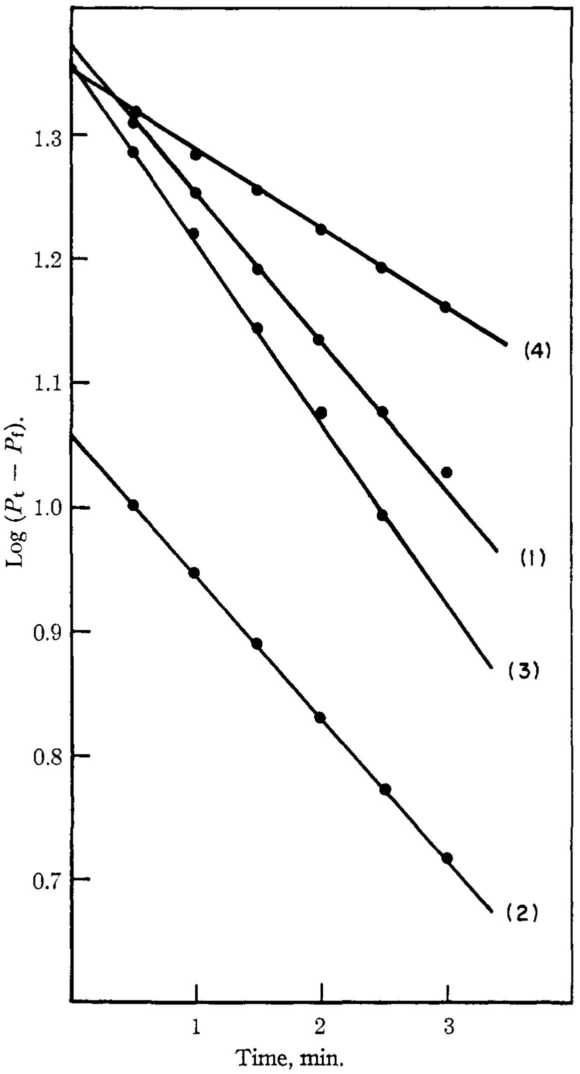

FIG. 1.—First-order rate curves for reaction between nitric oxide and triethyl phosphite in toluene at 0°. Initial conditions: (1) NO, 400 and TEP 1.2; (2) NO, 201 and TEP 1.2; (3) NO, 409 and TEP 1.7; (4) NO, 400 min. and TEP 0.6 moles/liter.

We attempted to obtain evidence for the transient existence of a reactive radical intermediate by running the reaction with styrene as the solvent. The formation of polystyrene would be evidence for the formation of a reactive radical. Reactions carried out at 0° and at room temperature yielded no polystyrene but only the normal products nitrous oxide and triethyl phosphite.

---

[4] (a) C. E. Griffin, *Chem. and Ind.* (*London*), 915 (1958); (b) C. Walling and R. Rabinowitch, THIS JOURNAL, **81**, 1243 (1959).

This indicates that the radical formed in the first step reacts more quickly with nitric oxide than with styrene. The failure of the reaction to catalyze the polymerization of styrene does not disprove the existence of a radical intermediate since the reaction between the proposed intermediate and nitric oxide is a reaction between two radicals and hence would have a negligible activation energy, whereas the reaction between a radical and styrene and the propagation step in the polymerization of styrene have activation energies of 10 to 20 kcal. per mole.

Experimental

Triethyl phosphite was purified by storing over sodium and distilling at reduced pressure through a Vigreux column. It was found by gas chromatography that after this treatment it contained no significant amount of impurity. Solvents were dried and distilled before use and checked for purity by gas chromatography. The nitric oxide was passed through a bed of Ascarite before entering the reaction flask. This removed the major impurity, nitrogen dioxide, as evidenced by the complete absence of the brown color characteristic of nitrogen dioxide.

The reactions were carried out in a 500-ml., three-neck flask, one neck of which was connected to a vacuum line, the middle neck to a magnetic stirrer and the third neck to a mercury manometer. The teflon stirring blade was cut so that it fitted the contour of the flask. A Mixmaster motor was used to turn the magnet which was coupled to the stirrer. There are ten possible settings of the motor by which one can vary the speed in a stepwise manner. It was found that when the setting was at 6 or higher, the reaction rate was independent of stirring speed. All subsequent runs were made with the setting at 7 or 8.

The appropriate amount of triethyl phosphite was pipetted into a 25-ml. volumetric flask and was diluted with the solvent. The solution was introduced into the reaction flask and allowed to stand in an ice bath for about 30 minutes until temperature equilibrium was achieved. The flask was then evacuated and filled with nitrogen and evacuated again to ensure the complete removal of air. The nitric oxide was then introduced to the desired pressure. The connection between the vacuum line and the reaction flask was closed by a stopcock and the stirrer was started. The manometer was read every 30 seconds until the completion of the reaction.

At the end of the reaction a sample of gas taken and analyzed both by infrared and mass spectrometer. It was found to contain over 99% nitrous oxide. The liquid reaction mixture was then subjected to gas chromatography and yielded three fractions—the solvent, unreacted triethyl phosphite and triethyl phosphate. The last was identified by comparing its infrared spectrum with that of a known sample of triethyl phosphate and by showing that the retention time in the chromatographic column was the same for the reaction product as for the known compound.

It is necessary to know the solubility of the nitric oxide in the various solvents in order to calculate the rate constant. The solubilities were determined in the same apparatus as the rate measurements were made. Fifty ml. of solvent were introduced into the 500-ml. flask which was cooled to 0°. After removal of air and flushing with nitrogen several times, nitric oxide was introduced and the pressure was measured. The stirrer was then started and the solution was stirred until the pressure reached a constant value.

It was assumed that our system obeys Henry's law

$$P = HX$$

where P is the pressure of nitric oxide above the liquid at equilibrium, H is a dimensionless constant and X is the mole fraction of nitric oxide in solution. In dilute solutions such as those used here, X is essentially equal to the concentration. The values of H for the various solvents at 0° which are given in Table II were determined by the relationship

$$P(\text{NO}) \text{ at equilibrium } = \frac{(\text{mm. NO absorbed})(\text{volume of gas})}{(\text{volume of liquid})} H$$

TABLE II

SOLUBILITY OF NITRIC OXIDE IN VARIOUS SOLVENTS AT 0°

Solvent	*H*
Benzene	1.0
Toluene	1.0
n-Butyl ether	0.92
Amyl acetate	0.87
Cyclohexene	1.05
n-Hexane	1.10
Ethanol	1.25

The second order rate constants given in Table I were calculated from the equation

$$\frac{2.303\ \Delta \log (P_{\text{t}} - P_{\text{p}})\Delta t}{(\text{TEP})\ V_1/(\text{H}V_{\text{g}} + V_1)} = k_2$$

where P_{t} and P_{f} are the pressure in the system at time t and the final pressure, respectively, (TEP) is the concentration of triethyl phosphite in moles per liter, H is Henry's constant given in Table II, V_1 is the volume of liquid (25 ml. in our experiments) and V_{g} is the volume of gas (500 ml.). The numerator was determined from the slope of the first order rate curves such as shown in Fig. 1.

[CONTRIBUTION FROM THE CALIFORNIA RESEARCH CORPORATION, RICHMOND, CALIFORNIA]

The Kinetics of the Disproportionation of Sodium Thiosulfate to Sodium Sulfide and Sulfate

BY WILLIAM A. PRYOR*

RECEIVED FEBRUARY 17, 1960

Sodium thiosulfate has been found to disproportionate irreversibly to form sulfide and sulfate in water or in aqueous buffers at 250–280° (equation 1). The reaction is pseudounimolecular with first order dependence on $S_2O_3^=$. The first order rate constant k_1 measured at 270° is nearly proportional to the hydrogen ion concentration measured at either 22 or 75°, and it seems reasonable to assume k_1 is proportional to the hydrogen ion concentration at 270°. It appears that k_1 is not dependent on the acetate ion concentration in sodium acetate buffers but only on the hydrogen ion concentration. The Arrhenius activation energy is 57 kcal. in sodium phosphate buffers. Sulfite is not an intermediate in this reaction. The mechanism is discussed.

Sodium thiosulfate has been found to undergo irreversible disproportionation in water or in aqueous buffers at 250–280°. The products are mainly sulfide and sulfate but small amounts of sulfur, polysulfide and sulfite are formed

$$S_2O_3^= + OH^- \longrightarrow SO_4^= + HS^- \qquad (1)$$

or

$$S_2O_3^= + H_2O \longrightarrow SO_4^= + HS^- + H^+ \qquad (1A)$$

---

* Department of Chemistry, Purdue University, Lafayette, Indiana.