

have assigned also the cyclic oxyphosphorane structure.⁴ These assignments are, therefore, mutually strengthened by the results summarized in this communication.

Diketol Cyclic Phosphate (IIA).—M.p. 106–112° (slow crystallization from ether or benzene-hexane). *Anal.* Calcd. for C₉H₁₆O₆P: C, 43.2; H, 6.0; P, 12.4; mol. wt., 250. Found: C, 43.2; H, 6.0; P, 12.4; mol. wt., 250 (alkaline titration at pH 7.0). Infrared in CCl₄ (μ): split CO at 5.77, 5.81 (s); PO at 7.68 (s); CH₃OP at 9.52 (vs); no OH. H¹ n.m.r. in CDCl₃ vs. TMS (fresh solution) (τ): CH₃OP at 6.07, J_{HP} = 12 c.p.s.;

CH₃CO at 7.65; CH₃C— at 8.42. IIA is sensitive to

moisture. Complete hydrolysis of IIA (benzene, excess water, reflux) gave 3,4-dimethyl-3,4-dihydroxy-2,5-hexanedione,² m.p. 95–96°.

Hemiketal Cyclic-Phosphate (III).—M.p. 114–115° (CH₂Cl₂-hexane). *Anal.* Calcd. for C₁₁H₁₉O₇P: C, 42.6; H, 6.8; P, 11.0. Found: C, 42.6; H, 7.1; P, 11.0. Infrared in CHCl₃ (μ): OH at 2.83 (broad); PO at 7.70 (s); POCH₃ at 9.50 (vs); no CO. H¹ n.m.r. (freshly prepared CDCl₃ solution vs. TMS) (τ): OH at

5.77; CH₃OP at 6.15, J_{HP} = 12 c.p.s.; CH₃O—C— (hemiketal): 6.65; CH₃C— at 8.50, 8.55 (double

intensity) and 8.58 (three of the four high-field methyl lines were resolvable). Under certain conditions, III can be recovered into IIA by removal of methanol.

Acknowledgment.—We are very grateful to Prof. E. Eliel (Univ. of Notre Dame) and to Mr. M. Banas (American Oil Co., Whiting, Indiana) for H¹-n.m.r. facilities and instruction.

(4) (a) F. Ramirez, N. B. Desai and N. Ramanathan, *Tetrahedron Letters*, No. 5, 323 (1963); (b) F. Ramirez and N. Ramanathan, *J. Org. Chem.*, **26**, 3041 (1961); (c) F. Ramirez and N. B. Desai, *J. Am. Chem. Soc.*, **82**, 2652 (1960).

(5) Alfred P. Sloan Fellow, 1961–1963

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RECEIVED JULY 23, 1962

Equalization of Electronegativity¹

Sir:

Recently, Hinze, Whitehead and Jaffé² have made real progress toward the derivation of an electronegativity scale for groups and radicals, based on an extension of the definition of electronegativity for atomic orbitals originally given by Pritchard and Sumner.³ However, Hinze, Whitehead and Jaffé neglect the effect of overlap between bonding orbitals, and are then led logically to the principle of equalization of the

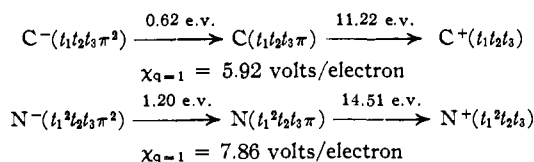
(1) Based on a lecture given at the Gordon Research Conference on Inorganic Chemistry at New Hampton, N. H., August 6–10, 1962.

(2) J. Hinze, M. A. Whitehead and H. H. Jaffé, *J. Am. Chem. Soc.*, **85**, 148 (1963).

(3) H. O. Pritchard and F. H. Sumner, *Proc. Roy. Soc. (London)*, **A235**, 136 (1956).

electronegativities of the orbitals forming the bond. In neglecting the overlap, they are in effect making a classical prediction of the electron distribution in the bond from the known (albeit quantum) properties of the constituent atoms, and the result must be in error to some extent. The order of magnitude of this error can be seen from the following calculation.

Consider an isolated π -bond between a carbon atom and a nitrogen atom in an extended organic system. (There is no difference in principle between π -bonds and σ -bonds.) This $>C=N-$ bond can be treated by the self consistent electronegativity molecular orbital approximation of Pritchard and Sumner³ in which the coulomb integral α_q for each atom is identified with the electronegativity χ_q of its π -orbital, where q is the occupation number of that orbital. The relevant valence state ionization energies for carbon and nitrogen are taken as⁴



In each cycle of the calculation the overlap integral and the values of α_q for the two atoms are adjusted according to the values of q obtained in the previous cycle, until a self consistent set of charge densities is obtained. The results for the C=N system, with $r_{CN} = 1.34 \text{ \AA.}$, are⁵

Atom	Charge	Electronegativity
C	0.946 electron	6.50 volts/electron
N	1.054 electron	7.13 volts/electron

Clearly the difference in electronegativity is considerably reduced in bond formation, but the electronegativities are not equalized. This would have required us to get $q_N = 1.082$, $q_C = 0.918$ and thus $\chi_q = 6.775$ volts/electron for both atoms.

This calculation suggests, therefore, that in general, the bond electronegativities of each atom will differ from the equalization value by something in excess of 10% of the original difference in electronegativity between the two constituent orbitals. This is quite a serious error and must be taken into account before a satisfactory electronegativity scale for radicals and groups can be finally established by the method of Hinze, Whitehead and Jaffé.

(4) G. Pilcher and H. A. Skinner, *J. Inorg. Nucl. Chem.*, **24**, 937 (1962).

(5) D. G. Rush, M. S. Thesis, Manchester, 1962. Apparently there was an error in the effective Z used for the overlap integrals for pyridine in ref. 3: the self consistent charge densities should be N atom 1.057, *ortho* C atoms 0.976, *meta* C atoms 0.997, *para* C atoms, 0.996; this is compatible with the strong preference of OH⁻ and NH₃⁻ for attack in the *ortho* position.

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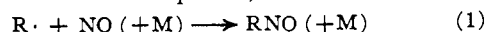
H. O. PRITCHARD

RECEIVED MAY 7, 1963

Mechanism of the Low-Temperature Scavenging of Methyl- \dot{d}_3 Radicals by Nitric Oxide

Sir:

The detailed mechanism by which nitric oxide scavenges free radicals has been a matter of considerable discussion since the discovery¹ of its inhibitory effect on free radical chain processes. Although it is generally agreed that the first step is one of direct addition to form a nitroso compound, *viz.*



(1) L. A. K. Staveland and C. N. Hinshelwood, *Proc. Roy. Soc. (London)*, **A154**, 335 (1936).

further reactions of RNO, particularly in high-temperature pyrolytic systems, are a matter of some controversy.²⁻⁷ At low temperatures (<ca. 200°) the complete scavenging mechanism, which must necessarily deal with further reactions of RNO, is not completely clear either, but is considerably more so than at high temperatures. While nearly all early work assumed the scavenging of only one free radical per nitric oxide molecule, more recent studies at low temperatures suggest that three radicals are scavenged per nitric oxide molecule. In studies of methyl radical abstraction of nitric oxide from methyl nitrite at 180°, Phillips^{8,9} has observed the formation of trimethylhydroxylamine, presumably *via* the successive addition of methyl radicals to nitrosomethane, *viz.*



This finding is consistent with the observation of Gingras and Waters¹⁰ that equation 2 occurs in solution when R is a 2-cyano-2-propyl radical. It is also in accord with recent studies of Hoare,¹¹ who found that in the photolysis of acetone-nitric oxide mixtures at 200° the number of radicals scavenged per nitric oxide molecule is between two and three. The purpose of this communication is to report evidence supporting the successive addition of methyl radicals to nitric oxide at room temperature.

We have photolyzed (at 3660 Å. and room temperature) mixtures of azomethane-*d*₆ and nitric oxide in a cell with a pin-hole leak into the ionization chamber of a Bendix Model 14-101 time-of-flight mass spectrometer, and have followed product formation continuously. In the absence of nitric oxide the only significant products are nitrogen and ethane-*d*₆. In the presence of 0.2-2% of nitric oxide we have observed the following products: CD₃NO, as indicated by the initial rapid appearance of a peak at mass 48; (CD₃)₂NOCD₃, as indicated by the appearance of peaks at masses 66 and 84 that arise from the same molecular species and which are in the ratio expected from inspection of the mass spectral cracking pattern⁹ of (CH₃)₂NOCH₃; and C₂D₆. The formation of CD₃NO is accompanied by a corresponding decrease in nitric oxide concentration (as observed by monitoring mass 30 at low ionizing voltage) to an immeasurably small value. No other products were found, although we specifically looked for peaks characteristic of (CD₃NO)₂,⁴ tetramethylhydrazine¹² and further addition products of CD₃NO with NO.¹³

The results of photolysis of a mixture of 11.8 mm. of azomethane-*d*₆ and ~0.2 mm. of nitric oxide are shown in Fig. 1. The general appearance of the pressure-time curves is typical of all photolyses carried out. The conversion of mass spectral peak heights to pressures was made by means of ethane and azomethane calibration and the following assumptions: (1) for a constant light intensity, the initial rate of formation of CD₃NO (the only observed product, initially) is twice the initial rate of formation of ethane-*d*₆ that is observed in the absence of nitric oxide; and (2) after depletion of the initial nitric oxide, NO is present only as CD₃NO and (CD₃)₂NOCD₃, so that the sum of pressures of CD₃NO

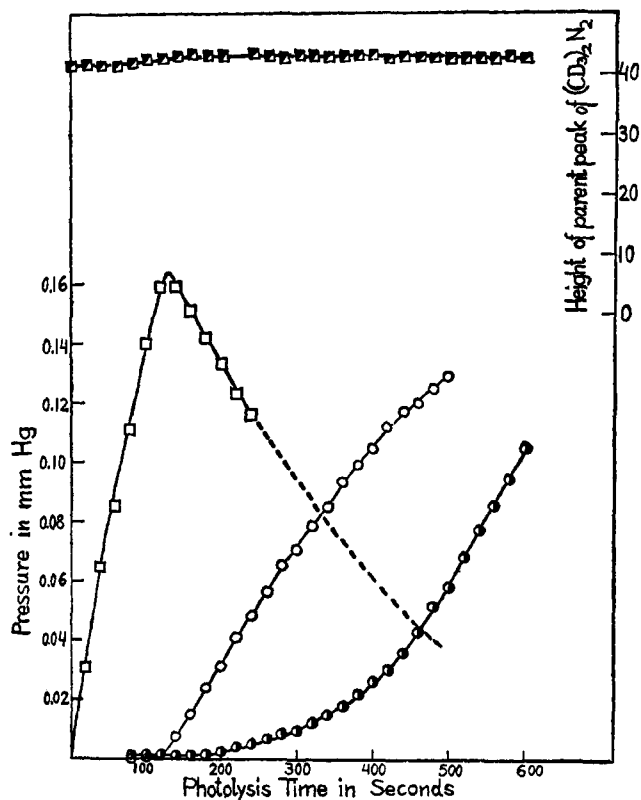
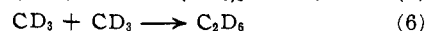
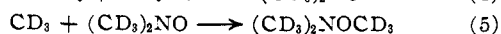
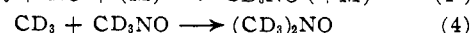
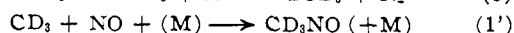
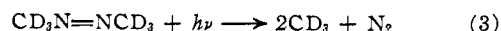


Fig. 1.—Photolysis of azomethane-*d*₆-nitric oxide mixture: □, CD₃NO; ○, (CD₃)₂NOCD₃; ●, C₂D₆; ■, *m/e* 64 (CD₃)₂N₂ in arbitrary units.

and (CD₃)₂NOCD₃ is constant and the rate of disappearance of CD₃NO is equal to the rate of appearance of (CD₃)₂NOCD₃. The dotted portion of the CD₃NO curve has been calculated using this second assumption.

As can be seen in Fig. 1, CD₃NO forms immediately and goes through a maximum. This maximum occurs at about the same time that we have observed essentially complete depletion of NO and at the same time as the occurrence of a very marked increase in (CD₃)₂NOCD₃ concentration. After NO is consumed CD₃NO can no longer be formed, and its concentration is then depleted, presumably by attack of CD₃ from the photolyzing azomethane-*d*₆. (CD₃)₂NOCD₃ is formed at a decreasing rate with time which is in accord with its precursor being a species whose concentration is continually decreasing. On the other hand, C₂D₆ is formed at an increasing rate which is in accord with the postulate that the continually decreasing CD₃NO is competing for CD₃ radicals. No species (CD₃)₂NO was detected. This is not surprising for (CD₃)₂NO is a free radical and would not be expected to reach a detectable concentration in our system. The most reasonable mechanism in accord with the experimental facts is as follows



The difference in shapes of the C₂D₆ and (CD₃)₂NOCD₃ formation curves allows us to rule out the possibility that NO might act as a chaperon¹⁴ in the recombination of methyl radicals.

The ratio of the slope of the CD₃NO disappearance curve (or the (CD₃)₂NOCD₃ appearance curve) to the

(2) H. W. Thompson and M. Meissner, *Nature*, **139**, 1018 (1937).

(3) H. A. Taylor and H. Bender, *J. Chem. Phys.*, **9**, 761 (1941).

(4) C. S. Coe and T. F. Doumani, *J. Am. Chem. Soc.*, **70**, 1516 (1948).

(5) J. H. Raley, F. F. Rust, and W. E. Vaughan, *ibid.*, **70**, 88 (1948).

(6) H. T. J. Chilton and B. G. Gowenlock, *Nature*, **172**, 73 (1953).

(7) J. B. Levy, *J. Am. Chem. Soc.*, **75**, 1801 (1953).

(8) L. Phillips, *Proc. Chem. Soc.*, 204 (1961).

(9) B. Bromberger and L. Phillips, *J. Chem. Soc.*, 5302 (1961).

(10) B. A. Gingras and W. A. Waters, *ibid.*, 1920 (1954).

(11) D. E. Hoare, *Can. J. Chem.*, **40**, 2012 (1962).

(12) H. A. Taylor and F. P. Jahn, *J. Chem. Phys.*, **7**, 470 (1939).

(13) M. I. Christie, *Proc. Roy. Soc., (London)*, **A249**, 248 (1958).

(14) G. Porter, *Discussions Faraday Soc.*, **33**, 198 (1962).

square root of the slope of the C_2D_6 appearance curve at a given CD_3NO pressure and assumption of the above mechanism leads to an estimate for $k_4/k_6^{1/2}$ of 2.5×10^{-9} [$cm.^3/molecule\cdot sec.$] $^{1/2}$. Combining this ratio with the value¹⁵ of 7.5×10^{-11} $cm.^3\cdot molecule^{-1}\cdot sec.^{-1}$ for k_6 yields a value for k_4 of 2.2×10^{-14} $cm.^3\cdot molecule^{-1}\cdot sec.^{-1}$. If we take the third-order rate constant¹¹ of 8.8×10^{-31} $cm.^6\cdot molecule^{-2}\cdot sec.^{-1}$ for equation 1' and assume azomethane to be as effective a third body as acetone, we are led to the interesting conclusion that, at 25° and 12 mm. pressure, nitric oxide is only 15 times more effective than nitrosomethane in scavenging methyl radicals.

Acknowledgment.—This work was supported in part by Petroleum Research Fund Grant 833-A1, and in part by Contract AF33(616)7716 with Office of Aerospace Research. A more complete report shall be forthcoming.

(15) R. Gomer and G. B. Kistiakowsky, *J. Chem. Phys.*, **19**, 85 (1951).

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RECEIVED MAY 3, 1963

Prostaglandins and Related Factors. 17.¹

The Structure of Prostaglandin E_3 ²

Sir:

The chemical structure (Fig. 1) of prostaglandin E_1 (PGE_1) has been reported.³ Recently, two new biologically active compounds were isolated from sheep vesicular glands and subjected to structural analysis.⁴

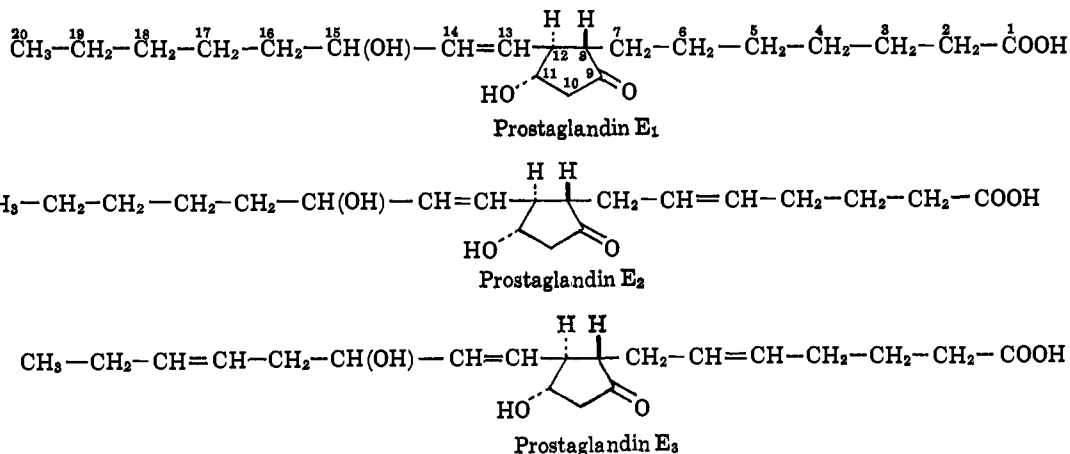


Figure 1.

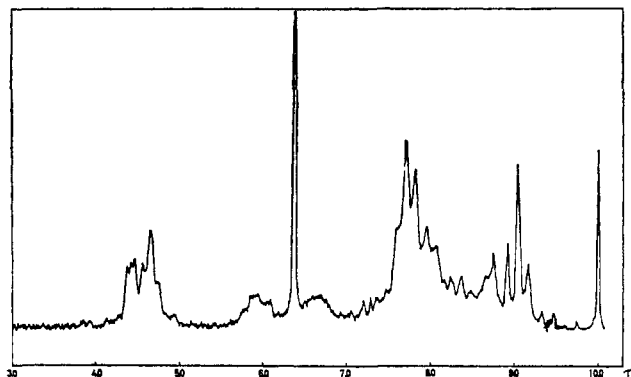
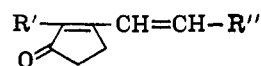


Fig. 2.—Proton n.m.r. spectrum of the methyl ester of prostaglandin E_3 .

(1) The prostaglandins belong to a new class of physiologically highly active compounds having smooth muscle stimulating and blood pressure depressing activity. For pertinent references, see S. Bergström and B. Samuelsson, *J. Biol. Chem.*, **237**, PC 3005 (1962). According to the nomenclature recently introduced (S. Bergström, R. Ryhage, B. Samuelsson and J. Sjövall, *ibid.*, in press) the parent C_{20} acid is called prostanic acid and prostaglandin E_1 , 11 α ,15-dihydroxy-9-keto-prost-13-enoic acid and prostaglandin E_2 , 11 α ,15-dihydroxy-9-keto-prosta-5,13-dienoic acid. X-Ray diffraction studies (S. Abrahamsson, S. Bergström and B. Samuelsson, *Proc. Chem. Soc.*, 332 (1962)) of a derivative of prostaglandin E_1 have provided the stereochemical features shown in Fig. 1.

This led to elucidation of the structure of prostaglandin E_2 (PGE_2) (Fig. 1) and afforded the following data on prostaglandin E_3 (PGE_3).

Mass spectrographic analysis of the methyl ester of PGE_3 demonstrated that its molecular weight is two units less than that of PGE_2 and four units less than that of PGE_1 . That the parent structure is the same for all three compounds followed from their conversion by catalytic reduction into the same derivative as judged by mass spectrographic analysis. The presence of two of the three double bonds of PGE_3 in the same positions as in PGE_2 was demonstrated by analysis of the mass spectra of all three compounds, by isolation of glutaric acid after chromic acid oxidation of both PGE_2 and PGE_3 and, finally, by the appearance of the same chromophore



($\lambda_{\text{max}}^{\text{EtOH}}$ 278 $m\mu$) on treatment of PGE_1 , PGE_2 or PGE_3 with alkali.⁴

A detailed analysis of the mass spectrum of PGE_3 further indicated that the third double bond in this compound is located in the terminal pentyl group.⁴ The present report is concerned with nuclear magnetic resonance studies, which in combination with the mass spectrographic analyses unequivocally demonstrate the structure of prostaglandin E_3 .

The n.m.r. spectra were determined with a Varian A-60 spectrophotometer on deuteriochloroform solutions of the methyl esters containing tetramethylsilane as standard. The n.m.r. spectrum of the methyl ester of PGE_3 is shown in Fig. 2.

Two of these protons appear at lower frequencies (4.25–4.5 τ) and in the same region as the two olefinic protons in PGE_1 . The other four olefinic protons in PGE_3 have approximately the same chemical shift as the protons attached to the double bonded carbon atoms in the carboxyl side chain of PGE_2 .

(2) This study has been supported by grants to Professor Sune Bergström from "Statens Medicinska Forskningsråd" and "Knut och Alice Wallenbergs Stiftelse."

(3) S. Bergström, R. Ryhage, B. Samuelsson and J. Sjövall, *Acta Chem. Scand.*, **16**, 501 (1962).

(4) S. Bergström, F. Dressler, R. Ryhage, B. Samuelsson and J. Sjövall, *Arkiv Kemi*, **19**, 563 (1962).