Instead, a quartet with the usual second-order splitting is observed. It would therefore seem that the small splitting of the methylene protons by the aldehydic protons, together with the second-order splitting of the quartet, have produced these four triplets. Also, the triplet of the aldehydic proton resonance of propionaldehyde in Figure 2a has collapsed to give a sharp signal. The changes in the resonances of the methylene and aldehydic protons may be explained by the fact there are two possible magnetic environments for the protons: (i) in propionaldehyde; (ii) in 1,1-dihydroxypropane. Owing to the reversible hydration, protons experience a rapid interchange of these environments. From the collapse of the aldehydic proton triplet, the mean lifetime of propionaldehyde was calculated to be 450 msec.

The equilibrium constant K_h was determined to be 1.4 from the ratio of the intensities of (i) the aldehydic and methylyne proton resonances and (ii) the methylene proton resonances of propionaldehyde and its hydrate. This value is in good agreement with that obtained by the ultraviolet photometric technique.[21] The equilibrium constant did not vary with concentration. The lowest concentration observed was determined by the detection limits of the instrument and the highest concentration, about 6 mol l.$^{-1}$ of propionaldehyde, by solubility.

Various changes were observed in the spectra obtained on addition of hydrochloric acid to the aqueous solution of propionaldehyde. The methylene quartets, the methyl triplets and the aldehydic resonances all broadened (see Figures 2a–d), owing to the hydration–dehydration exchange which became more rapid.

The reciprocal of the mean lifetime of propionaldehyde was obtained by observing the aldehydic and methylene resonances of propionaldehyde and comparing these with theoretical spectra which had been computed for various lifetimes. The theoretical triplets and quartets were computed from the imaginary part of the total complex magnetization as determined by McConnell's method.[13]

The reciprocal of the mean lifetime of propionaldehyde is plotted against the hydrochloric acid concentration in Figure 3. The straight-line graph obtained indicates a rate law of the type

$$\text{specific rate} = k_0 + k_{H^+}[H^+]$$

where k_0 is the spontaneous rate constant and k_{H^+} is the hydrogen ion dependent rate constant. This is consistent with the general acid–base catalysis observed for the hydration of carbonyl-containing compounds.

For the hydration, the hydrogen ion dependent rate constant was 460 l. mol^{-1} sec^{-1}, as determined from the slope of the straight line obtained in Figure 3.

It is reasonable to assume that the spontaneous rate constants for the hydration and dehydration are small compared to the hydrogen ion dependent rate constants. Therefore, the equilibrium constant K_h was employed to estimate the hydrogen ion dependent rate constant, which was found to be 650 l. mol^{-1} sec^{-1}. These results are in good agreement with those of Gruen and McTigue,[7] who employed a thermal method.

No anomalous behaviour similar to that of acetaldehyde was observed for the hydration of propionaldehyde.

Registry No.—Acetaldehyde, 75-07-0; propionaldehyde, 123-38-6.

Acknowledgment.—The author wishes to acknowledge helpful discussion with Professor V. Gold of King's College, London.

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Mechanism of Ozonation Reactions. IV. Carbon–Nitrogen Double Bonds

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A study of the mechanism of the ozonation of carbon–nitrogen double bonds has been carried out using product analysis data and competitive rate studies on dimethylhydrazones, oximes, and Schiff bases. It was found that variation of Y in I ($XC_6H_4CR{=}NY$) had a much larger effect on relative rates than variation of X. A generalized mechanism involving initial electrophilic attack of ozone on the carbon atom of the carbon–nitrogen double bond is proposed, and some specific suggestions are made as to pathways in the breakup of initial adducts. In all cases the complete reaction pathways are quite complex. Carbon–nitrogen double bonds, if properly substituted, are as reactive toward ozone as are carbon–carbon double bonds.

Previous work in this series has included one paper involving nitrones, a system which formally contains a carbon–nitrogen double bond.[3] At that time we showed that relative rate studies could be useful in distinguishing between nucleophilic and electrophilic ozone attack in such systems.

The literature contains ozonation studies on several other classes of compounds containing carbon–nitrogen double bonds in both acyclic and heterocyclic compounds. Acyclic systems include Schiff bases,[4] ni-

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(2) Abstracted in part from the M.S. thesis of P. Andrulis, Jr., Canisius College, 1964.

(3) R. E. Erickson and T. M. Myszkiewicz, *J. Org. Chem.*, **30**, 4326 (1965); for paper number III in this series, see R. E. Erickson, R. T. Hanson, and J. Harkins, *J. Amer. Chem. Soc.*, **90**, 6777 (1968).

(4) (a) A. H. Riebel, R. E. Erickson, C. J. Abshire, and P. S. Bailey, *ibid.*, **82**, 1801 (1960); (b) J. S. Belew and J. T. Person, *Chem. Ind.* (London), 1246 (1958); (c) R. E. Miller, *J. Org. Chem.*, **26**, 2327 (1961).

TABLE I
PRODUCT DATA

Substrate	Ozonation conditions	Products analyzed (yields, %)
Acetophenone dimethylhydrazone	CH_2Cl_2, −78°, 2–2.2 mol of O_3	Acetophenone (97), N-nitrosodimethylamine (65), chloride ion (1.7)
p-Bromoacetophenone dimethylhydrazone	CH_2Cl_2, −78°, 2–2.2 mol of O_3	*p*-Bromoacetophenone (98–100), N-nitrosodimethylamine (57–65)
Acetone dimethylhydrazone	CH_2Cl_2, −78°, 2–2.2 mol of O_3	Acetone (96), N-nitrosodimethylamine (51), chloride ion (1.1)
Cyclopentanone dimethylhydrazone	CH_2Cl_2, −78°, 2–2.2 mol of O_3	Cyclopentanone (62–65)
Cyclohexanone dimethylhydrazone	CH_2Cl_2, −78°, 2–2.2 mol of O_3	Cyclohexanone (90–91)
p-Nitroacetophenone O-methyl oxime	CH_2Cl_2, 0°, 2.1 mol of O_3	*p*-Nitroacetophenone (72)
Acetophenone O-methyl oxime	CH_2Cl_2, −78°, 2.1 mol of O_3	Acetophenone (83–86)
Acetone oxime	CH_2Cl_2, −78°, 1.3 mol of O_3	Acetone (77–83), chloride ion (1.3–1.5), nitric oxide, 2-nitroso-2-nitropropane (trace)
Acetone oxime	CH_2Cl_2, −78°, 1.3 mol of O_3, CF_3COOH added at end of reaction at −78°	Acetone (50–70), chloride ion (1.3), 2-nitroso-2-nitropropane (16–28)
Acetone oxime	CH_2Cl_2, −78°, CF_3COOH (equimolar with oxime)	No reaction
Acetone oxime	CH_2Cl_2–pyridine (1:1), −78°, 2.2 mol of O_3	Acetone (70–84), chloride ion (9–16), *no* 2-nitroso-2-nitropropane, pyridine salt (HNO_3) (33–35)
Acetone oxime	CH_3OH, −78°, 2.0 mol of O_3	Acetone (100), *no* 2-nitroso-2-nitropropane
Acetone oxime	CH_2Cl_2, −78°, 1.47 mol of O_3, pyridine added at −60° after ozonation	Acetone oxime (34), acetone (47), pyridine salt (HNO_3) (27)

trones,[4a] azines,[5] 2,4-dinitrophenylhydrazones,[6] N-methylphenylhydrazones,[5] and diazo compounds.[5,7] Wibaut and coworkers have ozonized several heterocyclic systems in which some products indicate that carbon–nitrogen double-bond cleavage occurs[5,8] while Moriconi and Spano[9] have carried out a definitive study of the ozonation of several azaaromatics and their N-oxides. Quite recently Bachman and Strawn reported products and yields for the ozonation of selected oximes and Schiff bases.[10]

In this paper we report on the ozonation of Schiff bases, oximes, and dimethylhydrazones. Using product analysis, and, of greater pertinence, relative rate studies, a generalized mechanism for the ozonation of carbon–nitrogen double bonds is suggested.

Experimental Section

Materials.—Solvents were the best commercial grades available and were not purified further. Dimethylhydrazones,[11] Schiff bases,[12] and oximes[13] were prepared by standard methods and had physical constants and spectra identical with or consistent with literature values.

Product Analyses.—Some products were analyzed by gas chromatography as related in previous communications.[3] Several of the analyses in Table I were determined by nmr spectroscopy (Varian HA-60), using an internal standard for the determination of absolute yields.

Chloride ion analyses listed in Table I were determined using a standard titration method, after water extraction of the methylene chloride solutions. Blanks were determined by ozonizing pure methylene chloride for the equivalent period of time and were never more than 20% of the total amount of chloride ion found.

Active oxygen was determined iodometrically in the usual fashion. All of the solutions ozonized except the benzaldehyde Schiff bases contained only slight (1–4%) amounts of peroxidic materials. Product (and rate) studies gave essntially identical results whether ozone–oxygen or ozone–nitrogen streams were used.

Ozone stoichiometry was readily determined for oximes and dimethylhydrazones which absorbed ozone almost quantitatively. When the ozonized solution became blue or the potassium iodide trap darkened, the ozonation was stopped, the time of ozonation was noted, and excess ozone in the ozonized solution was flushed into the trap. Comparison of the trap titration with that of the known ozone output (concentration/minute) yielded the number of moles absorbed in a particular ozonation.

Identification of Colored Product from Acetone Oxime Ozonations.—Ozonation of acetone oxime in methylene chloride at −78° produced a colorless solution which became colored (blue-green) upon warming and gave off nitric oxide at about 0°. The color of the solution changed slowly to blue and remained blue for several days. An nmr spectrum of the solution showed a weak peak at 1.50 ppm (δ) in addition to a relatively strong signal for acetone but isolation of the material was not successful. However, addition of 1 ml of trifluoroacetic acid to a freshly ozonized solution of acetone oxime in methylene chloride produced a considerably more intense blue coloration. Quantitative analysis was carried out by nmr (Table I) while evaporation *in vacuo* of solvent and acetone gave a crystalline material which, after crystallization, was shown (mixture melting point and identical ir and nmr spectra) to be 2-nitroso-2-nitropropane.

Identification of Methyl Nitrite from Acetone O-Methyl Oxime Ozonation.—One of the expected products of O-methyl oxime ozonations, methyl nitrite, is quite volatile (bp −12°) and might well be lost during ozonations. Gas chromatographic analysis of acetone O-methyl oxime ozonations indicated the presence of a volatile substance (retention time slightly longer than air) and showed that methanol was not a product. Infrared spectra, both of an extremely small amount of condensate in a Dry Ice trap placed after the ozonation flask and of the ozonation mixture itself (which also showed acetone and the solvent, methylene chloride, absorptions) indicated methyl nitrite to be a product. Specifically bands at 1640 and 1610 (*trans*- and *cis*-N=O) and 800 and 815 cm^{-1} (N—O stretch) are known nitrite

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(5) J. P. Wibaut and J. W. P. Boon, *Helv. Chem. Acta*, **44**, 1171 (1961).

(6) R. E. Erickson, A. H. Riebel, A. M. Reader, and P. S. Bailey, *Ann.*, **653**, 129 (1962).

(7) A. M. Reader, P. S. Bailey, and H. M. White, *J. Org. Chem.*, **30**, 784 (1965); P. S. Bailey, A. M. Reader, P. Kolsaker, H. M. White, and J. C. Barborak, *ibid.*, **30**, 3042 (1965).

(8) Bailey [P. S. Bailey, *Chem. Rev.*, **58**, 925 (1958)] reviewed much of Wibaut's earlier work along with other ozonations of heterocyclic systems.

(9) E. J. Moriconi and J. A. Spano, *J. Amer. Chem. Soc.*, **86**, 38 (1964).

(10) G. B. Bachman and K. G. Strawn, *J. Org. Chem.*, **33**, 313 (1968).

(11) G. R. Newkome and D. L. Fishel, *ibid.*, **31**, 677 (1966); R. Wiley and G. Irick, *ibid.*, **24**, 1925 (1959).

(12) M. D. Hurwitz, U. S. Patent 2,582,128 (Jan 8, 1952); J. Walia, L. Heindl, H. Lader, and P. Walia, *Chem. Ind.* (London), 155 (1968); H. Weingarten, J. P. Chupp, and W. A. White, *J. Org. Chem.*, **32**, 3246 (1967); G. Charles and M. Mazet, *Compt. Rend. Congr. Soc. Savantes Paris Dept. Sect. Sci.*, **87**, 491 (1962).

(13) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," John Wiley & Sons, Inc., New York, N. Y., 1966, p 289.

absorptions[14a] while methyl nitrite is also reported[14b] to have bands around 1000 and 1150 cm^{-1} (found 1012 and 1155 cm^{-1}).

Low Temperature Nmr Studies.—Several ozonations were carried out on the acetone oxime and acetophenone oxime solutions (methylene chloride solvent) directly in an nmr probe at temperatures between −60 and −70°. An ozone–nitrogen stream (ozone adsorbed on silica gel at −78°) was used for these studies. The course of the reaction was followed by removing the capillary bubbler from the nmr tube and recording the nmr spectra at regular intervals during the ozonation. The methyl group of the ketonic product appeared as soon as ozonation had begun but the methyl peak for the oxime shifted continuously to lower field as is shown for one specific case in Table II. All signals were singlets and percentages in the table were calculated *via* integration and comparison with the area on an internal standard (*t*-butyl benzoate).

TABLE II

NMR OZONATION OF ACETOPHENONE OXIME[a] AT −70°

Sample no.	Acetophenone Chemical shift[b]	 % yield	Acetophenone oxime Chemical shift[b]	 % reacted
1	64	0	43.5	0
2	64	7.4	44	9.0
3	63	9.1	44	14.6
4	64	13.5	44	17.3
5	64	16.7	45	25.9
6	64	23.5	47	29.4
7	64	26.4	48	35.9
8	64	30.0	50	44.0
9	63	33.3	51	49.0
10	63	42.0	56	63.0
10[c]	63	58.8		>95

[a] Solution (0.5 ml) from 0.500 g of acetophenone oxime and 0.225 g of *t*-butyl benzoate in 7.5 ml of methylene chloride. [b] Cycles per second downfield from internal standard (*t*-butyl group in *t*-butyl benzoate). [c] Sample 10 warmed to 30° and then cooled to −70° before the spectrum was taken.

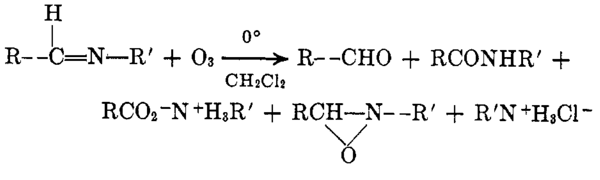
Relative Rate Methods.—Competitive ozonations were carried out using gas chromatography with an internal standard as has been described in previous publications.[3,15] The columns (40% Dow Corning high vacuum silicone grease on 60–80 mesh Chromosorb W, 5% SE-30 on Chromosorb G, 5% FFAP on 60–80 mesh DMCS-treated Chromosorb G, and 5% Carbowax 20M on 60–80 mesh Chromosorb G), gas chromatographic conditions, and internal standards (aromatic esters, aromatic nitro compounds, etc.) were varied widely to obtain good analytical data. Finding proper conditions for each analysis often involved an extensive series of gas chromatography experiments.

Relative rate constants were determined from a computer program for the least-squares analysis of the slope of a log concentration *vs.* log concentration plot.

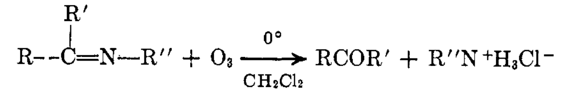
Reaction of Schiff Bases with Ozonized Oximes.—A methylene chloride solution of 1.50 g of cyclohexanone oxime and 1.31 g of methyl benzoate (internal standard) was ozonized at −78° until 27.8% of the oxime had reacted. At that point a solution (gas chromatographically analyzed) of 1.31 g of N-isobutylcyclohexanone imine and 1.04 g of *n*-propyl benzoate (internal standard) was cooled to −78° and added to the cold ozonized solution. Analysis within 1 min of the addition showed that 48.8% of the Schiff base had reacted with oxime ozonation products.

Results

Tables I, III, and IV list the major quantitative results of this investigation. Equations 1–5 indicate the general stoichiometry and show the major products of the ozonations.



$$\mathrm{R{-}\overset{H}{\overset{|}{C}}{=}N{-}R' + O_3 \xrightarrow[CH_2Cl_2]{0^\circ} R{-}CHO + RCONHR' + RCO_2^-N^+H_3R' + RCH{-}N{-}R' \,(O\ ring) + R'N^+H_3Cl^-} \quad (1)$$



$$\mathrm{R{-}\overset{R'}{\overset{|}{C}}{=}N{-}R'' + O_3 \xrightarrow[CH_2Cl_2]{0^\circ} RCOR' + R''N^+H_3Cl^-} \quad (2)$$

$$\mathrm{R_2{-}C{=}NN(CH_3)_2 + 2O_3 \xrightarrow[-78^\circ]{CH_2Cl_2} RCOR + O{=}NN(CH_3)_2} \quad (3)$$

$$\mathrm{R_2{-}C{=}NOH + 1.3O_3 \xrightarrow[-78^\circ]{CH_2Cl_2} RCOR + NO + R_2C(NO)(NO_2)} \quad (4)$$

$$\mathrm{R_2{-}C{=}NOCH_3 + 1.3O_3 \xrightarrow[-78^\circ]{CH_2Cl_2} RCOR + CH_3ON{=}O} \quad (5)$$

The products indicated in eq 1 were those found for the N-*t*-butyl benzaldimine system studied in earlier work.[4a] As titrations showed a maximum of 3% active oxygen in the ozonation of Schiff bases from cyclic ketones and acetophenones in this study, very little oxaziridine is formed. Ketone yields were generally high in the reactions described by 2–5, while yields of products containing nitrogen were generally lower.

The behavior of acetone oxime upon ozonation was very striking and seemed to indicate the possibility that some precursor to the products was formed. Ozonation at −78° in methylene chloride showed complete absorption of about 1.3–1.4 mol of ozone/mol of acetone oxime. The solution remained colorless until the end of the ozonation, whereupon it became blue (ozone color). The solution again became colorless when the excess ozone was swept out by nitrogen. On warming, the solution changed color again (blue-green) and at about 0° gave off large quantities of nitric oxide (shown by its typical reaction with oxygen in the air to form nitrogen dioxide). Gas chromatography and nmr showed that no starting material was present. The color of the solution was shown to be due to 2-nitroso-2-nitropropane and several experiments were carried out (see Table I) to determine the conditions necessary for its formation. Low temperature nmr studies (Table II) and product analysis (Table I) partially resolved this unusual ozonation behavior (see Discussion).

Competitive ozonations listed in Tables III and IV were carried out with no particular difficulty. However, attempts to determine the relative rates of ozonation of either oximes or O-methyl oximes and Schiff bases by the competitive method gave widely variable results, with the Schiff base normally reacting faster than the oxime. It was shown (see Experimental Section) that the disappearance of Schiff base in these competitive ozonations was in fact due to reaction with ozonation products of the oxime. Experiments involving competitive ozonations of oxime pairs gave erratic results (*e.g.*, relative rates varied from 1.5 to 5.5 for the system cyclohexanone oxime–cyclopentanone oxime) unless pyridine was used as a cosolvent. The trapping of the reaction product (nitric oxide) by the pyridine before it could react with the oximes is the obvious explanation for this solvent effect.

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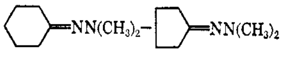
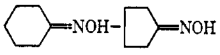
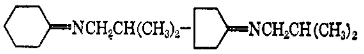
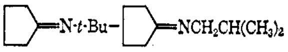
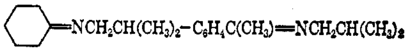
(14) (a) R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds," John Wiley & Sons, Inc., New York, N. Y., 1967, p 99. (b) P. Tarte, *Bull. Soc. Chim. Belges*, **60**, 227 (1951); *Chem. Abstr.*, **46**, 826*d* (1952).

(15) R. E. Erickson, D. Bakalik, C. Richards, M. Scanlon, and G. Huddleston, *J. Org. Chem.*, **31**, 461 (1966).

TABLE III
COMPETITIVE OZONATIONS. SUBSTITUENT EFFECTS

	Temp (°C), solvent	Relative rate	r
Schiff Bases			
$C_6H_5CH{=}N\text{-}t\text{-}Bu\text{–}3NO_2C_6H_4CH{=}N\text{-}t\text{-}Bu$	0, CH_2Cl_2	2.3 ± 0.2	0.976
$C_6H_5CH{=}N\text{-}t\text{-}Bu\text{–}4NO_2C_6H_4CH{=}N\text{-}t\text{-}Bu$	0, CH_2Cl_2	2.5 ± 0.2	0.945
$C_6H_5CCH_3{=}NCH_2CH(CH_3)_2\text{–}4BrC_6H_4CH{=}NCH_2CH(CH_3)_2$	0, CH_2Cl_2	1.7 ± 0.1	0.999
$C_6H_5CCH_3{=}NCH_2CH(CH_3)_2\text{–}4NO_2C_6H_4CH{=}NCH_2CH(CH_3)_2$	0, CH_2Cl_2	2.9 ± 0.1	0.992
N,N-Dimethylhydrazones			
$C_6H_5CCH_3{=}NN(CH_3)_2\text{–}4BrC_6H_4CCH_3{=}NN(CH_3)_2$	−78, CH_2Cl_2	1.06 ± 0.1	0.990
$4BrC_6H_4CCH_3{=}NN(CH_3)_2\text{–}3NO_2C_6H_4CCH_3{=}NN(CH_3)_2$	−78, CH_2Cl_2	1.06 ± 0.1	0.987
O-Methyl Oximes			
$C_6H_5CCH_3{=}NOCH_3\text{–}4BrC_6H_4CCH_3{=}NOCH_3$	−78, $CH_2Cl_2\text{–}CH_3OH$ (2:1)	1.4 ± 0.1	0.999
$C_6H_5CCH_3{=}NOCH_3\text{–}4NO_2C_6H_4CCH_3{=}NOCH_3$	0, $CH_2Cl_2\text{–}CH_3OH$ (2:1)	4.6 ± 0.5	0.930
Substitution on Nitrogen			
$C_6H_5CCH_3{=}NN(CH_3)_2\text{–}C_6H_5CCH_3{=}NCH_2CH(CH_3)_2$	−78, CH_2Cl_2	20.4 ± 0.4	0.902
$C_6H_5CCH_3{=}NN(CH_3)_2\text{–}c\text{-}C_6H_{10}{=}NOH$	−78, CH_2Cl_2	9.8 ± 0.6	0.800
$(CH_3)_2C{=}NN(CH_3)_2\text{–}(CH_3)_2C{=}NOCH_3$	−78, $CH_3COOCH(CH_3)_2$	14.2 ± 0.2	0.940

TABLE IV
COMPETITIVE OZONATIONS. STRAIN EFFECTS

	Temp (°C), solvent	Relative Rate	r
	−78, CH_2Cl_2	0.49 ± 0.08	0.990
	−78, CH_2Cl_2, pyridine	2.17 ± 0.07 2.06 ± 0.12	0.996 0.990
	−78, CH_2Cl_2	1.63 ± 0.18	0.978
	−78, CH_2Cl_2	9.3 ± 0.3	0.981
	−78, CH_2Cl_2	10.8 ± 0.3	0.985

Discussion

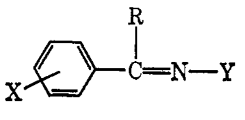
Several mechanisms for the ozonation of the carbon–nitrogen double bond have been considered in the literature. Riebel, *et al.*,[4a] suggested four principal ways in which initial ozone attack could occur: (1) an addition to the double bond as with carbon–carbon double bonds to give a four- or five-membered ring, (2) an electrophilic attack on the nitrogen atom of the double bond followed by loss of oxygen, (3) an electrophilic attack on the entire double bond followed by loss of oxygen, and (4) a nucleophilic attack on the carbon atom of the double bond followed by loss of oxygen. Wibaut and Boon[5] have proposed initial attack on nitrogen by the central atom of ozone followed by formation of a four-membered ring and breaking of the nitrogen–oxygen single bond. Present understanding of ozonation mechanisms rules out attack by the central oxygen atom and the existence of four-membered rings.

Another possibility, electrophilic attack on carbon for nitrones, was suggested by Riebel, *et al.*,[4a] and confirmed by us in an earlier study.[3]

The product analysis data from both Riebel, *et al.*,[4a] and from Moriconi and Spano's investigation of aza-aromatics and their N-oxides[9] were interpreted in favor of the fourth possibility listed above, nucleophilic attack of ozone on carbon.

At the beginning of this research we hoped to discover if all carbon–nitrogen double bonds react with ozone by a similar mechanism. Although the hypothesis of a single mechanism for the initial attack of ozone on the variety of systems investigated is an appealing one, we recognized that the possibility of secondary reactions, either of ozone with products or of highly unstable products with starting material, may complicate the over-all mechanism of any carbon–nitrogen double-bond ozonation. For example, earlier work has shown that nitrosobenzene, one of the major products of nitrone ozonation itself, reacts with ozone and that chlorinated solvents are attacked by an ozonation product of Schiff bases (a nitrene was suggested as the reactive ozonation product).[4a] In this work it has been shown that N,N-dimethylhydrazone ozonations are complex in that 2 mol of ozone are absorbed/mol of hydrazone. Attack on the solvent (methylene chloride) is evident for both oximes and dimethylhydrazones and oxime ozonations reveal particularly unusual secondary reactions.

Substituent effects were studied with several classes of compounds represented by formula I.



I

The choice of substituents X, R, and Y was based on the following factors. Since the electrophilic attack of ozone on the aromatic ring was a possible competing reaction,[16] the X substituent used was generally an electron-withdrawing group such as the nitro group or a bromine atom. The known reactivity of aldehydic hydrogen to ozone-catalyzed autoxidation[15,17] led to the use of acetophenone derivatives (R = CH_3) rather than benzaldehyde derivatives for most of the systems

[16] T. W. Nakagawa, L. J. Andrews, and R. M. Keefer, *J. Amer. Chem. Soc.*, **82**, 269 (1960).

[17] H. M. White and P. S. Bailey, *J. Org. Chem.*, **30**, 3037 (1965).

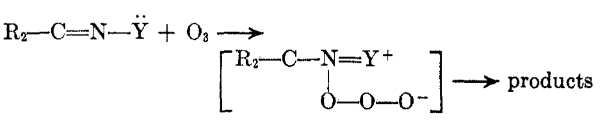
investigated. The Y group was varied from carbon to oxygen to nitrogen to test electron donation to the nitrogen as a factor on the rate of ozonation. Acetophenone oximes had unfavorable gas chromatographic behavior and the O-methyl oximes were used instead. As previous studies on the ozonation of 2,4-dinitrophenylhydrazones[6] indicated possible involvement of the nitrogen–hydrogen bond in the ozonation, the simplest dialkylhydrazones, the acetophenone dimethylhydrazones, were used.

Table III shows that changing the substituent (X) on the aromatic ring to a more electron-withdrawing group has a rate-retarding effect for Schiff bases and O-methyl oximes and essentially no effect on dimethylhydrazones. Rate differences for all compounds are relatively small as has been found previously for aldehyde, nitrone, and ether ozonations.[3,15] No relative rate sequence studied thus far has given any evidence for nucleophilic ozone attack (which has been suggested for some ozonation mechanisms on the basis of product studies).[18]

The data in Table III indicate that changing the substituent on the nitrogen end of the double bond can have a large effect on the relative rate of ozonation. The order found (dimethylhydrazones > O-methyl oximes ≫ Schiff bases) indicates electron donation from an atom α to the nitrogen to be significant.

This pattern (small rate effect on variation of X, large rate effect on variation of Y) is the same as that found by Hegarty and Scott in the bromination of substituted benzaldehyde arylhydrazones.[19] Specifically they found ρ −0.62 for substituents on the phenyl group on the benzylidene carbon *vs.* ρ −2.17 for substituents on the phenyl group on the hydrazone. In a similar study on the reaction of aryl diazonium ions on substituted benzaldehyde hydrazones the same authors found ρ −1.3 for substitution on the hydrazone ring and ρ −0.38 for substitution on the benzylidene ring.[19]

Our data indicate that initial attack of ozone on carbon–nitrogen double bonds is electrophilic and may be strongly assisted by an electron-donating group on nitrogen as is shown in eq 6.



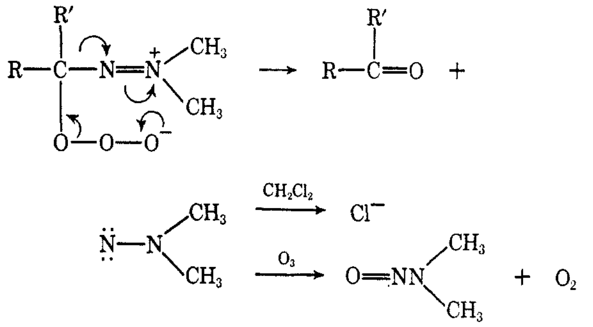
$$R_2\text{—C=N—}\ddot{Y} + O_3 \longrightarrow \left[\begin{array}{l} R_2\text{—C—N=Y}^+ \\ \quad\;\; | \\ \quad\;\; \text{O—O—O}^- \end{array}\right] \longrightarrow \text{products} \qquad (6)$$

For Schiff bases where Y cannot donate a lone pair of electrons, the initial adduct might be a five-membered ring, similar to the initial ozonide formed in the ozonation of alkenes[20] in which attack is also electrophilic.

The use of cyclic systems as models in structure reactivity relationships has been widespread.[21] One generalization has been that a change in hybridization in a cyclic compound from sp^2 to sp^3 during a reaction will lead to a relative rate sequence of cyclic C_6 > cyclic C_5 rings. For example cyclohexanone reacts considerably faster than cyclopentanone with all addition reagents, supposedly because of the increased number of nonbonded interactions in the five-membered ring containing all sp^3-hybridized atoms. The only example of which we are aware that does not follow this pattern is the finding of Garbisch, *et al.*, that methylenecyclopentane reacts slightly faster than methylenecyclohexane with diimide.[21]

Table IV shows that for Schiff bases and oximes the six-membered rings are more reactive than the five-membered rings as expected. However, cyclopentanone dimethylhydrazone definitely reacts faster with ozone than does the cyclohexanone analog.

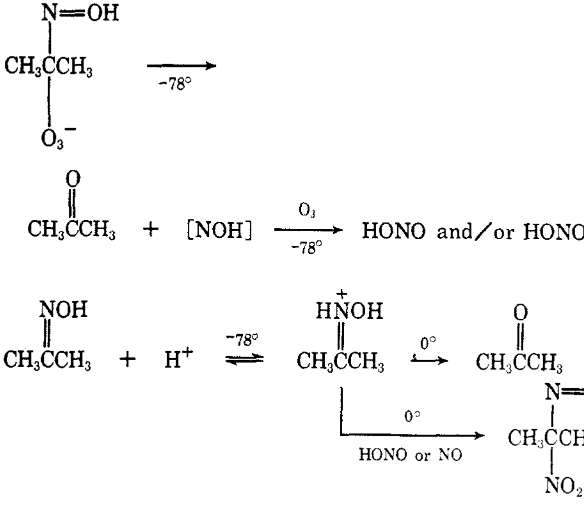
Although several explanations might be suggested to explain this finding and speculative correlations with the product data in Table I are possible, we prefer to hypothesize our current views on dimethylhydrazone ozonations with the aid of a single equation, eq 7,



(7)

Equation 7 is similar in some regard to earlier hypothesis for the ozonation of Schiff bases[4a] and accounts qualitatively for all of the data in the paper.

The complete mechanistic pathway for the ozonation of oximes is also of interest. After initial electrophilic attack on carbon (with assistance by electron donation from oxygen), the exact pathway is still speculative. However, careful inspection of the quantitative data on the acetone oxime ozonations of Table I and the nmr data in Table II leads to a minimal assumption of eq 8 and 9 to describe the reaction.



(8)

(9)

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[18] Dr. Bryant W. Rossiter (Eastman Kodak Co., Rochester, N. Y.) has informed us (private communication) that substituted pyrazolone–azomethine dyes also undergo electrophilic attack by ozone at the carbon–nitrogen double bond of the azomethine linkage.

[19] A. F. Hegarty and F. L. Scott, *J. Chem. Soc., B*, 672 (1966); *J. Org. Chem.*, **32**, 1957 (1967).

[20] P. S. Bailey, J. A. Thompson, and B. A. Shoulders, *J. Amer. Chem. Soc.*, **88**, 4098 (1966); L. J. Durham and F. L. Greenwood, *J. Org. Chem.*, **33**, 1629 (1968).

[21] H. C. Brown, J. H. Brewster, and H. Shechter, [*J. Amer. Chem. Soc.*, **76**, 467 (1954)] originally discussed the usefulness of relative rate studies with ring systems for structure reactivity correlation. Semiquantitative calculations involving angle strain, torsional strain, and polar effects for the relative rates of diimide additions to cyclic and acyclic alkenes [E. V. Garbisch, Jr., S. M. Schildcrout, D. B. Patterson, and C. M. Sprecher, *ibid.*, **87**, 2932 (1965)] are perhaps the most sophisticated made for this type of study.

The mechanism of the Schiff base ozonation remains as the most perplexing of all of the carbon–nitrogen double-bond systems. The original product analysis data could be rationalized reasonably well by any of six different types of initial attack as noted above.[4a,5] The major problem with both product analysis and competitive ozonation studies lies in the reactivity of Schiff bases. They react very slowly with ozone but may react quite rapidly with ozonation products. Thus, although amides and oxaziridines are very likely primary products, they account for only 39% of products even in favorable cases, and major cleavage products may well be derived from secondary processes. Relative rate studies are also inconclusive. Originally we attempted to carry out competitive rate studies on benzaldehyde Schiff bases at −78° in methylene chloride. Ozonation was extremely slow; less than half of either Schiff base reacted in a 12-hr period. Dimethylhydrazones and oximes, on the other hand, react quantitatively with ozone at −78°. Thus, although the results in Table III are "real" in that they show Schiff bases to react considerably more slowly with ozone than do dimethylhydrazones, we believe the true relative rate spread may be considerably larger.[22] In other words, the decreasing concentration of Schiff base measured in our experiments may be caused by reaction with products of either the competing system or of the Schiff base itself.[23]

It has been believed generally that carbon–nitrogen double bonds are considerably less reactive than carbon–carbon double bonds. The data from these experiments appear to suggest, however, that carbon–nitrogen double-bond reactivity is dependent on the group attached to nitrogen. In fact *trans*-stilbene and acetophenone dimethylhydrazone have essentially equivalent rates of ozonation (competitive rate 1.01 ± 0.05).

Registry No.—Methyl nitrite, 624-91-9; acetophenone oxime, 613-91-2.

Acknowledgment.—Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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[22] True rate comparisons could be made if experiments with stop-flow systems such as used by Williamson and Cvetanovic [D. G. Williamson and R. J. Cvetanovic, *ibid.*, **90**, 3668 (1968)] for alkene ozonations were carried out with dimethylhydrazones and oximes. The Schiff base ozonations are slow enough to be treated by conventional kinetic methods.

[23] A referee has suggested that nucleophilic attack on carbon to yield cleavage products may be competing with electrophilic bond attack on Schiff bases. The notion that ozone can act as a nucleophilic reagent is, of course, tantamount to calling it a reducing agent. Although such a situation is conceivable, we believe that rigorous proof would be necessary before postulating such a mechanism. As the proceeding paragraphs have indicated, such experimental justification is lacking.

New Carbonyl Compounds from Dehydrogenation of *p*-Cresol

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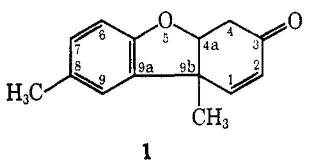
Chemical one-electron-type oxidation of *p*-cresol with ferric chloride yielded a previously unreported diphenyl ether **4** and three new ketonic trimers **5**, **6**, and **7**, the structures of which are related to Pummerer's ketone **1**, which was also formed in the reaction mixture as were the known compounds **2** and **3**. When *p*-cresol was oxidized enzymatically by peroxidase and peroxide, **5** was the only new unknown compound which could be isolated.

It is well established that the oxidation of *p*-cresol by one-electron-type chemical oxidants yields 4a,9b-dihydro-8,9b-dimethyl-3(4H)-dibenzofuranone (Pummerer's ketone) (**1**), 2,2′-dihydroxy-5,5′-dimethyldiphenyl (**2**), and 2,2′,2″-trihydroxy-5,5′,5″-trimethylterphenyl (**3**).[2–5] These products have also been isolated from the peroxidase-catalyzed oxidation of *p*-cresol with hydrogen peroxide.[6] A general review of the oxidative coupling of phenols, including *p*-cresol, and the significance of this type of reaction in biosynthesis have been published.[7]

Hayes reported that in the oxidation of phenols by one-electron-type oxidants, more than 1 equiv of the oxidizing agent is consumed and that this must be the result of further oxidation of the low molecular weight products initially formed.[5] Mixtures of higher molecular weight substances were isolated in that work, but the constituents of the mixture were not identified. We have now oxidized *p*-cresol with 1.4 equiv of ferric chloride in aqueous solution, and have found that at least 10 compounds are present.



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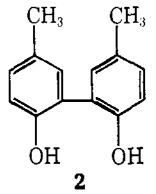

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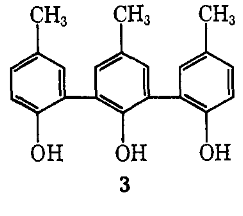

3

The reaction mixture was separated into alkali- and ether-soluble fractions, and further separation was

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(1) (a) 1967 Summer Student Trainee, Forest Products Laboratory. (b) Maintained at Madison, Wis., in cooperation with the University of Wisconsin.

(2) R. Pummerer and F. Frankfurter, *Ber.*, **47**, 1472 (1913).

(3) R. Pummerer, H. Puttfarcken, and P. Schopflocher, *ibid.*, **58B**, 1808 (1925).

(4) D. H. R. Barton, A. M. Deflorin, and O. E. Edwards, *Chem. Ind.* (London), 1039 (1955).

(5) C. G. Haynes, A. H. Turner, and W. A. Waters, *J. Chem. Soc.*, 2823 (1956).

(6) W. W. Westerfield and C. Lowe, *J. Biol. Chem.*, **145**, 463 (1942).

(7) A. I. Scott, *Quart. Rev.* (London), XIX, 1 (1965).