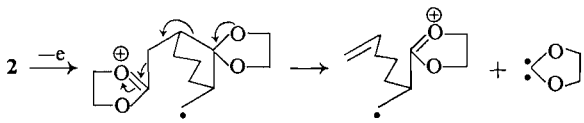
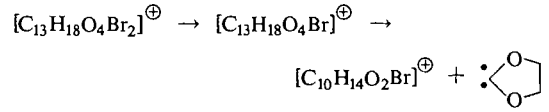
A mechanism may be drawn for **2** with the same structure for the *m/e* 168 ion. However, the substantial difference in the relative abundances of the ions between *m/e* 99 and *m/e* 168 suggests that a different *m/e* 168 ion may be involved.

Compound **3** yields an extremely rich spectrum in which the characteristic ketal peaks (*m/e* 99, etc.) are relatively weak. The strong peaks at *m/e* 317, 319 represent a monobromo species which differs from the parent (*P* = 396, 398, 400) only in the loss of one bromine atom. The



m/e 240 *m/e* 168

presence of a similar doublet at *m/e* 245, 247 and the broad metastable ion centered at *m/e* 190.5 (calcd. *m/e* 189.3 and 191.3) provides some evidence that loss of the ethylenedioxycarbene is involved here as well. Note that here the *m/e* 245 peak is the base peak.



3 *m/e* 396, 398, 400 *m/e* 317, 319 *m/e* 245, 247

Acknowledgment

Financial support of this work by the National Research Council of Canada is gratefully acknowledged.

1. Gordon Wood and E. P. Woo. Can. J. Chem. **46**, 3713 (1968).
2. H. Audier, A. Diara, M. de J. Durazo, M. Fétizon, P. Foy, and W. Vetter. Bull. Soc. Chim. France, 2827 (1963).
3. Z. Pelah, D. H. Williams, H. Budzikiewicz, and C. Djerassi. J. Am. Chem. Soc. **86**, 3722 (1964).
4. H. Audier, J. Bottin, A. Diara, M. Fétizon, P. Foy, M Golfier, and W. Vetter. Bull. Soc. Chim. France, 2292 (1964).
5. H. Audier, M. Fétizon, J-C. Gramain, J. Schalbar, and B. Waegel. Bull. Soc. Chim. France, 1880 (1964).
6. H. Audier, M. Fétizon, and J-C. Gramain. Bull. Soc. Chim. France, 3088 (1965).
7. D. M. Lemal, E. P. Gosselink, and S. D. McGregor. J. Am. Chem. Soc. **88**, 582 (1966).

Structure and reactivity of the mono-oxime of 2,6-dimethoxy-1,4-benzoquinone

H. I. Bolker and F. L. Kung[1]

Department of Chemistry, McGill University, Montreal, Quebec and Organic Chemistry Division, Pulp and Paper Research Institute of Canada, Montreal, Quebec

Received August 9, 1968

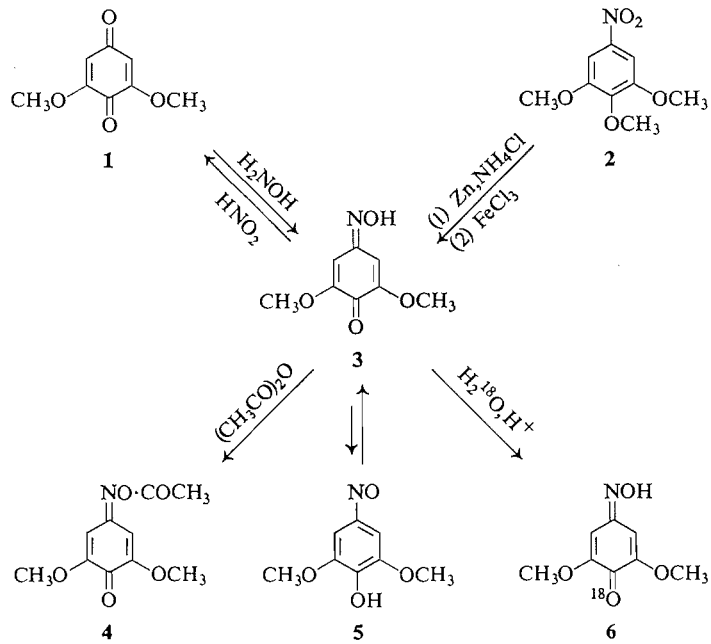
Reaction of 2,6-dimethoxy-1,4-benzoquinone with hydroxylamine yielded 2,6-dimethoxy-4-oximino-2,5-cyclohexadienone-1 (**3**), as confirmed by spectroscopic analysis, and by independent synthesis from 5-nitro-1,2,3-trimethoxybenzene. Infrared and proton magnetic resonance spectra in solution showed no significant proportion of the tautomeric nitrosophenolic form of **3**. When **3** was heated for 3 min at 90–95° in 1.0 *N* HCl in $H_2{}^{18}O$, the N—OH group was stable, but the keto oxygen underwent complete exchange. Mass spectra of **3**, its ^{18}O- and deuterium-substituted derivatives indicated that a major process leading to fragmentation upon electron impact was loss of oxygen from N—OH to form the corresponding quinone imine.

Canadian Journal of Chemistry, 47, 2109 (1969)

In research aimed at elucidating the mechanism whereby 2,6-dimethoxy-1,4-benzoquinone (**1**) is formed by the action of nitrous acid on 1,2,3-trimethoxybenzene, we have found (1) that 2,6-dimethoxy-4-oximino-2,5-cyclohexadienone-1 (2,6-dimethoxy-1,4-benzoquinone-4-oxime) (**3**), a compound unknown until now, is an intermediate. Its relevance to current studies on the keto–enol equilibrium of nitrosophenols (2), and our findings concerning the exchangeability of its oxygen, have prompted separate publication of this part of the work.

Unsubstituted *p*-nitrosophenol is known to exchange 82% of one oxygen after only 5 min at

[1]From the Doctoral Thesis of F.L.K.; present address: College of Forestry, Syracuse University, Syracuse, New York.



100° in 0.2 *N* alcoholic hydrogen chloride, and 1-nitroso-2-naphthol exchanges 84% in 5 min at 80° in the same solvent (3). However, the existence of the tautomeric keto-oximes has complicated interpretation of these reactions by suggesting that two exchangeable oxygens could be present. Nevertheless, it is proposed that only the carbonyl group of the keto-oxime is exchanged (3,4). In the present work, application of mass spectroscopy to compound **3** and its derivatives has produced evidence to support the original proposal.

The Structure of the Oxime (3)

Although the product **3** obtained by treating **1** with hydroxylamine in pyridine (5) was clearly a monoxime, an alternative synthesis (6) from 5-nitro-1,2,3-trimethoxybenzene (**2**) proved that the oximino group had been introduced in position-4, and not position-1. The products of the two reactions were identical in all respects, and, on acetylation, yielded the same acetate (**4**).

The proton magnetic resonance (p.m.r.) spectrum of **3** in deuteriodimethylsulfoxide showed the expected singlet at δ 3.58 corresponding to the 6 hydrogens of the methoxyl groups, and another singlet at δ 12.62 (eliminated on deuteration) due to a single hydroxyl proton. However, neither the spectrum of **3** in pure deuteriodimethylsulfoxide nor that in deuteriodimethylsulfoxide containing 50% D_2O exhibited any trace of the single peak which might have been expected to arise from the two identical phenyl ring protons of the tautomeric nitrosophenol (**5**). Rather, spectra of the compound in both solvents had a doublet at δ 6.30 and δ 6.64, corresponding to two phenyl ring protons with $J_{3,5} = 1.5$ c.p.s. This AB pattern suggests that the protons at positions-3 and -5 are not equivalent, undoubtedly because of the rigidity and non-linearity of the C=N—O group on position-4. Hence, even in aqueous solution, the oxime form of **3** is overwhelmingly predominant, as would be predicted from the literature already cited (2).

The oxime **3**, treated with nitrous acid, produced no 2,6-dimethoxy-4-nitrophenol but only 2,6-dimethoxy-1,4-benzoquinone (**1**) in 98% yield. In contrast, treatment of 2-methoxy-4-nitrosophenol with nitrous acid gave rise to the corresponding nitro compound (although it forms an oxime acetate upon acetylation (7)). In general, most other quinone monoximes (or *p*-nitrosophenols) are reported to exhibit reactions of both tautomers (2*c*, 8). In this respect the behavior of **3** is unusual.

Interpretation of Mass Spectra

From the mass spectra of **3** (Fig. 1) and

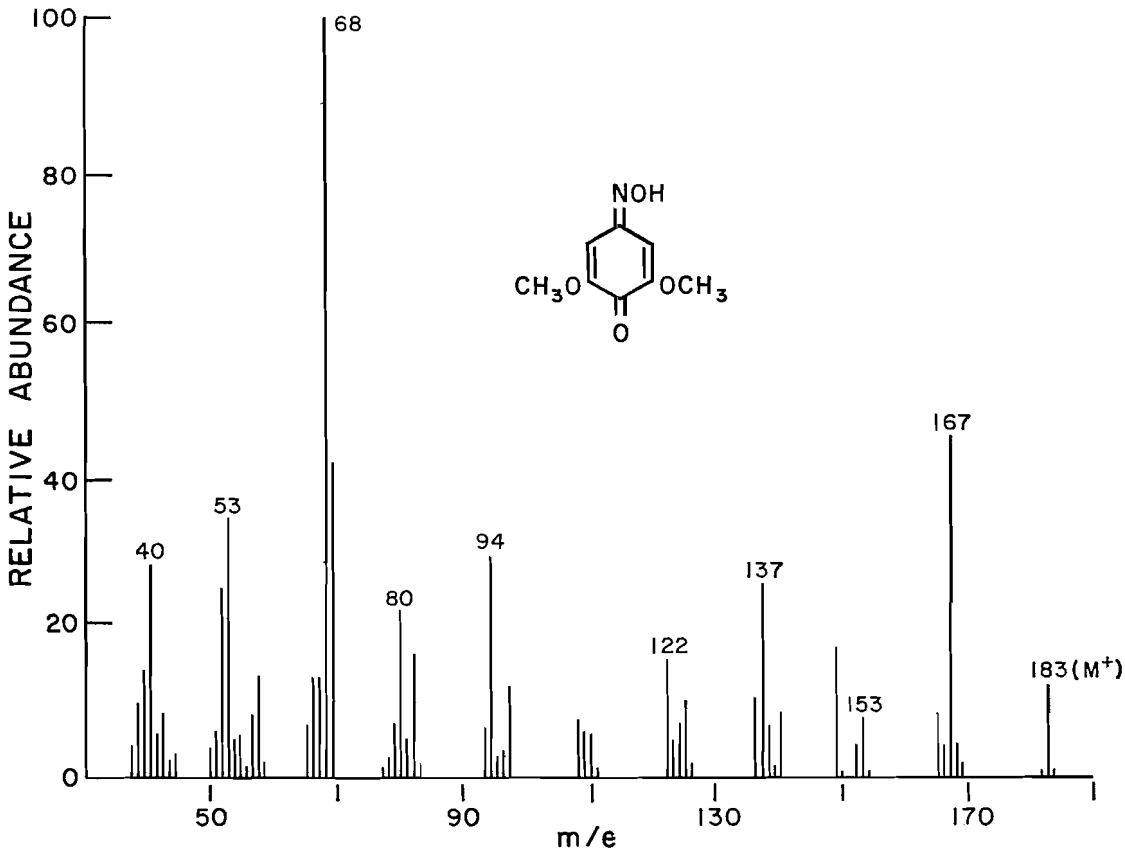


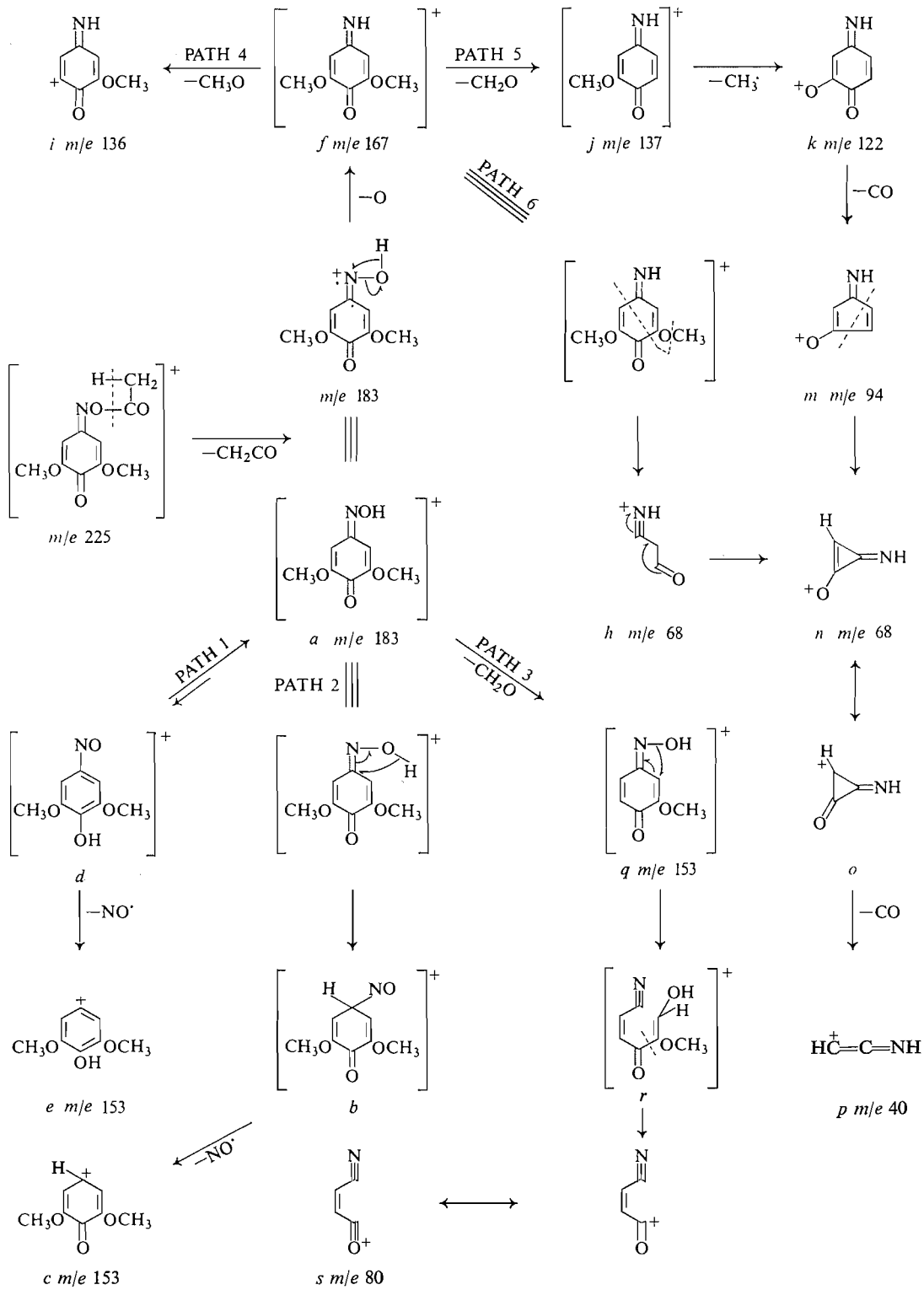
FIG. 1. Mass spectrum of 2,6-dimethoxy-4-oximino-2,5-cyclohexadienone-1 (**3**).

deuterated **3** (i.e. as =N—OD), we have deduced many of the details of the pattern of fragmentation (Scheme 1) arising from electron-impact, and have related this interpretation to the spectrum of the acetate (**4**), and hence deduced, in turn, the position of ^{18}O on compound **6** after exchange in acidified $H_2{}^{18}O$.

In the spectrum of deuterated **3**, all the peaks representing species listed in Scheme 1, except Path 3, exhibit intensification of the next higher mass unit ($m/e + 1$) over the corresponding peaks in the spectrum of the undeuterated **3** (Fig. 1). Therefore, these species have retained the deuterium introduced by exchange.

Thus, Path 1 demands tautomerization of species *a* to permit the expulsion of NO and formation of *e* ($m/e = 153$) without loss of label. In the light of the known tendency of **3** to retain its oxime form, Path 2 (by analogy with the fragmentation of benzophenone oxime (9)) requires transfer of the hydroxyl hydrogen to the ring, but may be a better interpretation for this compound. Paths 4, 5, and 6 have a common starting point, fragment *f*, which appears to have arisen in a one-step process (metastable ion is present) involving transfer of hydrogen to nitrogen simultaneously with the loss of oxygen. We have also observed the formation of a quinone imine corresponding to *f* in the fragmentation of the 4-monoxime of 2-methoxy-1,4-benzoquinone. We are therefore led to suggest that the quinone imine mechanism may prove to be common to the fragmentation processes of all quinone monoximes.

In the first step in each of the three pathways, 4, 5, and 6, whereby *f* undergoes further fragmentation, the products *h*, *i*, and *j* all retain their deuterium labels. The cleavage giving rise to *h* is similar to that of methoxybenzoquinones (10). In Path 5, the first two steps from *f* are the same



SCHEME 1. Fragmentation of 2,6-dimethoxy-4-oximino-2,5-cyclohexadienone-1 (**3**) and its acetate (**4**).

as those known for phenolic methyl ethers (11): loss of formaldehyde, then methyl. Two more steps are required to form *n* (*m/e* = 68), an isomer of *h*. The formation of *n* through two different paths, and the fact that it is resonance-stabilized, may account for *m/e* = 68 being the base peak of the spectrum.

In contrast with the other mechanisms, Path 3 alone leads to a product, *s*, which has lost its deuterium label.

With the exception of the transitions $183^+ \rightarrow 153^+ + 30$, $167^+ \rightarrow 68^+ + 99$, $153^+ \rightarrow 80^+ + 73$, all the fragmentation processes deduced from the spectra of **3** are further supported by the presence of appropriate metastable ions.

Exchange of Oxygen

For the experiment on the exchange of oxygen, **3** was dissolved in 1.0 *N* hydrochloric acid containing 10% of $H_2{}^{18}O$; the solution was rapidly heated to 90–95° and kept at that temperature for 3 min. Accurate measurement of the isotope content of the product by mass spectroscopic analysis (12) presented some difficulties, and it proved necessary to acetylate the compound to facilitate purification.

In the ^{18}O-containing acetate, the ratios of the peaks at *m/e* 225/227, 183/185, and 153/155 were all 100/12, while the same peaks in the unexchanged compound were in the ratio of 100/2. Thus 10% of ^{18}O had been incorporated in each of these species. (Natural relative isotopic abundance (13) of P_m/P_{m+2} for $C_{10}H_{11}NO_5$ (*m/e* 225) is 100/1.6, for $C_9H_9NO_4$ (*m/e* 183) is 100/1.2, and for $C_8H_9O_3$ (*m/e* 153) is 100/1.0.) The complete absence of spectral bands above *m/e* 225 + 2 clearly ruled out the possibility that ^{18}O might have been incorporated into more than one oxygen atom of **4**.

The main features of the spectra of the acetate are the same as those of the unacetylated oxime (Fig. 1), with the necessary exception that the first step in fragmentation is the loss of ketene (M-42), as has been observed in the spectra of *N*-acetyl alkylamines (14), and of sugar acetates (15). This loss occurred with retention of ^{18}O. Subsequent fragmentation through Paths 1, 2, 3, and 4 also led to retention of ^{18}O, as measured from the peaks for *c*, *e*, *i*, *s* (Scheme 1). However, in Paths 5 and 6, once the keto oxygen is lost (*h* in Path 6, *m* and subsequent fragments in Path 5) the ratios of *m/e*:*m/e* + 2 are the same for each *m/e* whether or not the compound originally contained ^{18}O.

The mass spectra of the oxime acetate (**4**), both with and without ^{18}O, thus serve on the one hand to confirm the previous interpretations of the spectrum of the free oxime, and, on the other, to demonstrate that, in accordance with earlier conjecture, the keto oxygen is the one which is exchangeable, in this instance, completely so.

Nucleophilic displacement of ring oxygen has also been reported to occur (16) as a minor pathway in the mechanism of direct alkylation of benzoquinone oxime by acidified alcohols (17). The major mechanism involves attack by protonated alcohol on carbonyl oxygen.

Experimental

All melting points were determined on a calibrated Fisher–Johns apparatus unless otherwise specified. Infrared (i.r.) spectra were recorded on a Perkin–Elmer spectrometer, model 337. The proton magnetic resonance (p.m.r.) spectra were recorded on a Varian A-60 spectrometer, with tetramethylsilane as an internal standard. Mass spectra were determined by the Morgan Schaffer Corp., Montreal, on a Hitachi Perkin–Elmer RMU60 mass spectrometer operating at 70 eV. Elemental analyses were done by Schwarzkopf Microanalytical Laboratory of Woodside, N.Y. Magnesium sulfate was used to dry all solvent extracts before concentration. Deuterium oxide and hydrogen oxide-^{18}O were products of Merck-Sharpe and Dohme. Known methods (1) were used to prepare 2,6-dimethoxy-1,4-benzoquinone (**1**) and 5-nitro-1,2,3-trimethoxybenzene (**2**). Solutions of nitrous acid were prepared according to the published procedure (18).

Preparation of 2,6-Dimethoxy-4-oximino-2,5-cyclohexadienone-1 (3) from 2,6-Dimethoxy-1,4-benzoquinone (1)

A solution of 20 g (0.12 mole) of **1** and 20 g (0.30 mole) of $NH_2OH \cdot HCl$ in 100 ml of anhydrous pyridine and 150 ml of anhydrous ethanol was boiled under reflux for 1 h with exclusion of moisture. The solution was then made alkaline with aqueous sodium hydroxide and concentrated by complete removal of the remaining pyridine under reduced pressure. Water (200 ml) was added and then the pyridine-free aqueous solution was extracted with methylene chloride (5 × 300 ml). Drying and evaporation of the combined extracts yielded 6.8 g (31%) of brown powder with m.p. 212–216°. Two recrystallizations from water containing 5% methanol gave 4.1 g, m.p. 218.8° (decomp.), of yellow plates. This compound was insoluble in ether and carbon tetrachloride, moderately soluble in cold water and chloroform, soluble in hot water, ethanol and methanol.

Anal. Calcd. for $C_8H_9NO_4$: C, 52.46; H, 4.92; N, 7.65. Found: C, 52.57; H, 5.01; N, 7.83.

The i.r. spectrum (KBr), 3270 cm^{-1} broad (OH), 1635 cm^{-1} (C=O), 1570 cm^{-1} (C=N), 1010 cm^{-1} (N—OH str.) and the absence of —N=O str. band at 1500 cm^{-1}, accorded with an oxime structure (19,20).

Preparation of 2,6-Dimethoxy-4-oximino-2,5-cyclohexadienone-1 (3) from 5-Nitro-1,2,3-trimethoxybenzene (2)

In a solution of 1.0 g of NH_4Cl in 50 ml of water

containing 20% methanol, 1.5 g of **2** were dissolved. The solution was heated to 60–65°, and zinc powder (2.5 g) was added over a period of 10 min with stirring. After rapid filtration by suction, the filter cake was washed with hot ethanol, the filtrate was cooled, and then was poured with stirring into 200 ml of water containing 10% ferric chloride. Steam distillation led to the recovery of 80 mg of starting material, **2**, in the distillate. The residue in the still (pH 2) was cooled and extracted with chloroform (3 × 100 ml). Drying and evaporation of the extract gave 1.1 g (85%) of light brown solid material with m.p. 210–215° (decomp.). One recrystallization from water containing 5% methanol gave 0.85 g of yellow plates with m.p. 218.0–218.5° (decomp.). This material exhibited an i.r. spectrum identical to that of a sample of **3**, prepared according to the method described in the preceding section, and showed no depression of melting point upon admixture.

Reaction of 2,6-Dimethoxy-4-oximino-2,5-cyclohexadienone-1 (3) with Nitrous Acid

This reaction was conducted in a flask fitted with a reflux condenser, with the top of the condenser connected, by means of rubber tubing, to two wash bottles in series. The first wash bottle was empty, and acted as a safety bottle. The second contained water, and its purpose was twofold: (*a*) to inhibit the escape of gases so that decomposition of nitrous acid would be retarded, and (*b*) to trap whatever oxides of nitrogen might otherwise tend to escape. A suspension of 10 mg of **3** in 20 ml of nitrous acid (pH 1) was placed in the flask and boiled under reflux for 1 h. The reaction mixture was then extracted with chloroform (3 × 10 ml). After drying and evaporation of the solvent, the yellow solid residue, 9 mg (98%), m.p. 250–252° was identified as **1** (by mixture m.p. and i.r. spectrum).

Reaction of 2-Methoxy-4-nitrosophenol with Nitrous Acid

A suspension of 10 mg of 2-methoxy-4-nitrosophenol (18) in 20 ml of nitrous acid (pH 1) was boiled under reflux for 1 h in the apparatus described in the previous section. The product solution was then extracted with chloroform (3 × 10 ml). Drying and evaporation of the extract yielded 10 mg (91%) of yellow solid, m.p. 90–96°. Two recrystallizations from ether with a few drops of petroleum ether added each time gave 7.3 mg of yellow needles, m.p. 100.3–100.4°, which proved to be identical (i.r. spectrum and mixture m.p.) with a sample of 4-nitroguaiacol prepared according to Pollecoff and Robinson (21). Thin-layer chromatography (on silica gel with methanol:benzene:acetic acid:petroleum ether (8:45:3.5:20) showed that the crude yellow solid contained a trace of 4,6-dinitroguaiacol (18).

Preparation of 2,6-Dimethoxy-4-oximino-2,5-cyclohexadienone-1 Acetate (4)

A solution of 1.0 g of **3** in 25 ml of acetic anhydride was boiled under reflux for 2 h. The hot solution was poured into 200 ml of ice water and extracted with chloroform (4 × 50 ml). Drying and evaporation of the extract, yielded a residue, which, after thorough washing with methanol and subsequent drying, was a yellowish material weighing 0.85 g (69%) with m.p. 179–181°. After two recrystallizations from ethanol, the product (0.61 g) appeared as yellow prisms, m.p. 181.8–182.0°.

Anal. Calcd. for $C_{10}H_{11}NO_5$: C, 53.33; H, 4.89; N, 6.22. Found: C, 52.84; H, 4.83; N, 6.31.

The i.r. spectrum (KBr) exhibited a band at 1795 cm^{-1} corresponding to C=O stretching vibration of acetoxyl (22).

Oxygen-18 Exchange Reaction of 2,6-Dimethoxy-4-oximino-2,5-cyclohexadienone-1 (3) Followed by Acetylation

To a solution of 1 ml of 6 *N* aqueous hydrochloric acid in 8 ml of water containing 10.6% ^{18}O, **3** (400 mg) was added. The resulting mixture was heated to 90–95° with constant stirring for 3 min. Extraction with chloroform, drying of the extract, and evaporation gave a yellowish product which was then acetylated by the same procedure as described in the preceding section. The purified labeled oxime acetate weighed 150 mg, m.p. 178.5–181.8°. The i.r. spectrum of the ^{18}O-containing compound showed no detectable difference from its unlabeled precursor (**3**). However, its mass spectrum indicated that 10% ^{18}O had been incorporated into the molecule.

Deuterium Exchange Reaction of 2,6-Dimethoxy-4-oximino-2,5-cyclohexadienone-1 (3)

A suspension of 100 mg of **3** in 3 ml of deuterium oxide was heated to boiling and filtered. The filtrate was allowed to stand at room temperature and the partially deuterated oxime gradually separated as yellow plates, m.p. 216.0–218.5° (turns brown at 210°), yield 75%. The i.r. spectrum exhibited an O—D stretching band at 2400 cm^{-1} (23).

Acknowledgment

This paper is based on results of research supported in part by a grant from the Department of Forestry of Canada.

1. H. I. Bolker and F. L. Kung. To be published.
2. (*a*) H. Uffmann. Tetrahedron Letters, **38**, 4631 (1966). (*b*) H. Uffmann. Z. Naturforsch. **22b**, 491 (1967). (*c*) R. K. Norris and S. Sternhell. Australian J. Chem. **19**, 841 (1966). (*d*) R. K. Norris and S. Sternhell. Tetrahedron Letters, **2**, 97 (1967).
3. (*a*) I. P. Gragerov and A. F. Levit. Zh. Obshch. Khim. **30**, 3726 (1960). (*b*) D. Samuel and B. L. Silver. Oxygen isotope exchange reactions of organic compounds. *In* Advances in physical organic chemistry. Vol. 3. *Edited by* V. Gold. Academic Press, Inc., New York. 1965. p. 176.
4. (*a*) S. Oae, T. Fukumoto, and R. Kiritani. Bull. Chem. Soc. Japan, **36**, 346 (1963). (*b*) S. Oae and R. Kiritani. Bull. Chem. Soc. Japan, **37**, 770 (1964).
5. S. J. Metro. J. Am. Chem. Soc. **77**, 2901 (1955).
6. E. Havinga and A. Schors. Rec. Trav. Chim. Pays-Bas, **69**, 466 (1950).
7. A. Pfob. Monatsh. Chem. **18**, 467 (1897).
8. E. H. Rodd. (Editor.) Chemistry of carbon compounds. Vol. III. Part A. Elsevier Publishing Co., Inc., New York. 1954. p. 446.
9. D. Goldsmith, D. Becher, S. Sample, and C. Djerassi. Tetrahedron, Supplement No. **7**, 145 (1966).
10. G. M. Clarke, R. Grigg, and D. H. Williams. J. Chem. Soc. 338 (1966).
11. H. Budzikiewicz, C. Djerassi, and D. H. Williams. Interpretation of mass spectra of organic compounds. Holden-Day, San Francisco. 1964. p. 179.

12. C. G. SWAIN, G. TSUCHIHASHI, and L. T. TAYLOR. Anal. Chem. **35**, 1415 (1963).
13. J. H. BEYNON and A. E. WILLIAMS. Mass and abundance tables for use in mass spectrometry. Elsevier Publishing Co., Inc., New York. 1963.
14. H. BUDZIKIEWICZ, C. DJERASSI, and D. H. WILLIAMS. Interpretation of mass spectra of organic compounds. Holden-Day, San Francisco. 1964. p. 67.
15. H. BUDZIKIEWICZ, C. DJERASSI, and D. H. WILLIAMS. Structure elucidation of natural products by mass spectrometry. Vol. 2. Holden-Day, San Francisco. 1964. p. 208.
16. Y. FURUYA, D. MORIKAWA, and K. ITOHO. Bull. Chem. Soc. Japan, **40**, 1425 (1967).
17. A. SCHORS, A. KRAAIJEVELD, and E. HAVINGA. Rec. Trav. Chim. **74**, 1243 (1955).
18. H. I. BOLKER, F. L. KUNG, and M. L. KEE. Tappi, **50**, 199 (1967).
19. D. HADZI. J. Chem. Soc. 2725 (1956).
20. H. STERK and E. ZIEGLER. Monatsh. Chem. **97**, 1131 (1966).
21. F. POLLECOFF and R. ROBINSON. J. Chem. Soc. 645 (1918).
22. L. J. BELLAMY. The infrared spectra of complex molecules. John Wiley and Sons, Inc., New York. 1958. p. 178.
23. D. M. W. ANDERSON, L. J. BELLAMY, and R. L. WILLIAM. Spectrochim. Acta, **12**, 233 (1958).