

1.5549; lit.<sup>2</sup> b.p. 91° (1.2 mm.),  $n_D^{20}$  1.5583. The infrared spectrum often showed a weak to medium band at 13.8  $\mu$  and a shoulder at 3.3  $\mu$  which were absent in pure samples. The proton magnetic resonance spectrum of the compound in carbontetrachloride with internal tetramethylsilane showed an octet centered at 5.67  $\tau$ . This spectrum was obtained some years after completion of the remainder of the work, and no pure material remained. The spectrum was obtained on a sample that contained about 10% of I, judging from the area of the vinyl hydrogen absorption. Hence some of the finer features of the recorded spectrum may be due to impurity.

**Bicyclo[4.2.0]oct-7-ene (V).**—The olefin was prepared by treating dibromide IV with magnesium, b.p. 131–133°,  $n_D^{25}$  1.4729; lit.<sup>4</sup> b.p. 132.5°,  $n_D^{20}$  1.4761. Addition of bromine to V in methylene chloride at 0° gave an 80% yield of the dibromide IV, a colorless liquid, b.p. 94° (1.2 mm.),  $n_D^{25}$  1.5517. The infrared spectrum (2–15  $\mu$ ) was superimposable upon that of authentic IV.

**cis and trans-1,2-Dibromocyclobutane.**—These compounds were prepared according to standard procedures.<sup>8,17</sup> The *trans*-dibromide had b.p. 93–94° (55 mm.),  $n_D^{25}$  1.5344; lit.<sup>8</sup> b.p. 74–75° (26.5 mm.),  $n_D^{25}$  1.5352. The *cis* isomer, obtained by addition of hydrogen bromide to 1-bromocyclobutene in the presence of benzoyl peroxide, was purified by gas chromatog-

raphy, and was pure by that criterion,  $n_D^{25}$  1.5485; lit.<sup>17</sup>  $n_D^{25}$  1.5478. The infrared spectra were in good agreement with those obtained by Abell and Chiao.<sup>17,18</sup>

**Dipole Moments.**—The moments were calculated by essentially the method of Halverstadt and Kumler,<sup>19</sup> utilizing an IBM 7070 computer programmed as described earlier.<sup>20</sup> The molar refractivities were calculated from tables<sup>21</sup> and atomic polarization was neglected. The apparatus has been described previously.<sup>22</sup>

**Acknowledgment.**—The authors are indebted to Dr. M. A. DaRooge and Mr. C. L. Neumann for the dipole moment determinations, to Dr. M. Emerson and Mr. R. Ford for the n.m.r. spectra, to Dr. N. A. LeBel and Mr. P. M. Subramanian for the sample of *cis*-1,2-dibromocyclobutane, and to Dr. A. T. Blomquist and Dr. V. Georgian for correspondence regarding various aspects of the present work.

(18) Personal communication from Professor Abell.

(19) I. F. Halverstadt and W. D. Kumler, *J. Am. Chem. Soc.*, **64**, 2988 (1942).

(20) N. L. Allinger and J. Allinger, *J. Org. Chem.*, **24**, 1613 (1959).

(21) A. I. Vogel, W. T. Cresswell, G. J. Jeffery, and J. Leicester, *Chem. Ind. (London)*, 358 (1950).

(22) N. L. Allinger, H. Blatter, M. A. DaRooge, and L. A. Freiberg, *J. Org. Chem.*, **26**, 2550 (1961).

(17) P. I. Abell and C. Chiao, *J. Am. Chem. Soc.*, **82**, 3610 (1960).

## The Pulegone Oxides

WILLIAM REUSCH AND CALVIN KEITH JOHNSON

*Kedzie Chemical Laboratory, Michigan State University, East Lansing, Michigan*

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The diastereoisomeric pulegone oxides have been isolated as crystalline solids. These isomers are assigned configurations Ia and IIa on the basis of the n.m.r. spectra, the optical rotatory dispersion curves, the thermal isomerization occurring at 200°, and a consideration of the available conformations.

Over three decades ago, Prileschaev reported<sup>1</sup> the preparation of a crystalline oxide, m.p. 44°, from pulegone by oxidation with perbenzoic acid. This work was recently confirmed by Pigulevsky and Mironova,<sup>2</sup> who also found that this dextrorotatory oxide was converted to a more strongly dextrorotatory liquid modification when heated at 200° for ten hours. On the basis of the Raman spectra and the change in specific rotation the latter workers concluded that isomerization of the crystalline pulegone oxide (Ia or IIa) to its diastereoisomer (IIa or Ia) was taking place, and that no deep structural changes occurred during heating. The lack of convincing evidence for this assertion combined with our interest in the high temperature reactions of oxiranes<sup>3</sup> has led us to re-examine these

facts and interpretations. In this paper we report the isolation of and assignment of configurations to the diastereoisomers Ia and IIa.

Good yields of pulegone oxide mixtures were obtained from pulegone either by oxidation with perbenzoic acid<sup>1,2</sup> or by reaction with alkaline hydrogen peroxide.<sup>4</sup> These mixtures yielded to analysis by vapor phase chromatography (v.p.c.) and proved to be almost identical in composition (33% Ia and 67% IIa). The crystalline modification, m.p. 44°, was readily isolated, but v.p.c. analysis showed this to be a compound consisting of equal proportions of the two diastereoisomers. These isomers were eventually separated by careful distillation at reduced pressure, followed by crystallization from petroleum ether. A survey of appropriate physical properties is given in Table I.

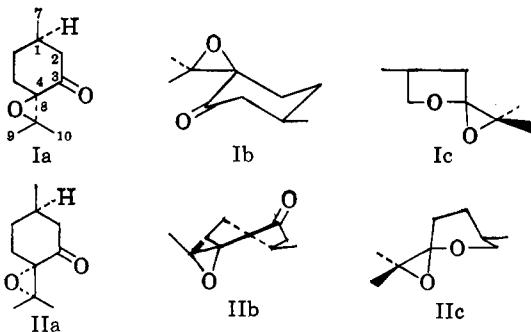


TABLE I

Isomer	M.p., °C.	$\lambda_{\max}^{\text{heptane}}$	$m\mu$ ( $\epsilon$ )	$\nu_{\max}^{\text{CCl}_4}$ cm. <sup>-1</sup>	$[\alpha]_D^{25}$ C <sub>2</sub> H <sub>5</sub> OH
Ia	59	209	(225)	1727	+48.0°
		303	(31)		
IIa	55	209	(221)	1728	-19.6°
		303	(31)		

In contrast to the report by Prileschaev, both Ia and IIa, prepared in this manner, are stable indefinitely under normal laboratory conditions. However, heating either Ia or IIa at 200° in an inert atmosphere does

(1) M. N. Prileschaev, *Bull. soc. chim.*, (iv) **41**, 687 (1927).

(2) G. V. Pigulevsky and I. K. Mironova, *Zh. Obshch. Khim.*, **27**, 1101 (1957).

(3) W. Reusch and C. K. Johnson, *J. Am. Chem. Soc.*, **84**, 1759 (1962).

(4) W. Treibs, *Ber.*, **66**, 1492 (1933).

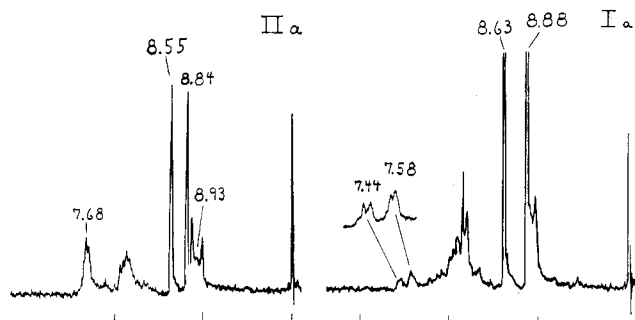


Fig. 1.—Nuclear magnetic resonance spectra of the pulegone oxides.

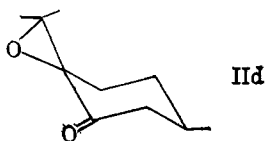
produce a transformation similar to that described by Figulevsky and Mironova. This reaction is considerably more complex than originally believed,<sup>2</sup> since extensive rearrangement and fragmentation accompany the isomerization. After ten hours of heating, more than half the pulegone oxide has decomposed, and at least ten products have been observed by v.p.c. analysis. The isolation and identification of the major rearrangement products will be described in a future paper.

The assignment of configurations Ia and IIa, as described in Table I, rests upon four arguments. First, the similarity of the ultraviolet spectra and the group frequency region of the infrared spectra for the two isomers suggests that the principle conformations in each case have almost identical or enantiomeric configurations in the neighborhood of the carbonyl group. Furthermore, the bathochromic shift of the  $n \rightarrow \pi^*$  transition, with respect to that found in menthone,  $\lambda_{\max}^{\text{heptane}} 296 \mu$  ( $\epsilon 21$ ), is an indication that the oxirane oxygen atom is oriented above (or below) the plane of the carbonyl group.<sup>5</sup> An examination of molecular models has enabled us to conclude that the chair conformation Ib is a major contributor to the isomer of configuration Ia, while twist boat conformation IIb predominates in isomer IIa. These conformations not only satisfy the previous points, but also have minimal nonbonded interactions.<sup>6</sup>

Secondly, there are significant differences in the n.m.r. spectra of the two isomers which can reasonably be explained in terms of conformations Ib and IIb. In the chair conformation Ib, the equatorial hydrogen at C-2 is almost eclipsed by the adjacent carbonyl group, and is therefore deshielded with respect to the axial

(5) The bathochromic influence of an axial polar substituent at the  $\alpha$ -position in cyclohexanones has been well substantiated [R. C. Cookson and S. H. Dandegaonker, *J. Chem. Soc.*, 352 (1955)].

(6) Measurements made with the aid of Dreiding Models indicate the following unfavorable steric interactions: Ib, C-9-C-5 1.9 Å., C-10-carbonyl oxygen, 1.6 Å.; IIb, C-9-C-5 2.0 Å., C-10-carbonyl oxygen, 1.7 Å. Only distances less than 2.5 Å. are reported, and the values refer to the distance at which maximum compression occurs. It is doubtful that these measurements are reliable to less than  $\pm 0.05$  Å. In considering other conformations, such as the chair conformation of IIa having an equatorial methyl group at C-1 (IIId), one should keep in mind that steric compression is not the only important destabilizing factor. In the case of IIId, the electrostatic repulsion resulting from the eclipsed oxygen bonds at C-3 and C-4 also is important.



C-2 hydrogen, which is located above the plane of the carbonyl group.<sup>7</sup> The former is thus expected to show a resonance pattern which is essentially the low field portion of an ABC system. The observed spectrum (Fig. 1) agrees with this interpretation in exhibiting a pair of doublets at 7.44 and 7.58  $\tau$ ,  $J_{\text{vic}} = 2.2$  c.p.s.,  $J_{\text{gem}} = 9.0$  c.p.s. The area of these doublets is only one fourth that of the methyl group at 8.63  $\tau$ ; however, it is likely that the latter resonance is reinforced by parts of other multiplets.

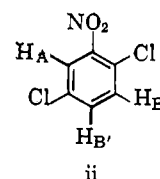
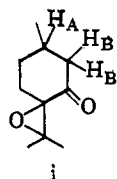
On the other hand, one of the distinguishing features of the twist conformation IIb is that the carbonyl group bisects the H-C<sub>2</sub>-H bond angle. The hydrogens at C-2 will, therefore, have similar chemical shifts, and may be expected to exhibit an AB<sub>2</sub> relationship with the tertiary hydrogen at C-1.<sup>8</sup> The observed spectrum (Fig. 1) agrees with this suggestion to the extent that the lowest field absorption is a doublet, 7.68  $\tau$ ; however, the apparent coupling constant for this doublet, 2 c.p.s., is smaller than that anticipated from earlier studies.<sup>8</sup> Furthermore, the integrated areas of the doublet in question and the methyl group at 8.55  $\tau$  are not in exact agreement with this assignment, the ratio being 2.5/3, respectively. Despite these difficulties, the previous interpretations seem generally sound and should require only minor modification.

The most striking variation in the physical properties listed in Table I is seen in the opposite signs of the specific rotations of Ia and IIa. We have learned that this difference is a consequence of opposite Cotton effects near 300  $m\mu$  (having amplitudes of roughly 2000°), and the third argument in favor of our assignment rests upon this evidence. The application of the Octant Rule<sup>9</sup> to conformations Ib and IIb is readily made, using projection formulas Ic and IIc. The oxirane oxygen and the C-7 methyl group occupy positive quadrants in Ic and negative quadrants in IIc; the agreement with the positive and negative Cotton effects observed for Ia and IIa, respectively, is, thus, excellent. Alternately, the axially oriented oxirane oxygen atom and the adjacent carbonyl function may be viewed as an inherently disymmetric chromophore, similar to those which gave rise to the "axial halo ketone rule."<sup>10</sup> If this is the case, the nature of the anomalous dispersion curve is determined primarily by the configuration of the disymmetric chromophore. An interpretation paralleling the "axial halo ketone rule" agrees with the observed dispersion curves.

The fourth and final argument concerns the isomeri-

(7) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p. 122.

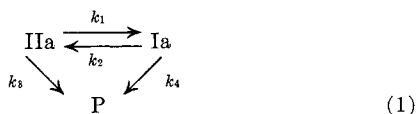
(8) That the chemical shifts may not be identical and that  $J_{AB} \neq J_{AB'}$  are apparently of little consequence in this case (i); indeed, a parallel situation (ii) has been reported by R. Richards and T. Schaefer, *Mol. Phys.* **1**, 331 (1958). In the latter work the B hydrogens appeared as a doublet;  $J_{\text{apparent}} = (J_{AB} + J_{AB'})/2$ .



(9) W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne, and C. Djerani, *J. Am. Chem. Soc.*, **83**, 4013 (1961).

(10) C. Djerassi and W. Klyne, *ibid.*, **79**, 1506 (1957).

zation of Ia and IIa observed at elevated temperatures. This isomerization and the accompanying rearrangements and fragmentations (leading irreversibly to products P) are illustrated in equation 1. By heating samples of pure Ia and IIa at 200° for varying lengths of time,



we have found that the ratio Ia/IIa approaches a limit of approximately 3. Because of the concurrent rearrangement reactions, this ratio does not necessarily represent the equilibrium constant,  $K_{\text{eq}} = k_1/k_2$ . Utilizing the fact that such a limiting ratio exists, however, the relationship expressed in equation 2 may be derived.<sup>11</sup> Although quantitative values for

$$K_{\text{eq}} = 3 - \frac{(3k_3 - 3k_4)}{4k_2} \quad (2)$$

the rate constants are not available, a few qualitative relationships may be pointed out. Thus,  $k_1 > k_2$ ,  $k_3 > k_4$ , and  $k_4 > k_2$ . These differences do not appear to be large and  $(3k_3 - 3k_4)/4k_2$  is thought to be no greater than one. In this event, the equilibrium constant would be greater than unity and  $\Delta F^\circ$ , for the isomerization, would be negative. These conclusions agree well with the assignment of configuration presented in Table I. Although the qualitative nature of the previous reasoning makes a detailed conformational analysis of doubtful value, one may conclude from an inspection of models<sup>6</sup> that only slight differences in nonbonded interactions exist between Ib and IIb.<sup>12a</sup> The main difference lies, therefore, in the torsional strain<sup>12d</sup> present in the twist boat conformation (IIb) but not in the chair form (Ib). Measurements<sup>12b,c</sup> and calculations<sup>12d</sup> indicate that at 200° a standard free energy difference of approximately 3 kcal./mole would be anticipated for an equilibrium between the twist boat and chair conformations of cyclohexane.

## Experimental

Melting points were determined on a Kofler hot stage. The infrared spectra were recorded by a Perkin-Elmer, Model 21, spectrophotometer, and the ultraviolet spectra were measured with a Cary, Model 11, spectrophotometer. Optical rotatory dispersion measurements were made at Wayne State University. The n.m.r. spectra were determined in carbon tetrachloride solution using a Varian Associates, A-60, high resolution spectrometer. Vapor phase chromatography analyses were made using an Aerograph, A-90-P, gas chromatograph. A 0.25-in., 5-ft. column of 5% P.D.E.A.S. (phenyldiethanolamine succinate) on Chromosorb W served very well for the v.p.c. analyses. Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan.

**Preparation of Pulegone Oxide Mixtures.** A.—A mixture of pulegone<sup>13</sup> (30 g.), methanol (160 ml.), and 30% hydrogen peroxide (34 g.), in a 50-ml., three-necked flask equipped with a stirrer, a dropping funnel, and a thermometer, was cooled to 15°. A solution of sodium hydroxide (1.0 g. in 10 ml. of water) was

added dropwise with stirring over a 15-min. period. Stirring was continued for 4 hr. with the temperature being maintained at 20–25°. The reaction mixture was then poured into 400 ml. of brine and extracted with three 200-ml. portions of benzene. After the combined benzene extracts were washed and dried, the solvent was removed under reduced pressure and the residue was analyzed by v.p.c. The crude product, which consisted of 32% Ia and 68% IIa, was distilled (5 mm.) over a short path to give 20 g. (67%) of a mixture of diastereoisomeric pulegone oxides.

**B.**—Pulegone<sup>13</sup> (1.0 g.) was added to a 0.48 M benzene solution of perbenzoic acid (15 ml.), and the reaction mixture was kept at 5–10° for 24 hr. with occasional stirring. The benzene solution was washed with 10% sodium hydroxide followed by water, and was then dried over anhydrous magnesium sulfate. The solvent was removed by distillation, and the residue proved to be a mixture of 34% Ia and 66% IIa when analyzed by v.p.c. Distillation over a short path at a pressure of 5 mm. gave an 86% yield of pulegone oxides. Benzoic acid was shown not to isomerize the pulegone oxides under the described conditions.

**Isolation and Properties of Ia and IIa.**—Treatment of the crude oxide mixture, described in the previous section, with chilled pentane gave a low melting crystalline solid, which, after several crystallizations from pentane, exhibited physical properties identical to those previously attributed<sup>1,2</sup> to one of the diastereoisomeric pulegone oxides; m.p. 42–43°;  $[\alpha]_{\text{D}}^{25} + 15.2^\circ$  (*c* 5.445, in 95% ethanol).

*Anal.* Calcd. for C<sub>10</sub>H<sub>16</sub>O<sub>2</sub>: C, 71.39; H, 9.59. Found: C, 71.69; H, 9.60.

Analysis by v.p.c. proved this material to be an equimolar mixture of Ia and IIa.

Isolation of the pure diastereoisomers was achieved by careful distillation of the oxide mixture through a 16-in., vacuum jacketed, tantalum spiral column. The fraction boiling at 95–97° (5 mm.) was crystallized twice from pentane to give IIa; m.p. 55–56°;  $\lambda_{\text{max}}^{\text{heptane}}$  209 ( $\epsilon$  221) and 303 m $\mu$  ( $\epsilon$  31);  $\nu_{\text{max}}^{\text{CCl}_4}$  1728 cm.<sup>-1</sup>. Rotatory dispersion in 95% ethanol (*c* 0.028), 25°;  $[\alpha]_{700} - 24.9$ ,  $[\alpha]_{589} - 14.2$ ,  $[\alpha]_{527} - 1177.9$ ,  $[\alpha]_{293} + 786.5$ ,  $[\alpha]_{290} + 562.3$ .

*Anal.* Calcd. for C<sub>10</sub>H<sub>16</sub>O<sub>2</sub>: C, 71.39; H, 9.59. Found: C, 71.60; H, 9.58.

The fraction boiling at 100–102° (5 mm.) was redistilled, and the high boiling fraction was crystallized from petroleum ether (60–110°) to give Ia, m.p. 59°;  $\lambda_{\text{max}}^{\text{heptane}}$  209 ( $\epsilon$  225) and 303 m $\mu$  ( $\epsilon$  31);  $\nu_{\text{max}}^{\text{CCl}_4}$  1727 cm.<sup>-1</sup>. Rotatory dispersion in 95% ethanol (*c* 0.040), 25°;  $[\alpha]_{700} + 32.2$ ,  $[\alpha]_{589} + 50.0$ ,  $[\alpha]_{324} + 853.9$ ,  $[\alpha]_{285} - 1242.5$ ,  $[\alpha]_{283} - 1203$ .

**Thermal Isomerization.**—Samples of pure Ia and IIa were degassed and sealed in carefully cleaned Pyrex tubes under nitrogen. These tubes were heated for varying lengths of time in an aluminum block furnace kept at 200 ± 2°. The vials were then opened, and the mixtures within were analyzed by v.p.c. In many of the samples acetophenone, which was found to be stable under the conditions of these experiments, was added as an internal standard; the absence of very high boiling products and polymers was thus demonstrated. The reproducibility is not good, but some general trends may be discerned from the following data in Table II.

TABLE II

Isomer	Time heated, hr.	% decomposition	Ia/IIa
Ia	3	29	7.7
Ia	9	52	5.0
Ia	10	57	3.8
IIa	5	55	0.6
IIa	7	76	1.7
IIa	10	90	3.0

If the relationships of equation 1 are accepted and if it may be assumed that the ratio of the molar concentrations of Ia and IIa approach the limit *X*, the following derivation may be made.

$$\frac{d[\text{Ia}]}{dt} = k_1[\text{IIa}] - [\text{Ia}](k_2 + k_4)$$

$$\frac{d[\text{IIa}]}{dt} = k_2[\text{Ia}] - [\text{IIa}](k_1 + k_3)$$

$$X = \frac{[\text{Ia}]}{[\text{IIa}]} = \frac{[\text{Ia}] + d[\text{Ia}]}{[\text{IIa}] + d[\text{IIa}]}$$

(11) This derivation will be found at the end of the Experimental section.

(12) (a) A referee has pointed out that at high temperatures, significant concentrations of other conformations (e.g., II'd) will be present in IIa. This is certainly quite likely; however, we have based our argument upon IIb alone for simplicity; (b) W. S. Johnson, V. J. Bauer, J. L. Margrave, M. A. Frisch, L. H. Dreger, and W. Hubbard, *J. Am. Chem. Soc.*, **83**, 606 (1961); (c) N. L. Allinger and L. A. Freiberg, *ibid.*, **82**, 2393 (1960); (d) J. B. Hendrickson, *ibid.*, **83**, 4537 (1961).

(13) Pulegone, obtained from K and K Laboratories, was distilled carefully before being used.

$$k_2[\text{Ia}]^2 - [\text{Ia}][\text{IIa}](k_1 + k_3) = k_1[\text{IIa}]^2 - [\text{Ia}][\text{IIa}](k_2 + k_4)$$

$$k_2X - k_3 + k_2 + k_4 = k_1(1/X + 1)$$

$$k_1/k_2 = K_{\text{eq}} = X^2 - \frac{X \frac{k_3 - k_4}{k_2}}{X + 1}$$

**Acknowledgment.**—We are indebted to Mr. Fredrick Karkowski, Dr. Margaret DaRooge, and Dr. Norman L. Allinger of Wayne State University for the determination of the optical rotatory dispersion curves. We also wish to thank Drs. G. Karabatsos, D. McQuarrie, and M. Russell of this department for helpful discussions.

## Purine N-Oxides. XI. An Activating Effect on Some Displacement Reactions<sup>1</sup>

R. M. CRESSWELL AND GEORGE BOSWORTH BROWN

*Division of Nucleoprotein Chemistry, Sloan-Kettering Institute for Cancer Research,  
Sloan-Kettering Division of Cornell University Medical College, New York, New York*

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2-Mercaptoadenine 1-N-oxide was obtained from 4-aminoimidazole-5-carboxamidoxime and carbon disulfide. Methylation and oxidation afforded the 2-methylsulfinyladenine 1-N-oxide, which could be converted to the 2-chloro- or the 2-hydroxyadenine N-oxides, none of which are available by direct oxidations. A comparison has been made of the reactivity of the 2-methylsulfinyl and 2-chloro groups in the N-oxides and in the corresponding free bases.

Adenine and several amino or alkyl purine N-oxides are produced by the oxidation of the parent purine by hydrogen peroxide in acetic acid.<sup>2a,b</sup> Because N-oxides of purines containing hydroxy, mercapto, or chloro substituents in the pyrimidine ring have not been obtained by direct oxidation, other synthetic approaches to such purines seemed desirable.

A previous paper<sup>2b</sup> describing the synthesis of 2-azaadenine 1-N-oxide (II) from the reaction of nitrous acid with 4-aminoimidazole-5-carboxamidoxime (I) noted the selectivity of the reaction, in which the alternative 2-aza-6-hydroxylaminopurine was not produced. This same selectivity is found when I is refluxed in a mixture of ethyl orthoformate and dimethylformamide where a high yield of adenine 1-N-oxide (IV) is obtained. Under the latter conditions, Taylor, *et al.*,<sup>4</sup> obtained hypoxanthine 1-N-oxide from 4-aminoimidazole-5-hydroxamic acid.

Useful intermediate I, obtained from acid hydrolysis of adenine 1-N-oxide,<sup>2b</sup> was treated with carbon disulfide in an attempt to form a purine N-oxide with a mercapto substituent. The reaction in pyridine and methanol proceeded smoothly at room temperature; after four or five days, a crystalline product was collected and analyzed. It evolved hydrogen sulfide when fused with sodium formate,<sup>5</sup> and gave a dark green color with ferric chloride solution.<sup>6</sup> The N-oxide structure III was preferred to that of the alternative 6-hydroxylamino-2-mercaptapurine, since the product could be recovered unchanged from brief treatment with sodium dithionite at 90°. Such conditions are known to reduce hydroxylamino substituents in purines<sup>7</sup>

and pyrimidines,<sup>8</sup> but do not affect adenine N-oxide. Proof of the 2-mercaptoadenine 1-N-oxide structure (III) came from the desulfurization of III with Raney nickel to a mixture of adenine 1-N-oxide and adenine.

Previous<sup>3</sup> workers have noted the lack of reactivity of the 2-methylmercapto<sup>9,10</sup> or 2-carboxymethylmercapto<sup>11</sup> substituents in substituted adenines. In the hope that a 2-methylmercapto group adjacent to an N-oxide would prove to be more reactive, III was methylated with methyl iodide. This led to 2-methylmercaptoadenine 1-N-oxide (V) in good yield. This compound was highly resistant to hydrolysis in refluxing 25% hydrochloric acid. In a further attempt to render the substituent in the 2-position more susceptible to displacement, oxidation of the methylmercapto group to a sulfinato or sulfonate was investigated.

Todd and co-workers<sup>9</sup> obtained 2-methylsulfonyl-adenine (X) by the action of chlorine in aqueous solution on 2-methylmercaptoadenine (VIII). This derivative is likewise obtained in better yield when the chlorine oxidation is carried out in methanol, as in a recent modification<sup>12</sup> of this reaction. It is also obtained when 2-methylmercaptoadenine is oxidized with hydrogen peroxide in alkaline solution, but with hydrogen peroxide in acetic acid, the 2-methylsulfinyl analog IX and not the 2-methylsulfonyl derivative is obtained.

Treatment of 2-methylmercaptoadenine 1-N-oxide (V) with chlorine in methanol or with hydrogen peroxide in acetic acid gave good yields of 2-methylsulfinyl-adenine 1-N-oxide (VI). Further oxidation to the corresponding 2-methylsulfonyl derivative by prolonged reaction time or elevated temperature was unsuccessful, as were attempts to oxidize VI by hydrogen peroxide in alkaline solution. The failure to oxidize the 2-methylmercaptoadenine 1-N-oxide beyond the 2-methylsulfinato stage can presumably be explained on

(1) Some of the investigations referred to here were supported by grants from the National Cancer Institute, National Institutes of Health, Public Health Service (grant CY-3190), and from the Atomic Energy Commission [contract AT(30-1)-910].

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