methanol, and chilled. A scintillating crystalline product was filtered, washed with methanol, and recrystallized from nitrobenzene to yield only a few milligrams of pale yellow needles which were identified as 2,2′,4,4′,6,6′-hexanitrostilbene (1) by X-ray powder diffraction pattern.

Heating the reaction mixture to reflux temperature for a few minutes or for a prolonged period, or addition of a larger quantity of piperidine did not improve the yield of 1.

D. From 2,4,6-Trinitrotoluene.—A solution of 4.5 g. of 2,4,6-trinitrotoluene in 25 ml. of pyridine was prepared in a 300-ml. three-necked round-bottomed flask equipped with a thermometer and a mechanical stirrer. A solution of 8 g. of iodine in 75 ml. of methanol was added to the pyridine solution of TNT and the mixture was chilled to −10° in an ice–salt bath. A heavy red-gold precipitate formed which was replaced by a red-brown finely divided precipitate suspended in a blood red solution during the 0.5-hr. addition of 17 ml. of a 33% methanolic potassium hydroxide solution. After the addition of the alkali was completed the reaction mixture was stirred in the ice–salt bath for 0.5 hr., then for 15 min. after removal of the bath. The product was filtered, slurried with hot methanol and then with hot water, and dried. The dark red-brown material weighed 0.5 g., 10% of the theoretical yield. Recrystallized from nitrobenzene it yielded 0.2 g. of pale yellow needles, m.p. 315–316° dec. The X-ray powder diffraction pattern for this product was superimposable on that for A above.

Unit Cell Dimensions and Molecular Weight of 1.—X-Ray diffraction measurements on a single crystal of hexanitrostilbene showed that it had orthorhombic symmetry and the following unit cell dimensions: $a = 20.93$, $b = 5.57$, and 14.67 Å. The unit cell volume is therefore 1710 Å.^{3}. The crystal density was measured by flotation to be 1.740 g./cm.^{3}. The unit cell weight is therefore 2975×10^{-24} g. or 1792 molecular weight units. Since the unit cell must contain an integral number of molecules and orthorhombic symmetry indicates that the number is 2, 4, or 8, the most probable molecular weights are 896, 448, and 224. The calculated molecular weight of hexanitrostilbene, 450.3, agrees to within 1% of the observed value corresponding to 4 molecules per unit cell.

X-Ray powder diffraction pattern, interplanar spacing, Å. (relative intensity): 6.06 (23), 5.27 (37), 4.98 (58), 4.46 (27), 4.33 (13), 4.27 (12), 4.11 (20), 3.85 (97), 3.78 (100), 3.69 (73), 3.64 (60), 3.52 (25), 3.42 (8), 3.28 (15), 3.23 (17), 3.13 (48), 2.99 (28), 2.92 (27), 2.88 (15), 2.79 (37), 2.78 (35), 2.63 (47), 2.49 (17), 2.38 (17), 2.24 (13), 2.16 (5), 2.14 (3), 2.05 (10), 2.02 (8).

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Pyrazines. IV. Nucleophilic Substitutions on Chloropyrazine and Alkyl Chloropyrazine N-Oxides[1a,b]

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The rapid formation of hydroxypyrazine N-oxides by the action of alkali on chloropyrazine N-oxides and alkyl chloropyrazine N-oxides, contrasted with the prolonged time required to prepare similarly the unoxidized hydroxypyrazines, suggests that the N→O group increases the reactivity of the halogen. Examples illustrating this effect are given. This activation is not noted in the preparation of ethoxypyrazine and alkyl ethoxypyrazine N-oxides by varied reagents.

Several accounts of nucleophilic substitutions on chloropyrazine and alkyl-substituted chloropyrazines have appeared in recent years.[2-6] It was of additional interest, therefore, to compare the behavior of chloropyrazine N-oxides[7] with nucleophilic reagents. The effect of the presence of N→O in this heterocyclic series has been indicated[8] by the preparation of 2-hydroxypyrazine 1-oxide in 60% yield from 2-chloropyrazine 1-oxide by heating with aqueous alkali for 2 hr. By contrast, Erickson and Spoerri[9] had to heat 2-chloropyrazine with aqueous alkali in a sealed vessel for 7 hr. (150°) to produce 2-hydroxypyrazine in comparable yield.

Attempts have been made in this laboratory to prepare 3-hydroxypyrazine 1-oxide by alkaline hydrolysis of 3-chloropyrazine 1-oxide. Although spectroscopic evidence is available for the facile formation of the desired compound within 45 min., *e.g.*, a probe sample of the reaction mixture shows absorptions at 231, 259, and 315 mμ, consistent with the predicted spectrum for this compound,[7,10] efforts to isolate good quality homogeneous material have been unsuccessful thus far. The preparation of 3-hydroxypyrazine 1-oxide has been reported by Palamidessi and Bernardi[8] by nitrous acid treatment of 3-aminopyrazine 1-oxide. Further studies are in progress.

The influence of the N→O was further illustrated by action of aqueous alkali on 3-chloro-2-methylpyrazine 1-oxide. The course of the reaction was followed spectrophotometrically and probe samples examined at intervals showed that the formation of the fully developed absorption peak at 310–315 mμ, characteristic of hydroxypyrazines, occurred within the first 15 min.

(1) (a) Portions of this work were presented at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963. (b) The work reported here was supported in part by a grant (CY-5343) from the National Institutes of Health.

(2) G. Karmas and P. E. Spoerri, *J. Am. Chem. Soc.*, **78**, 4071 (1956); **79**, 680 (1957).

(3) G. W. H. Cheeseman, *J. Chem. Soc.*, 242 (1960).

(4) A. Hirshberg and P. E. Spoerri, *J. Org. Chem.*, **26**, 2356 (1961).

(5) (a) H. Gainer, M. Kokorudz, and W. K. Langdon, *ibid.*, **26**, 2360 (1961); (b) W. B. Lutz, S. Lazarus, S. Klutzko, and R. I. Meltzer, *ibid.*, **29**, 415 (1964).

(6) J. D. Behun, P. Kan, P. Gibson, C. Lenk, and E. Fujiwara, *ibid.*, **26**, 4981 (1961).

(7) B. Klein, N. E. Hetman, and M. E. O'Donnell, *ibid.*, **28**, 1682 (1963).

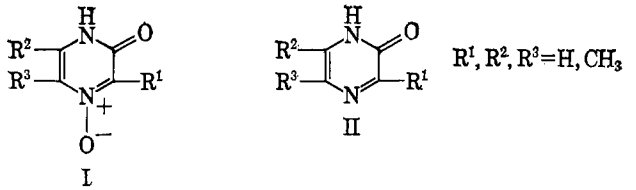
(8) G. Palamidessi and L. Bernardi, *Gazz. chim. ital.*, **93**, 343 (1963).

(9) A. E. Erickson and P. E. Spoerri, *J. Am. Chem. Soc.*, **68**, 400 (1946).

(10) R. A. Baxter, G. T. Newbold, and F. S. Spring, *J. Chem. Soc.*, 1859 (1948).

Again, this is in marked contrast to the work of Gainer, *et al.*,[5] who boiled 2-chloro-3-methylpyrazine with concentrated aqueous alkali for 9 hr. to replace the chloro group. Similar resistance to replacement of the halogen of 2-chloro-3,6-dimethylpyrazine by hydroxyl (and in poor yield) has been reported by the same authors and by Baxter and Spring.[11] In the present work, when the course of this reaction was followed spectrophotometrically, it was observed that alteration of the ultraviolet spectrum with the appearance of the characteristic hydroxypyrazine absorption at 310–320 mμ did not commence until at least 23 hr. had elapsed. This observation can be contrasted with the formation of 3-hydroxy-2,5-dimethylpyrazine 1-oxide in 59.5% yield by heating the chloro N-oxide compound in aqueous alkali for 1 hr., although spectrophotometrically considerable conversion was apparent within 15 min. Approximately, 59 hr. of boiling with aqueous alkali was required to replace the chloro group of 2-chloro-3,5-dimethylpyrazine with hydroxyl.

The hydroxypyrazine N-oxides undoubtedly exist as the cyclic amide in the solid state since their infrared



absorption spectra in every case showed the amide-type absorption at about 6.0–6.1 and at about 6.4–6.5 μ described by Gainer, *et al.*,[5] for the hydroxypyrazines. This was true for the other hydroxypyrazines examined in this investigation.

Albert and Phillips[12] concluded that hydroxypyrazine in solution existed predominently in the amide form. This was later corroborated by Cheeseman[3] in similar studies. In the examples studied here, with one ring nitrogen substituted by the oxide function, it might be possible to apply the Albert and Phillips approach to determine the amide–enol ratio.[13] It would be more accurate, therefore, to refer to these compounds as the alkyl-3,4-dihydro-substituted pyrazinone 1-oxides (I) and alkyl-1,2-dihydro-substituted pyrazinones (II),[3] respectively, but the compounds are named in their traditional sense.

Experiments designed to determine whether the N→O group increased the reactivity of the halogen toward alkoxide were not clear cut. Initially, sodium ethoxide was used. Later, when Gainer, *et al.*,[5] showed that alcoholic sodium or potassium hydroxide also converted alkylchloropyrazines to alkylethoxypyrazines, these reagents were substituted, again without significant difference.

3-Chloropyrazine 1-oxide on treatment with sodium ethoxide rapidly formed 3-ethoxypyrazine 1-oxide. This was identical with the product obtained by direct oxidation of 2-ethoxypyrazine. In the latter reaction, a small amount of the dioxide was also obtained. The

Chart I

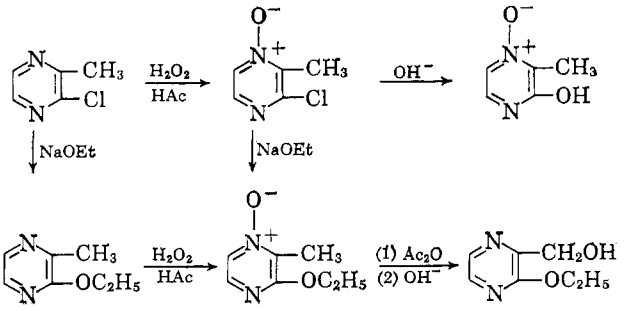


Chart II

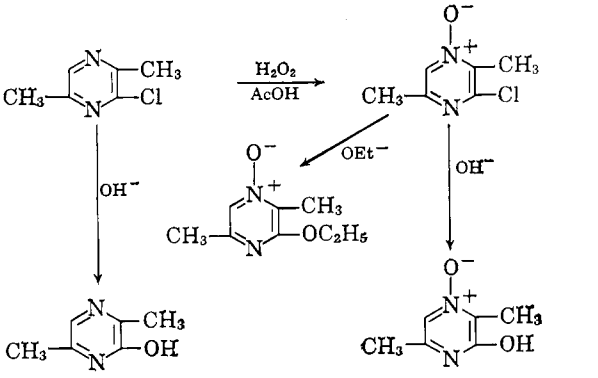
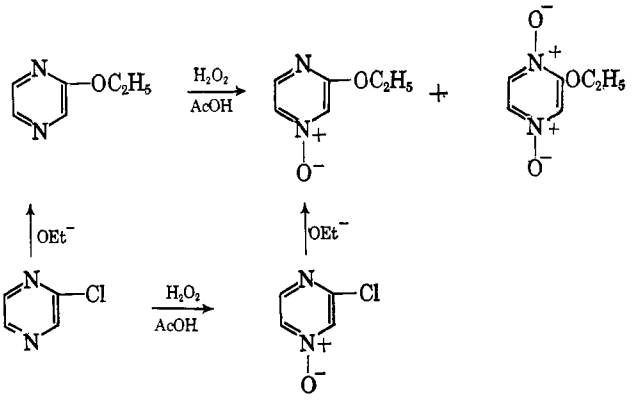


Chart III



formation of the dioxide was an unexpected finding since previously recorded attempts to prepare di-N-oxides of halogen or ethoxypyrazine derivatives were unsuccessful.[14] On the other hand, 2-ethoxy-3-methylpyrazine, on direct oxidation formed only the 1-oxide[15] (adjacent to the methyl) again, identical with the ethoxylation product of 3-chloro-2-methylpyrazine 1-oxide. The position of the N-oxide was established by rearrangement with acetic anhydride[16] to 2-ethoxy-3-pyrazylmethyl acetate and hydrolysis to the pyrazinemethanol. The reactions studied are given in Charts I–III.

(11) R. A. Baxter and F. S. Spring, *J. Chem. Soc.*, 1179 (1947).

(12) A. Albert and J. N. Phillips, *ibid.*, 1294 (1956).

(13) The ultraviolet spectra of pyrazine and alkyl pyrazine N-oxides upon addition of strong acid are remarkably altered in a stepwise manner to indicate that first protonation of the unoxidized nitrogen occurs, followed by protonation of the N→O (B. Klein and B. Schneider, unpublished observation, manuscript in preparation).

(14) See ref. 10. In this laboratory, for example, deliberate efforts to prepare 2-chloropyrazine di-N-oxide using more vigorous conditions [F. Linsker and R. L. Evans, *J. Am. Chem. Soc.*, **68**, 403 (1946)] were unsuccessful.

(15) The authors consider a steric effect unlikely since in an earlier paper [B. Klein and J. Berkowitz, *ibid.*, **81**, 5160 (1959)] the formation of di-N-oxides of trisubstituted pyrazines was shown to occur readily and in good yield. The positional designation used in this paper, wherein the N→O function is given the lowest number, is in accord with an earlier editorial suggestion.

(16) B. Klein, J. Berkowitz, and N. E. Hetman, *J. Org. Chem.*, **26**, 126 (1961).

Experimental[17,18]

3-Hydroxy-2-methylpyrazine 1-Oxide.—A suspension of 4.0 g. (0.027 mole) 3-chloro-2-methylpyrazine 1-oxide[7] in 10.8 ml. of 20% sodium hydroxide was heated under reflux for 2 hr.[19] The cooled mixture was exactly neutralized and taken to dryness *in vacuo*. The residue was distilled twice with 50 ml. of benzene to remove traces of water and then extracted twice with 100 ml. of boiling absolute ethanol and once with 50 ml. On chilling, some crystallization occurred. The solution was taken to dryness under reduced pressure and the residue was taken up in 70 ml. of hot absolute ethanol, filtered, and chilled, affording 1.7 g. of product, m.p. 194–200°. From the mother liquor on concentration and chilling, another 0.9 g. was obtained; total yield, 2.6 g. (76.6%). Several recrystallizations from 95% ethanol (charcoal) raised the melting point of the light tan crystals to 216–218°.

Anal. Calcd. for $C_5H_6N_2O_2$: C, 47.61; H, 4.80; N, 22.2. Found: C, 47.89; H, 4.87; N, 22.07.

3-Chloro-2,5-dimethylpyrazine 1-Oxide.—This compound was prepared in 74% yield from 2-chloro-3,6-dimethylpyrazine by the procedure described earlier,[7] recrystallized from petroleum ether (preferred) (b.p. 60–70°) or absolute methanol, and had m.p. 117–117.5°; Baxter, Newbold, and Spring[10] give m.p. 113–115°.

3-Hydroxy-2,5-dimethylpyrazine 1-Oxide.—A mixture of 9.8 g. (0.06 mole) of chloro compound and 53 ml. of water containing 10.1 g. of potassium hydroxide (0.18 mole) was heated under reflux for 1 hr. and worked up as described above. There was obtained after recrystallization from absolute methanol 5.0 g. product (59.5%), m.p. 270–272° dec. Baxter and associates[10] who prepared this compound by decomposition of the 3-ethoxy derivative with acid noted the decomposition point as "above 250°."

Anal. Calcd. for $C_6H_8N_2O_2$: C, 51.4; H, 5.75. Found: C, 51.39; H, 5.50.

2-Hydroxy-3,6-dimethylpyrazine.—A mixture of 8.6 g. (0.06 mole) of 2-chloro-3,6-dimethylpyrazine[20] and a solution of 10.1 g. potassium hydroxide in 60 ml. of water (0.18 mole) was heated in a 100-ml. stainless steel bomb for 23 hr. at 120°. The solution was brought to pH 5 with concentrated hydrochloric acid and evaporated to dryness *in vacuo*. The residue, dried by distillation twice with benzene, was extracted with boiling absolute ethanol. Removal of the solvent left a colorless residue also containing inorganic material. This was extracted with boiling benzene which on charcoaling and concentration deposited 3.5 g. (46.7%) of colorless needles, m.p. 207–208° (lit.[5] m.p. 206–207°).

2-Hydroxy-3,5-dimethylpyrazine.—A mixture of 7.3 g. (0.051 mole) of 2-chloro-3,5-dimethylpyrazine[7] and 73 ml. of water containing 14.6 g. (0.26 mole) of potassium hydroxide was heated under reflux for 59 hr. and worked up as described. After two recrystallizations from absolute ethanol, 1.9 g. (30%) of pale yellow crystals, m.p. 149.5–152°, was obtained. Karmas and Spoerri[21] give m.p. 146–147°.

3-Ethoxypyrazine 1-Oxide. A. From 3-Chloropyrazine 1-Oxide.—To a warm solution of sodium ethoxide [prepared from 1.38 g. (0.06 g.-atom) of sodium in 30 ml. of absolute ethanol] a solution of 3.9 g. (0.03 mole) of 3-chloropyrazine 1-oxide[7] in 30 ml. of absolute ethanol was added in several portions, and the suspension was heated under reflux for 15 min. At this time a probe sample showed an absorption at 217, 261, and 307 mμ, but the heating was continued for another hour.

The suspension was filtered, and the combined filtrate and hot absolute ethanol washings were concentrated to about 30 ml. The residue was diluted with an equal amount of water, and extracted with chloroform and ether. Removal of the solvent left 3.5 g. (83.3%) of a pale yellow oil, which soon solidified, m.p. 75–77°. Recrystallization from hexane raised the melting point to 76–77°. For analysis, a portion was sublimed *in vacuo*, m.p. 76–77°.

Anal. Calcd. for $C_6H_8N_2O_2$: C, 51.4; H, 5.74; N, 19.95. Found: C, 51.58; H, 5.93; N, 20.10.

B. From 2-Ethoxypyrazine.—2-Ethoxypyrazine, b.p. 90–92° (90 mm.), $n^{26}D$ 1.4960–1.4962, was prepared in 77% yield by the Erickson and Spoerri[9] procedure. They give b.p. 72–73° (30 mm.), $n^{26}D$ 1.4960.

To 14.0 g. (0.11 mole) of 2-ethoxypyrazine in 30 ml. of glacial acetic acid, 25 ml. of 30% hydrogen peroxide was added, and the solution was heated on a steam bath under a reflux condenser for 20 hr. The solution was concentrated to 1/4 volume in a flash evaporator, diluted with an equal quantity of water, and reconcentrated. This was repeated and taken to dryness, leaving a pale yellow crystalline mass, which melted mostly at 68–72° with a small remainder that melted at about 180°.

The residue was extracted with boiling hexane, which on partial concentration and cooling gave 7.1 g. (45%) of 3-ethoxypyrazine 1-oxide, m.p. 76–76.5°. Mixture melting point with material prepared under A showed no depression.

The remaining residue recrystallized from methanol gave 0.6 g. of 3-ethoxypyrazine 1,4-dioxide, m.p. 180–180.5°.

Anal. Calcd. for $C_6H_8N_2O_3$: C, 46.2; H, 5.1; N, 17.9. Found: C, 46.15; H, 5.26; N, 18.1.

2-Ethoxy-3-methylpyrazine.—One mole (128.6 g.) of 2-chloro-3-methylpyrazine, 250 ml. of 45% potassium hydroxide, and 200 ml. of 95% ethanol was heated under reflux with stirring for a total of 16 hr., and the layers were separated. The lower portion was neutralized with concentrated hydrochloric acid, extracted with chloroform, which was washed with water and dried ($MgSO_4$). The upper layer, to which 100 ml. of ether was added and dried over Drierite, was combined with the chloroform extract. The solvent was stripped at atmospheric pressure, and the residue was distilled. A total of 119.1 g. (86.3%) was collected, b.p. 83–88° (38–40 mm.), $n^{25}D$ 1.4934–1.4938. Hirshberg and Spoerri give b.p. 88–90° (40 mm.), $n^{26}D$ 1.4938.[22]

3-Ethoxy-2-methylpyrazine 1-Oxide. A.—A solution of 2-ethoxy-3-methylpyrazine, 34.5 g. (0.25 mole) in 70 ml. of glacial acetic acid was heated with 50 ml. of 30% hydrogen peroxide for a total of 24 hr. at 65–75°, and worked up as above. On cooling and shaking, a colorless crystalline mass settled out, which on collection afforded 24.7 g., m.p. 113–120°. Neutralization of the mother liquor with ammonia yielded an additional 7.0 g.; total yield, 31.7 g. (82.5%). The air-dried material was recrystallized from 95% ethanol to give 29.3 g. of product, m.p. 121–122.5°. For analysis, a small portion was sublimed, 120° (15 mm.), m.p. 121–122°.

Anal. Calcd. for $C_7H_{10}N_2O_2$: C, 54.53; H, 6.54; N, 18.17. Found: C, 54.75; H, 6.80; N, 18.04.

B.—A mixture of 13.8 g. (0.095 mole) of crude 3-chloro-2-methylpyrazine 1-oxide[7] (m.p. 53–72°) and 70 ml. of ethanol containing 12.5 g. of potassium hydroxide (0.19 mole) was heated under reflux for 7 hr., the hot mixture was filtered, and the precipitate was washed with boiling absolute ethanol. The filtrate and washings were concentrated under reduced pressure, and the material which precipitated was brought into solution with water. The solution was extracted with chloroform; the extract was washed with water and dried. Removal of the solvent left 3.7 g. of product, m.p. 116–121.5°. This was recrystallized from water to give 3.0 g., m.p. 118.5–121.5°. A mixture melting point with material produced in A caused no depression, and their infrared spectra were identical.

2-Ethoxy-3-pyrazylmethyl Acetate.—A solution of 8.7 g. (0.056 mole) of 3-ethoxy-2-methylpyrazine 1-oxide in 9.7 ml. of glacial acetic acid was heated under reflux with 16 ml. of acetic anhydride for 50 min. A probe sample taken at this time had an absorption at 215 and 295 mμ, indicating loss of the N-oxide.[16] Low-boiling materials were removed at 25 mm., and the residue was distilled giving a total of 8.8 g. (80%), b.p. 85–88° (0.5–0.85 mm.). This was redistilled to give 7.8 g. (71%), b.p. 100–102° (0.4 mm.), $n^{24}D$ 1.4979.

(17) Boiling points are uncorrected. Melting points were determined on a heated metal block and are uncorrected.

(18) Microanalyses were by Schwarzkopf Microanalytical Laboratory, Woodside 77, N. Y.

(19) A probe sample taken at 15 min. showed a shift in the shoulder at 305 mμ to a peak at 310–315 mμ which was fully developed in 2 hr.

(20) The authors are indebted to the Wyandotte Chemical Corp., Wyandotte, Mich., for a generous quantity of this compound. Redistilled material, b.p. 87° (32 mm.), $n^{25}D$ 1.5237, was used.

(21) G. Karmas and P. E. Spoerri, *J. Am. Chem. Soc.*, **74**, 1580 (1952). The infrared absorption spectra of a sample kindly furnished by Dr. George Karmas, Ortho Research Foundation, and the material prepared in this laboratory were identical.

(22) A. Hirshberg and P. E. Spoerri[4] obtained this compound in 33% yield by the conventional alkoxide synthesis. The procedure described above is based on the facile etherification of chloropyrazines when heated with alcoholic potassium hydroxide reported by Gainer, *et al.*[5]

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA

Pyrazine	Solvent[a]	λ_{max}, mμ	log ε
2-Chloro-3,6-dimethyl-	A	214, 281, 295 (sh)	4.90, 3.89, 3.74
2-Hydroxy-3,5-dimethyl-	A	228, 327	4.06, 3.92
2-Hydroxy-3,6-dimethyl-[b]	B	223, 321	3.97, 3.95
3-Chloro-2,5-dimethyl-, 1-oxide	B	221, 267, 308, 312	4.21, 4.04, 3.74, 3.72
3-Hydroxy-2-methyl-, 1-oxide	B	219, 266, 315	4.23, 3.79, 3.72
3-Hydroxy-2,5-dimethyl-, 1-oxide[c]	B	225, 272, 328	4.18, 3.79, 3.74
2-Ethoxy-	A	211.5, 279, 295 (sh)	3.93, 3.61
3-Ethoxy-, 1-oxide	B	217.5, 261, 305	4.31, 4.05, 3.68
2-Ethoxy-, 1,4-dioxide	B	212, 234, 256, 296, 337.5	4.05, 4.30, 3.74, 4.31, 4.08
2-Ethoxy-3-methyl-	A	214, 277 (sh), 292.5	3.94, ..., 3.75
2-Methoxy-3,6-dimethyl-	A	214, 295	3.93, 3.87
2-Ethoxy-3,6-dimethyl-[d]	A	216, 297	3.97, 3.89
3-Ethoxy-2-methyl-, 1-oxide	A	217, 264, 302.5, 306	4.22, 3.97, 3.54
3-Ethoxy-2,5-dimethyl-, 1-oxide	A	220, 262, 309	4.34, 4.01, 3.76
2-Ethoxy-3-pyrazylmethyl acetate	A	216, 294	4.04, 3.88
2-Ethoxy-3-pyrazinemethanol	B	215, 294	4.11, 3.90

[a] A = Spectro Grade methanol, B = water. [b] G. T. Newbold and F. S. Spring [*J. Chem. Soc.*, 373 (1947)] give λ_{max}^{EtOH} 227 mμ (log ε 3.88), 323 (3.56). [c] Ref. 10 gives λ_{max}^{EtOH} 225 mμ (log ε 4.18), 272 (3.79), 327 (3.68). [d] Ref. 10 gives λ_{max}^{EtOH} 298 mμ (log ε 3.92).

Anal. Calcd. for $C_9H_{12}N_2O_3$: C, 55.09; H, 6.18; N, 14.30. Found: C, 54.59; H, 6.39; N, 16.14.[23]

2-Ethoxy-3-pyrazinemethanol.—A mixture of 6.2 g. (0.032 mole) of 2-ethoxy-3-pyrazylmethyl acetate and 32 ml. of 10% sodium hydroxide was allowed to stand over a weekend at room temperature, although the phases became homogeneous within 2 hr. The solution was extracted with ether; the extract was washed with water and dried. Removal of solvent and sublimation of the residue gave 2.7 g. (55%) of product, m.p. 43°. For analysis, the product was sublimed several times, which raised the melting point to 46–47°.

Anal. Calcd. for $C_7H_{10}N_2O_2$: C, 54.5; H, 6.5; N, 18.2. Found: C, 54.84; H, 6.57; N, 17.88.

3-Ethoxy-2,5-dimethylpyrazine 1-Oxide.—Heating under reflux a mixture of 3.2 g. (0.02 mole) of 3-chloro-2,5-dimethylpyrazine 1-oxide and 17.5 ml. of absolute ethanol containing 3.46 g. of potassium hydroxide for 4 hr. and working up the reaction as described above yielded 1.52 g. (45%) of crude product, m.p. 93–96°. One recrystallization from petroleum ether (b.p. 30–60°) brought the melting point to 96–97°; Baxter and associates[10] give m.p. 92–94°.

2-Ethoxy-3,6-dimethylpyrazine.—A solution of 8.6 g. (0.06 mole) of 2-chloro-3,6-dimethylpyrazine in 50 ml. of absolute ethanol containing 10.1 g. (0.18 mole) of KOH was heated for 16 hr. in a stainless steel bomb at 120°. Half the solvent was removed at reduced pressure, an equal quantity of water was added, and the product was extracted into ether. Removal of the solvent after drying and distillation of the residue afforded 6.1 g. (66.3%) of product, b.p. 96–98° (31 mm.), $n^{25}D$ 1.4920.

2-Methoxy-3,6-dimethylpyrazine.—Heating a solution of 8.6 g. (0.06 mole) of 2-chloro-3,6-dimethylpyrazine in 60 ml. of absolute methanol containing 10.1 g. of potassium hydroxide for 2 hr. under reflux and working up the mixture as described gave a total of 5.4 g. (65%) of methyl ether, b.p. 86° (22 mm.), $n^{25}D$ 1.5026.

Absorption Spectra.—Ultraviolet absorption spectra were determined on a Bausch and Lomb Spectronic 505 recording spectrophotometer, calibrated with both mercury emission spectrum and holmium oxide. Infrared absorption spectra were determined on a Perkin-Elmer Model 21 recording spectrophotometer calibrated against a polystyrene film. The ultraviolet absorption spectra are given in Table I.

(23) This analysis, as well as the abrupt change in the boiling point on redistillation, showing the presence of material with a higher nitrogen content, indicates some deacetylation had occurred. The ease of hydrolysis of pyrazylmethyl acetates has been reported.[16]

Terpenes. XIV.[1] The Reaction of Pulegone with Lead Tetraacetate

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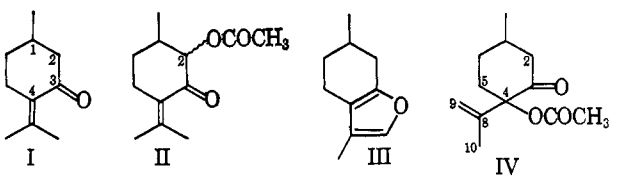
Pulegone (I) has been found to react with lead tetraacetate in benzene to yield predominantly *cis*- and *trans*-4-acetoxyisopulegone (IV) rather than 2-acetoxypulegone (II), the product of the reaction of pulegone with mercuric acetate.[3] Pyrolysis of IV gave menthofuran (III) in addition to the expected diene XII. The mechanisms involved in the formation of IV and its subsequent conversion to III are discussed.

In a recent communication[3] we reported on the formation of *cis*- and *trans*-2-acetoxypulegone (II) in the reaction of pulegone (I) with mercuric acetate in acetic acid and the surprising pyrolysis of II to yield optically pure menthofuran (III). We have now investigated the reaction of pulegone with lead tetraacetate in benzene and find that under these conditions II is produced



I II III IV

to only a minor extent and the major product is instead a mixture of *cis*- and *trans*-4-acetoxyisopulegone (IV).

Gas–liquid chromatography (g.l.c.) immediately showed that the product (IV) of the reaction of pulegone with lead tetraacetate had a lower retention time than

(1) Terpenes XIII: L. H. Zalkow and D. R. Brannon, *J. Chem. Soc.*, in press.

(2) National Institutes of Health Fellow, 1962–1964.

(3) L. H. Zalkow, J. W. Ellis, and M. R. Brennan, *J. Org. Chem.*, **28**, 1705 (1963).