Syntheses and Reactions of Some 2,3-Disubstituted Pyrazine Monoxides

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The reactions of 2,3-dimethyl- (**4**), 2,3-diphenyl- (**6**), and 2-methyl-3-phenyl-pyrazine monoxides (**8** and **9**) with phosphoryl chloride and acetic anhydride resulted in giving monochloro- and monacetoxy-pyrazines in almost all cases. However, the reaction of **6** with acetic anhydride afforded exceptionally a diacetoxydihydropyrazine. These products were converted further to hydroxy or dichloro derivatives.

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In our previous publications (1-3), we described the syntheses and reactions of some 2,5-di-substituted pyrazine monoxides, the transformation of the 2,5-disubstituted pyrazines to the corresponding 2,5-diketopiperazines, and the syntheses of 2-hydroxypyrazine 1-oxides. In relation to these works, this paper deals with the syntheses and reactions of the monoxides of 2,3-dimethylpyrazine (**1**) (4), 2,3-diphenylpyrazine (**2**) (5), and 2-methyl-3-phenylpyrazine (**3**) (6).

Although the preparation of 2,3-disubstituted pyrazines using α-haloketones, *N*-phenyltrifluoromethane sulfonamide, and ethylenediamine was recently reported by Bergeron and Hoffman (6), the preparation of the parent pyrazines was performed by the common condensation of the 1,2-dicarbonyl compounds with ethylenediamine and the successive dehydrogenation in this work. The dehydrogenation condition was different, however, between the cases of **1** and **2**, and **3**. In the former cases, the dihydro compounds were heated in the presence of sodium hydroxide in an ethanol solution, and in the latter with sulfur.

In order to prepare the *N*-oxides, **1** was heated with peracetic acid in acetic acid, and on the other hand, **2** and **3** were treated with permaleic acid in chloroform or methylene chloride. In all cases, monoxides and dioxides were obtained.

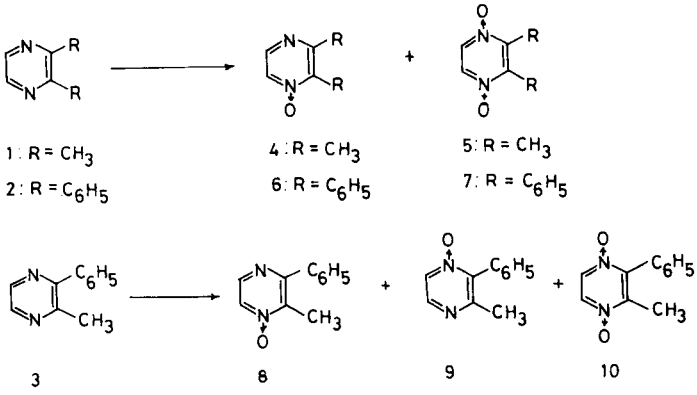


Chart 1

The pmr spectrum of 2,3-dimethylpyrazine 1-oxide (**4**) (7), taken in deuterium oxide, showed two singlets due to the methyl protons at 2.46 and 2.56 ppm, and two doublets due to the ring protons at 8.23 and 8.37 ppm. Among these signals, the one at 2.46 and 8.23 ppm would be ascribed to the methyl protons at C-2 and the ring protons at C-6, respectively. This assumption was supported by deuteration experiment in 1% sodium deuteroxide-deuterium oxide solution on pmr measurements, in which the signal at 2.46 ppm disappeared in 20 minutes at room temperature and a merely brief decrease of the signal at 2.56 ppm was observed. On the other hand, the signals due to the ring protons did not decrease under this condition and only the signal at 8.23 ppm disappeared finally in 60 minutes, when heated at 63°.

Among two monoxides derived from **3**, the one obtained in a higher yield is assumed to be the 1-oxide (**8**). The assumption was confirmed by the following deuteration experiment on pmr measurements. Though the solutions of the monoxides (**8** and **9**) in a mixture of deuterium oxide-methanol-d_4 (1:3) were heated, respectively, at 80-90° for 48 hours, any signals due to the methyl protons were not observed to be deuterated. However, by addition of a small amount of sodium deuteroxide (8), the methyl signal of **8** disappeared already in 10 minutes at 21°, while the deuteration of the methyl group of **9** was completed barely in 6 hours under the same conditions.

The mass spectra of **8** and **9** are of interest. In both cases, the M^+-17 (m/e 169) peak constitutes the base peak. The spectrum of **8** exhibits a small M^+-1 peak (4.3%), while a comparatively strong M^+-1 (60.0%) peak was observed in the spectrum of **9**. Probably a one-step elimination of the OH radical occurred in the spectrum of **8** to constitute the M^+-17 peak, and in the case of **9**, the M^+-17 peak was formed by deoxygenation *via* the M^+-1 ion (9,10).

The methyl signals of **8** and **9** appeared in a higher field (2.55 and 2.42 ppm) than that (2.65 ppm) of the parent compound (**3**) in deuteriochloroform. This high field shift of the methyl group of **8** can be explained by a back dona-

tion effect of an N-O group (11). On the other hand, the shift in **9** may be explained as follows. Since the phenyl group lies between the N-O and methyl groups, it can not be situated probably on a plane with the pyrazine ring. As a result, an anisotropy effect of the phenyl group would cause a high field shift of the methyl group. The ring protons of **8** and **9** appeared respectively as two doublets. The one, observed in a higher field, would be ascribed to the protons adjacent to the N-O group.

The monoxides were heated with phosphoryl chloride under the same conditions as previously reported (1,2), to afford monochloropyrazines. Differing from the reaction of 2,5-dimethylpyrazine 1-oxide (12), in which only the ring chlorination occurred, **4** gave interestingly two products, 5-chloro-2,3-dimethylpyrazine (**11**) (13) and 2-chloromethyl-3-methylpyrazine (**12**) (14), in a 1:2.5 ratio.

2,3-Diphenylpyrazine 1-oxide (**6**) (15) was also treated with phosphoryl chloride to afford a sole product, 5-chloro-2,3-diphenylpyrazine (**13**) (13). On the other hand, the reaction of **8** and **9** gave more complicated results. The former afforded three products, 6-chloro-2-methyl-3-phenylpyrazine (**14**), 5-chloro-2-methyl-3-phenylpyrazine (**15**), and 2-chloromethyl-3-phenylpyrazine (**16**) in a 3:1:12 ratio, and two products, **15** and **16**, were obtained in a 1:17 ratio by the reaction of the latter. In the reaction of 2,3-disubstituted pyrazine monoxides carrying an alkyl group at the α-position of the N-O group, chlorination seemed to take place preferentially on the alkyl group.

In the course of elucidation of the structures of **14** and **15**, *N*-oxidation of these compounds were achieved respectively to afford a monoxide and a dioxide. The monoxides, 6-chloro-2-methyl-3-phenylpyrazine 4-oxide (**17**) and 5-chloro-2-methyl-3-phenylpyrazine 1-oxide (**19**), behaved in a similar fashion respectively with **9** and **8** in the mass spectra. The strong M^+-17 peaks (89.3% in **17** and 100% in **19**) are observed in both spectra. However, there is a

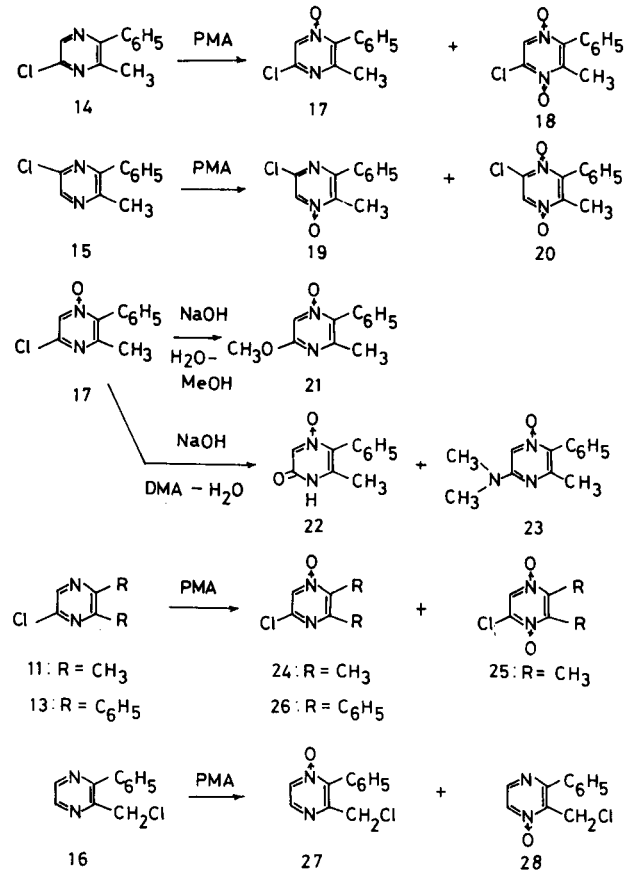


Chart 3

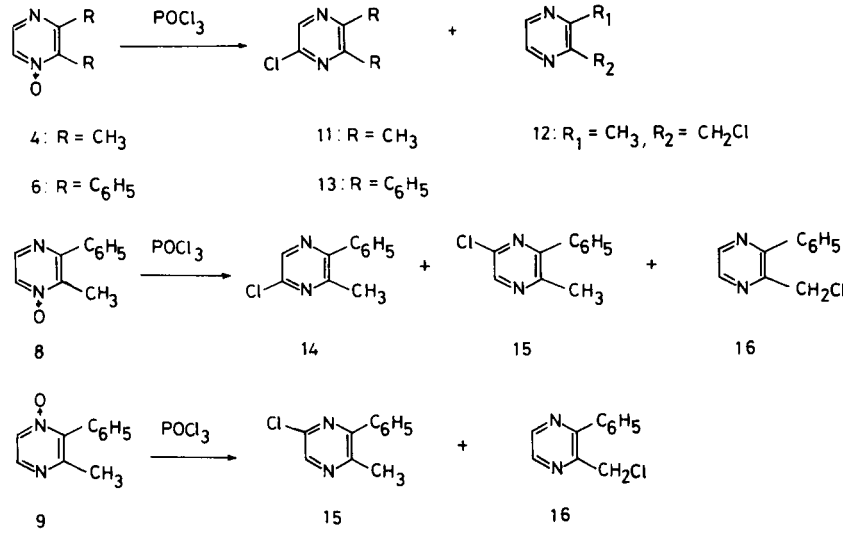


Chart 2

difference in intensity of the M^+-1 peak between the spectra of **17** (42.9%) and **19** (2.6%). This appearance would make clear the relation between the positions of the phenyl and N-O groups.

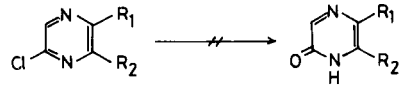
The alkaline hydrolysis of **17** in aqueous methanol resulted in yielding a methoxyl compound (**21**), and the one in a mixture of *N,N*-dimethylacetamide and water afforded a hydroxyl compound (**22**) together with a dimethylamino derivative (**23**). Since **22** indicated no coloration with ferric chloride owing to a hydroxamic acid structure, any hydroxyl group seems to be not existent at the neighboring position with the N-O group. The structure of **17** could be consequently ascertained.

N-Oxidation of **11**, **13**, and **16** was also performed by peracetic acid or permaleic acid. In the case of **11** and **13**, the *N*-oxidation would take place at the nitrogen, not adjacent to the chlorine atom, to afford 6-chloro-2,3-dimethylpyrazine 4-oxide (**24**) and 6-chloro-2,3-diphenylpyrazine 4-oxide (**26**), respectively. Also a dioxide (**25**) was obtained from **11**. The structures of 2-chloromethyl-3-phenylpyrazine 4-oxide (**27**) and 2-chloromethyl-3-phenylpyrazine 1-oxide (**28**), derived from **16**, were determined on the basis of the mass spectral data. Namely, an M^+-1 peak was observed only in the spectrum of **27**. This evidence made clear the relation between the positions of the phenyl and N-O groups.

The *N*-oxides, **24**, **26**, **17**, and **19** were also treated with phosphoryl chloride. In the reaction of **19**, chlorination took place interestingly only on the pyrazine ring, although a methyl group is existent at an α-position of an *N*-oxide group. On the other hand, **24** yielded 5,6-dichloro-2,3-dimethylpyrazine (**29**) (16) and 6-chloro-3-chloromethyl-2-methylpyrazine (**30**). The position of the secondly incorporated chlorine atom in **30** could not be determined. However, it may be presumed that the chlorination occurred at the neighboring methyl group of the N-O group.

In order to prepare hydroxypyrazines, chloropyrazines were submitted to hydrolysis in hydrochloric acid. Although **11** was converted to 2,3-dimethyl-5-hydroxypyrazine (**33**) (13) in a poor yield, **13**, **14**, and **15** gave no crystalline products.

11 33



13: $R_1 = R_2 = C_6H_5$ 34: $R_1 = R_2 = C_6H_5$

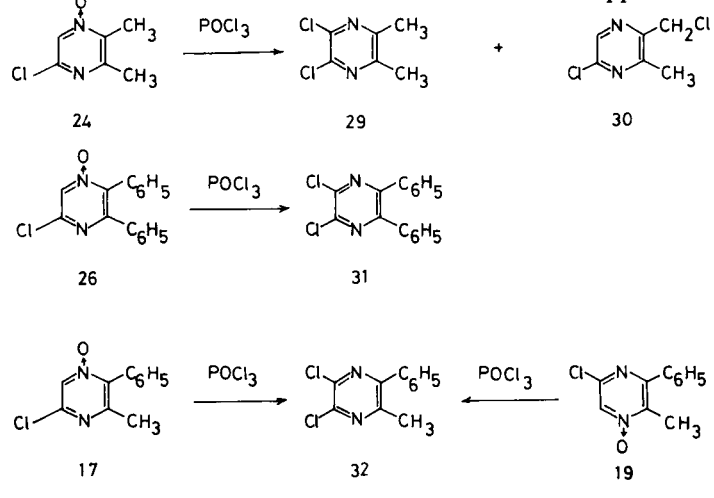
14: $R_1 = C_6H_5$, $R_2 = CH_3$ 35: $R_1 = C_6H_5$, $R_2 = CH_3$

15: $R_1 = CH_3$, $R_2 = C_6H_5$ 36: $R_1 = CH_3$, $R_2 = C_6H_5$

Chart 5

The reactions of the monoxides, **4**, **6**, **8**, and **9** with acetic anhydride were also investigated. In a similar manner as reported (1,2), **4** was treated with acetic anhydride and the products, whose pmr spectrum indicated no signal according to the acetoxyl group on the pyrazine ring, were purified by column chromatography to give solely 2-acetoxymethyl-3-methylpyrazine (**37**).

The reaction of **6** gave interestingly a crystalline substance (**38**) as a main product, possessing two acetoxyl groups. The uv spectrum of the product supports that the electronic situations of **38** resemble those of 5,6-diphenyl-2,3-dihydropyrazine (17) (Figure 1). In the pmr spectrum of **38**, two singlets appeared at 2.24 (6H) and 6.30 (2H) ppm could be ascribed respectively to the methyl and dihydropyrazine ring protons. The ^{13}C-nmr spectrum of **38** lends also some supports to this postulation. The probable



24 29 30

26 31

17 32 19

Chart 4

mechanism of the formation of **38** is proposed in Chart 6. Although the literature contains several references to the pmr spectra of 2,3-diphenyl-2,3-dihydropyrazines (18), the stereochemical relation between two acetoxyl groups in **38** could not be made clear on the basis of the pmr spectral data.

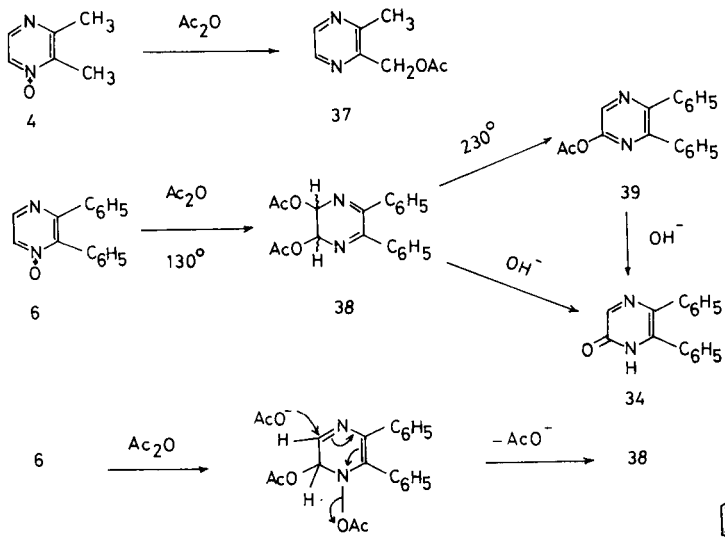


Chart 6

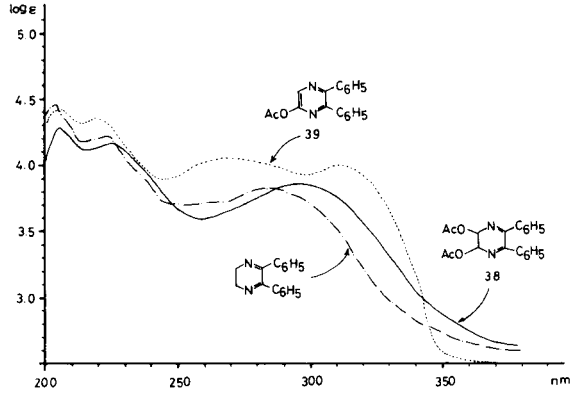


Figure 1

The heating of **38** at 230° afforded 5-acetoxy-2,3-diphenylpyrazine (**39**), eliminating acetic acid. By an alkaline treatment of **38** and **39**, 2,3-diphenyl-5-hydroxypyrazine (**34**) was obtained.

Differing from the two *N*-oxides described above, **8** and **9** gave respectively two products, which were converted to hydroxypyrazines, 5-hydroxy-2-methyl-3-phenylpyrazine (**36**) and 2-hydroxymethyl-3-phenylpyrazine (**40**), by an alkaline hydrolysis. In order to determine the structure, **36** was transformed to a chloropyrazine by a treatment with a mixture of phosphoryl chloride and phosphorus pentachloride, and the product was identical with **15**. Consequently, the acetoxylation of **8** and **9** occurred both on the pyrazine ring and side chain.

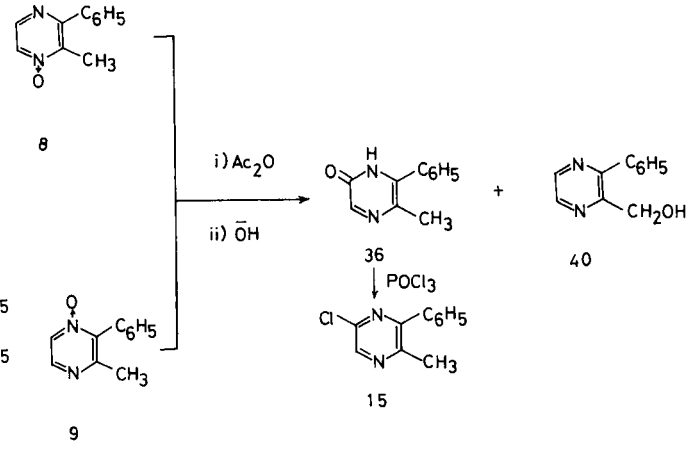


Chart 7

As shown in Chart 8, the modification of the side chain of **3** was attempted. The conversion of **16** to 2-cyanomethyl-3-phenylpyrazine (**41**) underwent by a treatment with potassium cyanide. However, the hydrolysis of **41** resulted in affording of **3**.

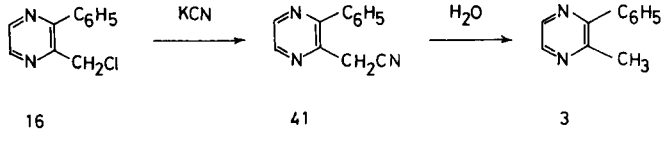


Chart 8

EXPERIMENTAL

Melting points were recorded on a Yanagimoto micro melting point apparatus and are uncorrected. Boiling points are also uncorrected. Uv spectra were recorded on a Hitachi 557 spectrophotometer, ir spectra on a Shimadzu IR-400 spectrometer. Pmr spectra were taken on a JEOL JNM-PS-100 and ^{13}C-nmr spectra on a JEOL FX-100 instrument with tetramethylsilane as an internal standard. Mass spectra were obtained on a Hitachi RMU-7L spectrometer.

1) 2,3-Diphenylpyrazine (**2**).

Ethylenediamine (17.2 g, 0.29 moles) was added slowly to a solution of benzil (50 g, 0.24 moles), dissolved in ethanol (250 ml), at room temperature under stirring and then the solution was refluxed for 0.5 hours. After cooling, yellow precipitates were collected by suction and recrystallized from ethanol to give 48.3 g (87%) of 2,3-dihydro-5,6-diphenylpyrazine as yellowish leaflets, mp 166-167° (lit 17, mp 160-161°).

A mixture of the 2,3-dihydropyrazine (23.4 g, 0.1 moles) and sulfur (6.4 g, 0.2 moles) was heated at 140° on an oil bath for 0.5 hours. The reaction mixture was chromatographed on silica gel (Wakogel C-200, 100 g), using hexane and benzene as developer. The fractions eluted with benzene gave 19.0 g (82%) of **2** as yellow prisms, mp 116-117° (from methanol) (lit 5, mp 112-115°).

2) 2-Methyl-3-phenylpyrazine (**3**).

Ethylenediamine (12.7 g, 0.21 moles) was added to a solution of acetylbenzoyl (26.1 g, 0.18 moles), dissolved in ethanol (250 ml), in 0.5 hours under stirring. The reaction mixture was allowed to stand at room temperature for 1 hour and after adding potassium hydroxide (10.5 g, 0.19 moles), refluxed for 5 hours. After removal of the solvent *in vacuo*, the

residue was extracted with ether. The ether layer was usually worked up to give a brownish oil, which was purified by distillation to yield **3** (14.7 g, 49%) as a pale yellow oil, bp 140°/7 torr (lit 6).

3) Oxidation of 2,3-Dimethylpyrazine (**1**).

A solution of **1** (33 g, 0.305 moles) and 30% hydrogen peroxide (240 ml) in acetic acid (120 ml) was heated at 50-60° for 16 hours. The solvent was removed by distillation *in vacuo*. Water was added and distillation was repeated. The residue was made alkaline with potassium carbonate and extracted with chloroform. The chloroform layer was worked up usually to give a pale yellow solid, which was triturated with hexane. The insoluble solid was collected by suction and recrystallized from 2-propanol to give **5** (18.1 g, 38%) as colorless prisms, mp 211°. The filtrate was evaporated and the residue was recrystallized from cyclohexane to yield **4** (17.6 g, 46%) as colorless prisms, mp 83-83.5°.

Compound **4**.

This compound had the following physical constants: uv (95% ethanol): λ max 223 (log ε = 4.17), 267 (4.00) nm; pmr (deuteriochloroform): δ 2.48 (3H, s, CH_3), 2.59 (3H, s, CH_3), 8.02 (1H, d, pyrazine H, J = 4 Hz), 8.20 (1H, d, pyrazine H, J = 4 Hz) ppm; pmr (deuterium oxide): (lit 19) δ 2.46 (3H, s, CH_3), 2.56 (3H, s, CH_3), 8,23 (1H, d, pyrazine H, J = 4 Hz), 8.37 (1H, d, pyrazine H, J = 4 Hz) ppm; ms: m/e 124 (M^+), 107 (M^+-OH).

Anal. Calcd. for $C_6H_8N_2O$: C, 58.05; H, 6.50; N, 22.57. Found: C, 58.23; H, 6.36; N, 22.76.

Compound **5**.

This compound had the following physical properties: uv (95% ethanol): λ max 232 (log ε = 4.24), 309 (4.27) nm; pmr (deuteriochloroform): δ 2.60 (6H, s, CH_3), 8.04 (2H, s, pyrazine H) ppm; ms: m/e 140 (M^+), 123 (M^+-OH).

Anal. Calcd. for $C_6H_8N_2O_2$: C, 51.42; H, 5.72; N, 19.99. Found: C, 51.72; H, 5.84; N, 20.04.

4) Oxidation of 2,3-Diphenylpyrazine (**2**).

A solution of **2** (6.97 g, 30 mmoles), 90% hydrogen peroxide (1.60 g, 60 mmoles), and maleic anhydride (4.55 g, 52.5 mmoles) in chloroform (150 ml) was refluxed for 2 hours and washed with water, 10% potassium bicarbonate, and water, successively. The usual work up of the chloroform layer gave a pale yellow solid (8.47 g), which was chromatrographed on silica gel (Wakogel C-200, 170 g), using chloroform and ethyl acetate as eluents. The fractions eluted with chloroform gave **6** (5.47 g, 73.4%) as colorless prisms, mp 184° (from cyclohexane) (lit 15, mp 171-172°). Further elution with a mixture of chloroform and ethyl acetate (9:1) yielded **7** (1.79 g, 23%) as colorless prisms, mp 258-259° dec (from 2-propanol) (lit 15, mp 262° dec).

5) Oxidation of 2-Methyl-3-phenylpyrazine (**3**).

A solution of **3** (17.0 g, 0.1 moles), 90% hydrogen peroxide (4.53 g, 0.12 moles), and maleic anhydride (14.71 g, 0.15 moles) in methylene chloride (300 ml) was allowed to stand for 2 days at room temperature and worked up as described in 4) to give a colorless solid (20.57 g), which was chromatographed on silica gel (Wakogel C-200, 400 g), eluting with chloroform, ethyl acetate, and methanol, successively. The ethyl acetate fractions gave **8** (11.47 g, 62%) as colorless prisms, mp 123-124° (from cyclohexane). The fractions eluted with a mixture of ethyl acetate and methanol (8:2) gave **9** (1.64 g, 9%) as colorless prisms, mp 113-115° (from hexane). Further elution with a mixture of ethyl acetate and methanol (6.5:3.5) afforded **10** (2.83 g, 14%) as colorless prisms, mp 203-204° (from 2-propanol).

Compound **8**.

This compound had the following physical constants: uv (95% ethanol): λ max 221 (log ε = 4.25), 253.5 (4.17), 309 (3.59) nm; pmr (deuteriochloroform): δ 2.55 (3H, s, CH_3), 7.19-7.68 (5H, m, benzene H), 8.15 (1H, d, pyrazine H, J = 4 Hz), 8.84 (1H, d, pyrazine H, J = 4 Hz) ppm; ms: m/e 186 (M^+, 31.5%), 185 (M^+—OH, 100%), 103 ($C_6H_5CN^+$, 22.8%).

Anal. Calcd. for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.05. Found: C, 70.80; H, 5.20; N, 15.00.

Compound **9**.

This compound had the following physical constants: uv (95% ethanol): λ max 226.5 (log ε = 4.26), 243.5 (4.13), 269-271 (4.05) nm; pmr (deuteriochloroform): δ 2.42 (3H, s, CH_3), 7.20-7.58 (5H, m, benzene H), 8.13 (1H, d, pyrazine H, J = 4 Hz), 8.33 (1H, d, pyrazine H, J = 4 Hz) ppm; ms: m/e 186 (M^+, 57.5%), 185 (M^+—H, 60.0%), 169 (M^+—OH, 100%), 103 ($C_6H_5CN^+$, 52.5%).

Anal. Calcd. for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.05. Found: C, 70.95; H, 5.39; N, 15.06.

Compound **10**.

This compound had the following physical characteristics: uv (95% ethanol): λ max 235.5 (log ε = 4.09), 250.5 (3.89), 272 (3.78), 313.5 (4.18) nm; pmr (deuteriochloroform): δ 2.30 (3H, s, CH_3), 7.18-7.60 (5H, m, benzene H), 8.10 (2H, s, pyrazine H) ppm; ms: m/e 202 (M^+).

Anal. Calcd. for $C_{11}H_{10}N_2O_2$: C, 65.33; H, 4.98; N, 13.86. Found: C, 65.58; H, 4.96; N, 14.14.

6) Reaction of 2,3-Dimethylpyrazine 1-Oxide (**4**) with Phosphoryl Chloride.

A mixture of **4** (8.68 g, 70 mmoles) and phosphoryl chloride (52.5 ml) was refluxed for 30 minutes, poured into ice water, made alkaline with potassium carbonate and extracted with methylene chloride. The brown oily product (8.06 g) was chromatographed on Florisil (160 g), eluting with a mixture of hexane and ether. The fractions eluted with a mixture of 95:5 ratio gave **11** (1.69 g, 17%) as a colorless oil, bp 81°/18 torr (lit 13, bp 86-88°/20 torr).

Further elution with the mixtures (9:1 and 8:1) gave **12** (4.01 g, 41%) as a colorless oil, bp 88°/17 torr; uv (95% ethanol): λ max 270 (log ε = 3.60), 274 (3.58, shoulder) nm; pmr (deuteriochloroform): δ 2.70 (3H, s, CH_3), 4.72 (2H, s, CH_2), 8.38 (1H, d, pyrazine H, J = 2 Hz), 8.46 (1H, d, pyrazine H, J = 2 Hz) ppm; ms: m/e 142 (M^+).

Anal. Calcd. for $C_6H_7ClN_2$: C, 50.54; H, 4.95; N, 19.65. Found: C, 50.69; H, 4.72; N, 20.03.

7) Reaction of 2,3-Diphenylpyrazine 1-Oxide (**6**) with Phosphoryl Chloride.

A solution of **6** (2.48 g, 10 mmoles) in phosphoryl chloride (20 ml) was refluxed for 20 minutes, poured into ice water, and made alkaline with potassium carbonate. The pale yellow precipitates (2.28 g, 86%) were collected by suction and recrystallized from methanol to furnish colorless prisms, mp 126-128° (lit 13, mp 123-124°).

8) Reaction of 2-Methyl-3-phenylpyrazine 1-Oxide (**8**) with Phosphoryl Chloride.

A solution of **8** (9.30 g, 50 mmoles) in phosphoryl chloride (180 ml) was refluxed for 1 hour and worked up as described in 6) to give a brown oil (9 g), which was chromatographed on silica gel (Wakogel C-200, 180 g), eluting with hexane, ether, and chloroform, successively. The fractions eluted with a mixture of hexane and ether (10:1) gave **14** (1.57 g, 15%) as a colorless oil, bp 120°/5 torr. The fractions eluted with an 8:2 mixture gave **15** (0.50 g, 5%) as a colorless oil, bp 140-150°/2 torr (oil bath temperature). The chloroform fractions yielded **16** (6.00 g, 59%) as colorless needles, mp 91° (from hexane).

Compound **14**.

This compound had the following physical properties: uv (95% ethanol): λ max 236.5 (log ε = 4.08), 287.5 (3.95), 301.5 (3.95) nm; pmr (deuteriochloroform): δ 2.64 (3H, s, CH_3), 7.40-7.64 (5H, m, benzene H), 8.48 (1H, s, pyrazine H) ppm; ms: m/e 204 (M^+, 66.7%), 203 (M^+-H, 100%), 103 ($C_6H_5CN^+$, 87.9%).

Anal. Calcd. for $C_{11}H_9ClN_2$: C, 64.56; H, 4.43; N, 13.69. Found: C, 64.44; H, 4.29; N, 13.90.

Compound **15**.

This compound had the following physical characteristics: uv (95% ethanol): λ max 230-232 (log ε = 3.90), 288.5 (3.87), 303 (3.86) nm; pmr (deuteriochloroform): δ 2.64 (3H, s, CH_3), 7.40-7.65 (5H, m, benzene H), 8.44 (1H, s, pyrazine H) ppm; ms: m/e 204 (M^+, 55.7%), 203 (M^+-H, 100%), 103 ($C_6H_5CN^+$, 96.2%).

Anal. Calcd. for $C_{11}H_9ClN_2$: C, 64.56; H, 4.43; N, 13.69. Found: C, 64.30; H, 4.18; N, 13.58.

Compound **16**.

This compound had the following physical characteristics: uv (95% ethanol): λ max 240 (log ε = 3.96), 280 (3.85), 310 (3.25, shoulder) nm; pmr (deuteriochloroform): δ 4.70 (2H, s, CH_2), 7.45-7.60 (3H, m, benzene H), 7.60-7.80 (2H, m, benzene H), 8.60 (2H, d, pyrazine H, J = 2 Hz) ppm; ms: m/e 204 (M^+).

Anal. Calcd. for $C_{11}H_9ClN_2$: C, 64.56; H, 4.43; N, 13.69. Found: C, 64.38; H, 4.37; N, 13.93.

9) Reaction of 2-Methyl-3-phenylpyrazine 4-Oxide (**9**) with Phosphoryl Chloride.

A solution of **9** (1.23 g, 6.6 mmoles) in phosphoryl chloride (10 ml) was refluxed for 0.5 hours and worked up as described in 6), to give a brown solid (1.40 g), which was chromatographed on silica gel (Wakogel C-200, 30 g) and eluted with hexane containing an increasing amount of ether. The 10:1 fractions afforded **15** (407 mg, 30%) as a colorless oil, bp 140-145°/2 torr (oil bath temperature). Further elution with an 8:2 mixture yielded **16** (680 mg, 51%) as colorless needles, mp 90-91° (from hexane).

10) Oxidation of 6-Chloro-2-methyl-3-phenylpyrazine (**14**).

A solution of **14** (1.04 g, 5.1 mmoles), 90% hydrogen peroxide (0.38 g, 10 mmoles), maleic anhydride (0.98 g, 10 mmoles) in chloroform (30 ml) was allowed to stand at room temperature for 2 days, then refluxed for 2 hours, and worked up as described in 4) to give a colorless solid (1.00 g), which was chromatographed on silica gel (Wakogel C-200, 40 g), eluting with benzene, ether, and methanol, successively. From the fractions eluted with a mixture of benzene and ether (100:1), the starting material (0.32 g, 31%) was recovered. A 20:1 mixture eluted **17** (0.647 g, 57%) as colorless prisms, mp 87-88° (from hexane). The methanol fractions yielded **18** (0.01 g, 0.8%) as colorless prisms, mp 187-188° (from 2-propanol).

Compound **17**.

This compound had the following physical constants: uv (95% ethanol): λ max 236.5 (log ε = 4.30), 268 (4.10, shoulder), 313 (3.56, shoulder) nm; pmr (deuteriochloroform): δ 2.38 (3H, s, CH_3), 7.34-7.70 (5H, m, benzene H), 8.24 (1H, s, pyrazine H) ppm; ms: m/e 220 (M^+, 82.1%), 219 (M^+-H, 42.9%), 203 (M^+-OH, 89.3%), 103 ($C_6H_5CN^+$, 100%).

Anal. Calcd. for $C_{11}H_9ClN_2O$: C, 59.88; H, 4.11; N, 12.69. Found: C, 59.93; H, 4.09; N, 12.81.

Compound **18**.

This compound had the following physical constants: uv (95% ethanol): λ max 242 (log ε = 4.29), 255 (4.16, shoulder), 312.5 (4.30) nm; pmr (deuteriochloroform): δ 2.42 (3H, s, CH_3), 7.40-7.70 (5H, m, benzene H), 8.47 (1H, s, pyrazine H) ppm; ms: m/e 236 (M^+).

Anal. Calcd. for $C_{11}H_9ClN_2O_2$: C, 55.82; H, 3.83; N, 11.83. Found: C, 55.97; H, 3.68; N, 11.78.

11) Oxidation of 5-Chloro-2-methyl-3-phenylpyrazine (**15**).

A solution of **15** (408 mg, 2 mmoles), 90% hydrogen peroxide (304 mg, 8 mmoles), and maleic anhydride (980 mg, 10 mmoles) in chloroform (20 ml) was allowed to stand overnight at room temperature, then refluxed for 4 hours, and worked up as described in 4), to give a pale yellow oil (390 mg), which was chromatographed on silica gel (Wakogel C-200, 12 g), using benzene, ethyl acetate, and methanol as eluents. The fractions eluted with a mixture of benzene and ethyl acetate (8:2) gave **19** (287 mg, 65%) as colorless needles, mp 64-65° (from hexane). Further elution with a mixture of ethyl acetate and methanol (8:2) yielded **20** (44 mg, 9%) as pale yellow prisms, mp 188-190° dec (from 2-propanol).

Compound **19**.

This compound had the following physical characteristics: uv (95% ethanol): λ max 231 (log ε = 4.26), 255 (4.26), 320 (3.74) nm; pmr (deuteriochloroform): δ 2.48 (3H, s, CH_3), 7.44 (5H, s, benzene H), 8.16 (1H, s, pyrazine H) ppm; ms: m/e 220 (M^+, 36.8%), 219 (M^+-H, 2.6%), 203 (M^+-OH, 100%), 103 ($C_6H_5CN^+$, 21.0%).

Anal. Calcd. for $C_{11}H_9ClN_2O$: C, 59.88; H, 4.11; N, 12.69. Found: C, 59.62; H, 4.09; N, 12.48.

Compound **20**.

This compound had the following physical characteristics: uv (95% ethanol): λ max 242.5 (log ε = 4.27), 256 (4.11, shoulder), 311 (4.30) nm; pmr (deuteriochloroform): δ 2.30 (3H, s, CH_3), 7.20-7.40 (2H, m, benzene H), 7.40-7.60 (3H, m, benzene H), 8.32 (1H, s, pyrazine H) ppm; ms: m/e 236 (M^+).

Anal. Calcd. for $C_{11}H_9ClN_2O_2$: C, 55.82; H, 3.83; N, 11.83. Found: C, 55.62; H, 3.74; N, 11.62.

12) Hydrolysis of 6-Chloro-2-methyl-3-phenylpyrazine 4-Oxide (**17**).

a) A solution of **17** (51 mg, 0.23 mmoles) in a mixture of 1 ml of 10% potassium hydroxide and 3 ml of methanol was refluxed for 1 hour. The solvent was evaporated off *in vacuo* and the residue was extracted with chloroform. The chloroform layer was worked up usually to give **21** as pale yellow crystals (41 mg, 83%), which was recrystallized from hexane to furnish colorless needles, mp 96-97°; uv (95% ethanol): λ max 229 (log ε = 4.32), 265 (4.01), 311 (3.78) nm; pmr (deuteriochloroform): δ 2.27 (3H, s, CH_3), 3.98 (3H, s, OCH_3), 7.20-7.50 (5H, m, benzene H), 7.76 (1H, s, pyrazine H) ppm; ms: m/e 216 (M^+).

Anal. Calcd. for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.82; H, 5.56; N, 13.11.

b) A solution of **17** (97 mg, 0.46 mmoles) and potassium hydroxide (267 mg, 4.8 mmoles) in a mixture of *N,N*-dimethylacetamide and water (1:2, 3 ml) was refluxed for 4 hours. The reaction mixture was dried off *in vacuo*. The residue was triturated with water and extracted with methylene chloride. The organic layer was worked up usually to give a semi-solid (35 mg), which was chromatographed on silica gel (Waqkogel C-200, 2 g), eluting with methylene chloride and then recrystallized from hexane to give **23** (62 mg, 27%) as colorless needles, mp 133-134°. The water layer was acidified with hydrochloric acid and the precipitates (**22**) were collected by suction and recrystallized from methanol to furnish colorless needles (38 mg, 43%), mp 264-265° dec.

Compound **22**.

This compound had the following physical properties: uv (95% ethanol): λ max 235.5 (log ε = 4.33), 287.5 (3.74, shoulder), 348 (4.36) nm; ir (potassium bromide): 1700 cm^{-1} (C=O); pmr (dimethylsulfoxide-d_6): δ 2.00 (3H, s, CH_3), 7.20-7.50 (5H, m, benzene H), 7.51 (1H, s, pyrazine H) ppm; ms: m/e 202 (M^+).

Anal. Calcd. for $C_{11}H_{10}N_2O_2$: C, 65.34; H, 4.98; N, 13.85. Found: C, 64.53; H, 4.87; N, 14.01.

Compound **23**.

This compound had the following physical properties: uv (95% ethanol): λ max 259 (log ε = 4.55), 366 (3.82) nm; pmr (deuteriochloroform): δ 2.20 (3H, s, CH_3), 3.07 (6H, s, $N(CH_3)_2$), 7.25-7.44 (5H, m, benzene H), 7.60 (1H, s, pyrazine H) ppm; ms: m/e 229 (M^+).

Anal. Calcd. for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33. Found: C, 68.01; H, 6.43; N, 18.60.

13) Oxidation of 5-Chloro-2,3-dimethylpyrazine (**11**).

a) A solution of **11** (490 mg, 34.5 mmoles) and 30% hydrogen peroxide (5 ml) in acetic acid (2.5 ml) was heated at 56° for 16 hours and worked up as described in 3) to give a brown semi-solid (181 mg), which was purified by Florisil column chromatography (6 g), eluting with hexane and ether. The fractions eluted with a mixture of both eluents (9:1 and 8:2) gave **24** (96 mg, 18%) as colorless prisms (from hexane).

b) A solution of **11** (285 mg, 2 mmoles), 90% hydrogen peroxide (432

mg, 11.4 mmoles), and maleic anhydride (1.34 g, 13.7 mmoles) in chloroform (25 ml) was allowed to stand overnight at room temperature, then refluxed for 5 hours and worked up as described in 4) to give a semi-solid (260 mg), which was chromatographed on silica gel (Wakogel C-200, 12 g), eluting with methylene chloride. The firstly eluted fractions gave **24** (145 mg, 46%), which was recrystallized from hexane to furnish colorless prisms, mp 58.5°. The secondly eluted fractions afforded **25** (97 mg, 28%), which was recrystallized from a mixture of hexane and chloroform to furnish colorless needles, mp 166-167°.

Compound **24**.

This compound had the following physical properties: uv (95% ethanol): λ max 209 (log ε = 3.99), 233 (4.11), 270 (4.08) nm; pmr (deuteriochloroform): δ 2.44 (3H, s, CH_3), 2.57 (3H, s, CH_3) 8.10 (1H, s, pyrazine H) ppm; ms: m/e 158 (M^+), 141 (M^+-OH).

Anal. Calcd. for $C_6H_7ClN_2O_2$: C, 41.28; H, 4.04; N, 16.05. Found: C, 41.33; H, 4.04; N, 16.30.

14) Oxidation of 5-Chloro-2,3-diphenylpyrazine (**13**).

A solution of **13** (213 mg, 0.8 mmoles), 90% hydrogen peroxide (150 mg, 3.2 mmoles), and maleic anhydride (330 mg, 3.2 mmoles) in chloroform (15 ml) was allowed to stand at room temperature for 2 days, and worked up as described in 4) to give yellowish crystals (206 mg), which were purified by silica gel (Wakogel C-200, 6 g) column chromatography, using benzene and chloroform as eluents. The fractions eluted with benzene and a mixture of benzene and chloroform (1:1) gave **26** (162 mg, 72%) as a colorless solid, which was recrystallized from ethanol to furnish colorless needles, mp 123-124°; uv (95% ethanol): λ max 227.5 (log ε = 4.29), 267 (4.45), 336 (3.67) nm; pmr (deuteriochloroform): δ 7.15-7.50 (10H, m, benzene H), 8.28 (1H, s, pyrazine H) ppm; ms: m/e 282 (M^+).

Anal. Calcd. for $C_{16}H_{11}ClN_2O$: C, 67.97; H, 3.92; N, 9.91. Found: C, 68.05; H, 3.92; N, 9.91.

15) Oxidation of 2-Chloromethyl-3-phenylpyrazine (**16**).

A solution of **16** (2.04 g, 10 mmoles), 90% hydrogen peroxide (0.456 g, 12 mmoles), and maleic anhydride (1.47 g, 15 mmoles) in chloroform (50 ml) was refluxed for 8 hours and worked up as described in 4) to give pale yellow crystals (2.29 g), which were chromatographed on silica gel (Wakogel C-200, 60 g) and eluted with benzene, containing an increasing amount of ethyl acetate. The fractions eluted with an 8:2 mixture gave the starting material (0.99 g, 43%). The 3:1 fractions afforded **27** (0.647 g, 29%) as colorless prisms, mp 142-142.5° (from methanol). Further elution with the 1:1 mixture yielded **28** (0.457 g, 21%) as colorless cotton crystals, mp 78-78.5° (from hexane).

Compound **27**.

This compound had the following physical characteristics: uv (95% ethanol): λ max 224.5 (log ε = 4.23), 255 (4.25), 272.5 (4.16, shoulder) nm; pmr (deuteriochloroform): δ 4.76 (2H, s, CH_2), 7.40-7.60 (3H, m, benzene H), 7.60-7.80 (2H, m, benzene H), 8.14 (1H, d, pyrazine H, J = 4 Hz), 8.46 (1H, d, pyrazine H, J = 4 Hz) ppm; ms: m/e 220 (M^+, 21.5%), 219 (M^+-H, 21.5%), 203 (M^+-OH, 3.2%), 185 (M^+-Cl, 12.9%), 167 $C_{11}H_7N_2^+$, 78 ($C_6H_6^+$, 100%).

Anal. Calcd. for $C_{11}H_9ClN_2O$: C, 59.87; H, 4.11; N, 12.70. Found: C, 59.52; H, 4.30; N, 12.47.

Compound **28**.'

This compound had the following physical characteristics: uv (95% ethanol): λ max 228 (log ε = 4.28), 247 (4.09, shoulder), 269.5 (4.05) nm; pmr (deuteriochloroform): δ 4.20 (2H, s, CH_2), 7.20-7.60 (5H, m, benzene H), 8.14 (1H, d, pyrazine H, J = 4 Hz), 8.40 (1H, d, pyrazine H, J = 4 Hz) ppm; ms: m/e 220 (M^+, 28.4%), 203 (M^+-OH, 21.1%), 185 (M^+-Cl, 13.7%), 167 ($C_{11}H_7N_2^+$, 100%).

Anal. Calcd. for $C_{11}H_9ClN_2O$: C, 59.87; H, 4.11; N, 12.70. Found: C, 59.75; H, 4.10; N, 12.69.

16) Reaction of 6-Chloro-2,3-dimethylpyrazine 4-Oxide (**24**) with Phosphoryl Chloride.

A mixture of **24** (220 mg, 1 mmole) and phosphoryl chloride (3 ml) was refluxed for 0.5 hours and worked up as described in 6) to give a brown oil (160 mg), which was chromatographed on silica gel (Wakogel C-100, 10 g), eluting with a mixture of hexane and ether. A 50:1 mixture eluted successively **29** and **30**.

Compound **29**.

This compound had the following physical characteristics: colorless prisms, mp 75-76° (from hexane), 66 mg (38%) (lit 16, mp 80-81°).

Compound **30**.

This compound had the following physical properties: colorless oil, bp 60-65°/1 torr (oil bath temperature); 34 mg (19%); uv (95% ethanol): λ max 278.5 (log ε = 3.84), 293 (3.65, shoulder) nm; pmr (deuteriochloroform): δ 2.64 (3H, s, CH_3), 4.66 (2H, s, CH_2), 8.34 (1H, s, pyrazine H); ms: m/e 176 (M^+).

Anal. Calcd. for $C_6H_6Cl_2N_2$: C, 40.70; H, 3.42; N, 15.82. Found: C, 40.66; H, 3.41; N, 15.91.

17) 5,6-Dichloro-2,3-diphenylpyrazine (**31**).

A solution of **26** (113 mg, 0.4 mmoles) in phosphoryl chloride (2 ml) was refluxed for 1 hour and worked up as described in 6) to give a brown oil (167 mg), which was purified by silica gel (Wakogel C-200, 3 g) column chromatography, using benzene as an eluent, to give **31** (103 mg, 86%) as colorless prisms, mp 182-183° (from hexane) (lit 16, mp 182-183°).

18) 5,6-Dichloro-2-methyl-3-phenylpyrazine (**32**).

a) A solution of **17** (110 mg, 0.5 mmoles) in phosphoryl chloride (2 ml) was refluxed for 1 hour and worked up as described in 6) to give a brown solid, which was purified by silica gel (Wakogel C-100, 3.6 g) column chromatography, eluting with hexane and ether. The fractions eluted with a mixture of hexane and ether (100:1) yielded **32** (100 mg, 84%) as colorless prisms, mp 69° (from methanol).

b) A solution of **19** (150 mg, 0.68 mmoles) in phosphoryl chloride (2 ml) was refluxed for 0.5 hours and worked up as above to give a brown solid (163 mg), which was chromatographed on silica gel (Wakogel C-100, 5 g) to afford **32** (151 mg, 93%) as colorless crystals, mp 69-70° (from methanol); uv (95% ethanol): λ max 242 (log ε = 4.01), 251 (3.99, shoulder), 284 (3.73, shoulder), 308.5 (4.05) nm; pmr (deuteriochloroform): δ 2.66 (3H, s, CH_3), 7.40-7.70 (5H, m, benzene H) ppm; ms: m/e 238 (M^+).

Anal. Calcd. for $C_{11}H_8Cl_2N_2$: C, 55.26; H, 3.37; N, 11.72. Found: C, 55.24; H, 3.42; N, 11.67.

19) 6-Hydroxy-2,3-dimethylpyrazine (**33**).

A suspension of **11** (601 mg, 4.2 mmoles) in 15% hydrochloric acid (12 ml) was refluxed for 4 hours, made alkaline with potassium carbonate, and extracted with ether. The aqueous layer was evaporated to dryness *in vacuo*. The residue was extracted with chloroform and the extract was worked up as usual to give a brownish solid, which was purified by sublimation at 130°/3 torr and the successive recrystallization from hexane-benzene to furnish **33** (52 mg, 9%) as pale yellow needles, mp 197° (lit 13, mp 201-202°).

20) Reaction of 2,3-Dimethylpyrazine 1-Oxide (**4**) with Acetic Anhydride.

A solution of **4** (1.24 g, 5 mmoles) in acetic anhydride (10 ml) was refluxed for 0.5 hours, poured into ice water, made alkaline with potassium carbonate, and extracted with ether. The ether layer was usually worked up to give a brown oil, which was purified by Florisil (20 g) column chromatography, eluting with a mixture of hexane and ethyl acetate. The fractions eluted with a 7:3 mixture gave **37** (1.28 g, 77%) as a colorless oil, bp 97-98°/6 torr; uv (95% ethanol): λ max 267.5 (log ε = 3.86), 271.5 (3.85, shoulder) nm; ir (liquid film, sodium chloride): 1740 cm^{-1} (C=O); pmr (deuteriochloroform): δ 2.16 (3H, s, CH_3), 2.60 (3H, s, CH_3), 5.24 (2H, s, CH_2), 8.40 (2H, s, pyrazine H) ppm; ms: m/e 166 (M^+).

Anal. Calcd. for $C_8H_{10}N_2O_2$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.69; H,6.11; N, 16.95.

21) Reaction of 2,3-Diphenylpyrazine 1-Oxide (**6**) with Acetic Anhydride.

A solution of **6** (1.24 g, 5 mmoles) in acetic anhydride (20 ml) was heated at 130° for 1.5 hours, poured into ice water. The yellow precipitates were collected by suction and recrystallized from methanol to afford **38** (1.36 g, 82%) as colorless prisms, mp 205-206°; uv (95% ethanol): λ max 224.5 (log ε = 4.15), 291.5-293.5 (3.80) nm; ir (potassium bromide): 1745 cm^{-1} (C=O); pmr (deuteriochloroform): δ 2.24 (6H, s, CH_3), 6.30 (2H, s, pyrazine H), 7.20-7.56 (10H, m, benzene H) ppm; ^{13}C-nmr (deuteriochloroform): δ 21.2 (CH_3), 82.5 (C-2 and C-3), 128.1 (benzene C), 128.4 (benzene C), 130.7 (benzene C), 135.3 (benzene C), 160.0 (C-5 and C-6), 169.9 (C=O) ppm; ms: m/e 248 (M^+-CH_3COOH-CH_2CO).

Anal. Calcd. for $C_{20}H_{16}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.59; H, 5.22; N, 8.09.

22) 5-Acetoxy-2,3-diphenylpyrazine (**39**).

After **38** (200 mg, 0.57 mmoles) was heated at 230° for 5 minutes on a metal bath, an oily product was triturated with hexane and allowed to stand overnight at room temperature. Colorless prisms (143 mg, 86%) were obtained, mp 77-77.5°; uv (95% ethanol): λ max 204 (log ε = 4.41), 219 (4.34), 268 (4.04), 311 (4.00) nm; ir (potassium bromide): 1780 cm^{-1} (C=O); pmr (deuteriochloroform): δ 2.32 (3H, s, CH_3), 7.12 (10H, m, benzene H), 8.33 (1H, s, pyrazine H) ppm; ms: m/e 290 (M^+, 9%), 248 (M^+-CH_2CO, 100%).

Anal. Calcd. for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.53; H, 4.97; N, 9.61.

23) 2,3-Diphenyl-6-hydroxypyrazine (**34**).

a) A solution of **38** (870 mg, 3 mmoles) in a mixture of 10% sodium hydroxide (10 ml) and methanol (50 ml) was refluxed for 1 hour, and then methanol was evaporated off *in vacuo*. The residual solution was acidified with 20% hydrochloric acid. The precipitates were collected by suction and recrystallized from ethanol to give **34** (303 mg, 41%) as yellow cotton needles, mp 247-248° (lit 13, mp 243-244°).

b) A solution of **39** (73 mg, 0.25 mmoles) in a mixture of 10% sodium hydroxide (1 ml) and methanol (2 ml) was refluxed for 1 hour, and worked up as before to give 55 mg (89%) of **34**.

24) Reaction of 2-Methyl-3-phenylpyrazine 1-Oxide (**8**) with Acetic Anhydride.

A mixture of **8** (10.50 g, 56 mmoles) and acetic anhydride (170 ml) was refluxed for 0.5 hours. After removal of acetic anhydride by distillation *in vacuo*, the resulting brown oil was poured into ice water, made alkaline with potassium carbonate, and extracted with ether. An usual work up of the extract gave a brown solid (12.89 g), which was refluxed in an alkaline medium (220 ml of 10% sodium hydroxide and 540 ml of methanol) for 1 hour. The solvent was evaporated off under a reduced pressure. The residue was triturated with water and extracted with methylene chloride. The organic layer was usually worked up to give **40** (6.26 g, 60%) as a pale yellow solid, which was recrystallized from cyclohexane to furnish pale yellow prisms, mp 101-102.5°. The aqueous layer was acidified with acetic acid and extracted with methylene chloride. The extract gave **36** (2.41 g, 23%) as pale yellow crystals, which was recrystallized from benzene to furnish colorless needles, mp 181-182.5°.

Compound **36**.

This compound had the following physical characteristics: uv (95% ethanol): λ max 245 (log ε = 3.82, shoulder), 325 (3.82, shoulder), 341-347 (3.85) nm; ir (potassium bromide): 1650 cm^{-1} (C=O); pmr (deuteriochloroform): δ 2.33 (3H, s, CH_3), 7.50 (5H, m, benzene H), 8.06 (1H, s, pyrazine H) ppm; ms: m/e 186 (M^+).

Anal. Calcd. for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.05. Found: C, 71.00; H, 5.43; N, 15.04.

Compound **40**.

This compound had the following physical characteristics: uv (95% ethanol): 232 (log ε = 3.99), 281 (3.97) nm; pmr (deuteriochloroform): δ 3.65 (1H, s, OH), 4.82 (2H, s, CH_2), 7.40-7.70 (5H, m, benzene H), 8.51 (1H, d, pyrazine H, J = 2.5 Hz), 8.62 (1H, d, pyrazine H, J = 2.5 Hz) ppm; ms: m/e 186 (M^+).

Anal. Calcd. for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.05. Found: C, 71.11; H, 5.36; N, 15.19.

25) Reaction of 2-Methyl-3-phenylpyrazine 4-Oxide (**9**) with Acetic Anhydride.

A mixture of **9** (556 mg, 2.98 mmoles) and acetic anhydride (5 ml) was refluxed for 0.5 hours and worked up as above to give a brown solid, which was heated in an alkaline medium (9 ml of 10% sodium hydroxide and 40 ml of methanol) for 1 hour. The same work-up as described in 24) yielded **36** (321 mg, 58%) and **40** (177 mg, 32%).

26) 5-Chloro-2-methyl-3-phenylpyrazine (**15**).

A mixture of **36** (231 mg, 1.24 mmoles), phosphoryl chloride (5 ml), and a small amount of phosphorus pentachloride was heated in a sealed tube at 140° for 1 hour, and worked up as described in 6) to yield a brown oil (182 mg), which was purified by silica gel (Wakogel C-200, 6 g) column chromatography, eluting with hexane and ether. The hexane-ether (10:1) fractions gave **15** (101 mg, 40%) as a colorless oil, bp 140-150°/2 torr (oil bath temperature).

27) 2-Cyanomethyl-3-phenylpyrazine (**41**).

A solution of **16** (408 mg, 2 mmoles) and potassium cyanide (160 mg, 2.4 mmoles) in ethanol (20 ml) was refluxed for 4 hours. After removal of the solvent by distillation *in vacuo*, the residual solid was triturated with water and extracted with methylene chloride. The usual work up of the extract gave a brown solid (439 mg), which was purified by silica gel (Wakogel C-200, 10 g) column chromatography, eluting with benzene and chloroform. The fractions eluted with a mixture of benzene and chloroform (8:2) gave **41** (356 mg, 91%) as a colorless solid, which was recrystallized from 2-propanol to furnish colorless needles, mp 126°; uv (95% ethanol): λ max 228.5 (log ε = 3.94), 278.5 (3.89) nm; ir (potassium bromide): 2250 cm^{-1} (CN); pmr (deuteriochloroform): δ 4.00 (2H, s, CH_2), 7.54 (5H, s, benzene H), 8.58 (1H, d, pyrazine H, J = 4 Hz), 8.66 (1H, d, pyrazine H, J = 4 Hz) ppm; ms: m/e 195 (M^+).

Anal. Calcd. for $C_{12}H_9N_3$: C, 73.83; H, 4.65; N, 21.52. Found: C,73.63; H, 4.65; N, 21.92.

28) Hydrolysis of 2-Cyanomethyl-3-phenylpyrazine (**41**).

A suspension of **41** (97.5 mg, 0.5 mmoles) in 20% hydrochloric acid (10 ml) was refluxed for 3 hours, neutrallized with potassium carbonate, and extracted with chloroform. The extract gave a brown oil, which was purified by silica gel (Wakogel C-100, 2 g) column chromatography, eluting with hexane and ether. The fractions eluted with a 20:1 mixture yielded **3** (56 mg, 66%) as a colorless oil, bp 130-140°/5 torr (oil bath temperature).

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