Syntheses of Some 2-Hydroxypyrazine 1-Oxides

Akihiro Ohta, Sawako Masano, Mayumi Tsutsui, Fusako Yamamoto, Sumie Suzuki, Hiromi Makita, Hideo Tamamura and Yasuo Akita

Tokyo College of Pharmacy, 1432-1 Horinouchi, Hachioji, Tokyo 192-03, Japan

Received October 21, 1980

A series of 2-hydroxypyrazine 1-oxides were prepared from the corresponding chloropyrazines by two methods, including oxidation processes in satisfactory yields. The treatment of 2,3-diphenylpyrazine 1,4-dioxide (**6**) led to 2,3-dichloro-5,6-diphenylpyrazine (**7**) and 2-chloro-5,6-diphenylpyrazine 1-oxide (**8**), and the latter was converted to 5,6-diphenyl-2-hydroxypyrazine 1-oxide (**9**) by an alkaline hydrolysis.

J. Heterocyclic Chem., **18**, 555 (1981).

Since aspergillic acid was characterized as a cyclic hydroxamic acid in 1944, several 2-hydroxypyrazine 1-oxides have been isolated as mold metabolites (1,2). Because of the antibiotic activity against gram-negative micro-organisms, these pyrazines have been of interest in the medicinal field.

Syntheses of some naturally occurring cyclic hydroxamic acids carrying a pyrazine ring have been already performed mainly by two methods, involving oxidation or condensation processes (1,2). This paper deals with the synthesis of a series of alkyl and phenyl 2-hydroxypyrazine 1-oxides starting from the corresponding 2-chloropyrazines by oxidation processes.

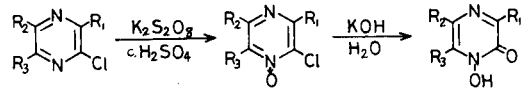
The preparation of the starting chloropyrazines was carried out mostly by modification of the reported manners (3-8). Among these 2-chloropyrazines, 2-chloro- and 2,5-dichloro-3,6-dialkylpyrazines were prepared from the corresponding 2,5-diketopiperazines (9) by the treatment with a mixture of phosphoryl chloride and phosphorus pentachloride. The separation of the chloro compounds was achieved by a usual method, in which a hexane solution of a mixture of mono- and dichloropyrazines was extracted with concentrated hydrochloric acid.

The oxidation of the chloropyrazines was undertaken by two ways, namely with potassium persulfate in a concentrated sulfuric acid solution and permaleic acid, as will be described next.

By Mixan and Pews (10), it was established that some 2-chloropyrazines are able to be converted to their 1-oxides under the treatment with potassium persulfate in concentrated sulfuric acid. In the present work, some other 2-chloropyrazines were submitted to this reaction to afford the corresponding 1-oxides. As shown in Table I, 2-chloro-3,6-dialkylpyrazines gave the aimed *N*-oxides in considerably good yields. In the case of phenylpyrazines, however, the yields were reduced, because of low basicity caused by the electron withdrawing effect of the phenyl groups. Some 2,5-dichloro-3,6-dialkylpyrazines were also

Table I

Syntheses of 2-Hydroxypyrazine 1-Oxides *via* 2-Chloropyrazine 1-Oxides



1 2 3

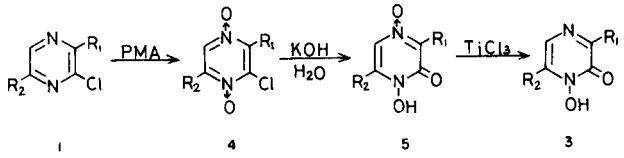
	Compound **1**	Product **2**	Yield (%)	Product **3**	Yield (%)
1a	$R_1 = R_3 = CH_3$, $R_2 = H$ (3)	**2a** (11)	97	**3a** (15)	94
1b	$R_1 = R_3 = C_2H_5$, $R_2 = H$ (4)	**2b**	84	**3b** (15)	84
1c	$R_1 = R_3 = n\text{-}C_3H_7$, $R_2 = H$	**2c**	97	**3c**	82
1d	$R_1 = R_3 = \text{iso-}C_3H_7$, $R_2 = H$	**2d**	97	**3d**	87
1e	$R_1 = R_3 = \text{iso-}C_4H_9$, $R_2 = H$ (5)	**2e** (12)	82	**3e** (16)	80
1f	$R_1 = C_6H_5$, $R_2 = H$, $R_3 = CH_3$ (6)	**2f** (6)	20	**3f** (6)	93
1g	$R_1 = R_3 = H$, $R_2 = C_6H_5$ (7)	**2g** (13)	37	**3g** (17)	95
1h	$R_1 = R_2 = C_6H_5$, $R_3 = H$ (8)	**2h**	13	**3h** (17)	95
1i	$R_1 = R_3 = C_2H_5$, $R_2 = Cl$ (6)	**2i** (6)	67 (30) (a)	**3i** (6)	81
1j	$R_1 = R_3 = n\text{-}C_3H_7$, $R_2 = Cl$	**2j**	74 (22) (a)	**3j**	43
1k	$R_1 = R_3 = \text{iso-}C_3H_7$, $R_3 = Cl$	**2k**	78 (8) (a)	**3k**	57
1l	$R_1 = R_3 = \text{iso-}C_4H_9$, $R_2 = Cl$ (5)	**2l** (14)	68 (17) (a)	**3l**	50

(a) Yields of the dioxides.

0022-152X/81/030555-04$02.25

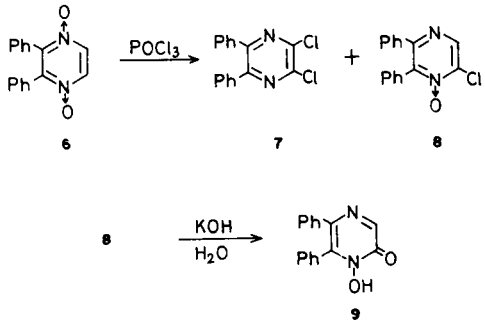
Table II

Syntheses of 2-Hydroxypyrazine 1-Oxides *via* 2-Chloropyrazine 1,4-Dioxides



1 4 5 3

	Compound **1**	Product **4**	Yield (%)	Product **5**	Yield (%)	Product **3**	Yield (%)
1b	$R_1 = R_2 = C_2H_5$ (4)	**4b** (6)	18	**5b** (6)	98	**3b** (15)	46
1e	$R_1 = R_2$ = iso-C_4H_9 (5)	**4e** (5)	42	**5e** (5)	97	**3e** (16)	50
1f	$R_1 = C_6H_5$, $R_2 = CH_3$ (6)	**4f** (6)	34	**5f**	94	**3f** (6)	57
1m	R_1 = iso-C_3H_7, R_2 = iso-C_4H_9 (19)	**4m** (19)	29	**5m** (19)	47	**3m** (19)	63
1n	R_1 = iso-C_4H_9, R_2 = iso-C_3H_7 (19)	**4n** (19)	41	**5n** (19)	42	**3n** (19)	64



6 7 8 8 9

Scheme I

treated with persulfuric acid to yield mono- and dioxides, which were separated by silica gel chromatography.

The 2-chloropyrazine 1-oxides, thus prepared, were converted to 2-hydroxypyrazine 1-oxides by an alkaline hydrolysis in good yields, and the results are given in Table I.

The present authors already synthesized some naturally occurring 2-hydroxypyrazine 1-oxides by two manners, in which 2-hydroxypyrazine 1,4-dioxides were deoxygenated directly with titanium trichloride (18), or their methyl esters were reduced with phosphorus trihalide (19). In this work, 2-hydroxypyrazine 1,4-dioxides were prepared also by the oxidation of the corresponding 2-chloropyrazines with permaleic acid and the following alkaline hydrolysis by the reported manners, as shown in Table II, and titanium trichloride was adopted as the reducing agent. The reduction was achieved at 30° or 50° in a tetrahydrofuran solution in good yields.

Lastly, the preparation of 5,6-diphenyl-2-hydroxypyrazine 1-oxide (**9**) will be described. This substance was prepared by a third method, including the chlorination of 2,3-diphenylpyrazine 1,4-dioxide (**6**) (20). As shown in Scheme I, the treatment of **6** with phosphoryl chloride led to 2,3-dichloro-5,6-diphenylpyrazine (**7**) (21) and 2-chloro-5,6-diphenylpyrazine 1-oxide (**8**). The latter was hydrolysed in an alkaline medium to give the aimed compound, which resulted in a red coloration with ferric chloride. It seems very interesting, that the chlorination of **6** occurs at a β position of the N-O group.

Conclusively, some 2-hydroxypyrazine 1-oxides could be easily synthesized with satisfactory yields. Because these compounds are expected to possess antibacterial activities, investigations for such activities are presently in progress.

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 Shimadzu IR-400 spectrometer and pmr spectra on a JEOL JNM-PS-100 instrument with tetramethylsilane as an internal standard. Mass spectra were obtained on a Hitachi RMU-7L spectrometer.

1) General Procedure for Preparation of 2-Chloro- and 2,5-Dichloro-3,6-dialkylpyrazines.

A mixture of DL-α-amino acid anhydrides (50 mmoles), phosphoryl chloride (40 ml.) and phosphorus pentachloride (5 g.) was heated at 140° for 1 hour in a sealed tube. The reaction mixture was poured into ice water, made alkaline with solid potassium carbonate, and extracted with hexane. The hexane layer was extracted with concentrated hydrochloric acid. The usual work-up of the organic layer gave dichloropyrazines, which were purified by distillation. The aqueous layer was made alkaline with potassium carbonate and extracted with ether to give monochloropyrazines.

Compound **1c**.

This compound was obtained as a colorless oil, b.p. 103-105°/6 torr (57% yield); pmr (deuteriochloroform): δ 0.98 (3H, t, J = 8 Hz, $CH_2CH_2CH_3$), 1.02 (3H, t, J = 8 Hz, $CH_2CH_2CH_3$), 1.80 (4H, m, $CH_2CH_2CH_3$), 2.84 (4H, m, $CH_2CH_2CH_3$) ppm; ms: m/e 198 (M^+); uv (95% ethanol): λ max 216 (log ε 3.89), 281 (3.92) nm.

Anal. Calcd. for $C_{10}H_{15}ClN_2$: C, 60.45; H, 7.61; N, 14.10. Found: C, 60.32; H, 7.67; N, 14.33.

Compound **1d**.

This compound was obtained as a pale yellow oil, b.p. 94-95°/6 torr (70% yield); pmr (deuteriochloroform): δ 1.28 (6H, d, J = 8 Hz, $CH(CH_3)_2$), 1.32 (6H, d, J = 8 Hz, $CH(CH_3)_2$), 3.06 (1H, m, J = 8 Hz, $CH(CH_3)_2$), 3.49 (1H, m, J = 8 Hz, $CH(CH_3)_2$), 8.29 (1H, s, pyrazine H) ppm; ms: m/e 198 (M^+); uv (95% ethanol): λ max 213 (log ε 4.01), 280 (3.92) nm.

Anal. Calcd. for $C_{10}H_{15}ClN_2$: C, 60.45; H, 7.61; N, 14.10. Found: C, 60.57; H, 7.81; N, 14.16.

Compound **1j**.

This compound was obtained as colorless prisms (methanol), m.p. 34° (39% yield); pmr (deuteriochloroform): δ 1.01 (6H, t, J = 8 Hz, $CH_2CH_2CH_3$), 1.79 (4H, m, $CH_2CH_2CH_3$), 2.86 (4H, t, $CH_2CH_2CH_3$) ppm; ms: m/e 232 (M^+); uv (95% ethanol): λ max 220 (log ε 4.04), 297 (3.92) nm.

Anal. Calcd. for $C_{10}H_{14}Cl_2N_2$: C, 51.52; H, 6.05; N, 12.02. Found: C, 51.58; H, 6.12; N, 12.03.

Compound **1k**.

This compound was obtained as colorless prisms (methanol), m.p. 52-53° (20% yield); pmr (deuteriochloroform): δ 1.30 (12H, d, J = 7 Hz, $CH(CH_3)_2$), 3.40 (2H, m, J = 7 Hz, $CH(CH_3)_2$) ppm; ms: m/e 232 (M^+); uv (95% ethanol): λ max 218 (log ε 3.90), 280-283 (3.73), 292 (3.78) nm. *Anal.* Calcd. for $C_{10}H_{14}Cl_2N_2$: C, 51.52; H, 6.05; N, 12.02. Found: C, 51.69; H, 6.01; N, 12.25.

2) General Procedure for Oxidation of 2-Chloro- and 2,5-Dichloropyrazines with Persulfuric Acid.

To a 2-chloropyrazine (10 mmoles) dissolved in 10 ml. of concentrated sulfuric acid, potassium persulfate (15 mmoles) was added portionwise at room temperature in 30 minutes under stirring and allowed to stand further for 24 hours. The reaction mixture was poured into ice water (30 ml.) and extracted with chloroform. The chloroform layer was washed with 10% potassium bicarbonate and water successively and worked up as usual. 2,5-Dichloropyrazines were treated with 4-5 molar equivalents of potassium persulfate and worked up as above.

Compound **2b**.

This compound was obtained as colorless needles (hexane), m.p. 135-138°; pmr (deuteriochloroform): δ 1.31 (6H, t, J = 8 Hz, CH_2CH_3), 2.89 (2H, q, J = 8 Hz, CH_2CH_3), 2.94 (2H, q, J = 8 Hz, CH_2CH_3), 8.24 (1H, s, pyrazine H) ppm; ms: m/e 186 (M^+), 169 (M^+-OH); uv (95% ethanol): λ max 206 (log ε 4.17), 230 (4.27), 260 (3.95) nm.

Anal. Calcd. for $C_8H_{11}ClN_2O$: C, 51.48; H, 5.94; N, 15.01. Found: C, 51.42; H, 5.80; N, 15.25.

Compound **2c**.

This compound was obtained as a colorless oil, b.p. 124.5°/3 torr; pmr (deuteriochloroform): δ 1.03 (6H, t, J = 7 Hz, $CH_2CH_2CH_3$), 1.79 (4H, m, $CH_2CH_2CH_3$), 2.88 (4H, m, $CH_2CH_2CH_3$), 8.23 (1H, s, pyrazine H) ppm; ms: m/e 214 (M^+), 197 (M^+-OH); uv (95% ethanol): λ max 208 (log ε 4.23), 232 (4.30), 270 (3.98) nm.

Anal. Calcd. for $C_{10}H_{15}ClN_2O$: C, 55.94; H, 7.04; N, 13.05. Found: C, 55.81; H, 7.08; N, 13.19.

Compound **2d**.

This compound was obtained as a pale yellow oil, b.p. 146°/9 torr; pmr (deuteriochloroform): δ 1.33 (6H, d, J = 7 Hz, $CH(CH_3)_2$), 1.37 (6H, d, J = 7 Hz, $CH(CH_3)_2$), 3.56 (2H, m, J = 7 Hz, $CH(CH_3)_2$), 8.31 (1H, s, pyrazine H) ppm; ms: m/e 214 (M^+), 197 (M^+-OH); uv (95% ethanol): λ max 206 (log ε 4.03), 230 (4.07), 270 (3.76) nm.

Anal. Calcd. for $C_{10}H_{15}ClN_2O$: C, 55.94; H, 7.04; N, 13.05. Found: C, 55.88; H, 7.07; N, 13.00.

Compound **2h**.

This compound was obtained as colorless needles (methanol), m.p. 179-180°; pmr (deuteriochloroform): δ 7.50 (5H, s, benzene H), 7.89 (5H, m, benzene H), 8.65 (1H, s, pyrazine H) ppm; ms: m/e 282 (M^+), 266 (M^+-O); uv (95% ethanol): λ max 202 (log ε 4.35), 267 (4.56), 335 (3.72) nm.

Anal. Calcd. for $C_{16}H_{11}ClN_2O$: C, 67.97; H, 3.92; N, 9.91. Found: C, 68.07; H, 3.96; N, 10.07.

Compound **2j**.

This compound was obtained as a pale yellow oil, b.p. 114-120°/8 torr; pmr (deuteriochloroform): δ 1.03 (3H, t, J = 7 Hz, $CH_2CH_2CH_3$), 1.05 (3H, t, J = 7 Hz, $CH_2CH_2CH_3$), 1.74 (4H, m, J = 7 Hz, $CH_2CH_2CH_3$), 2.97 (4H, m, $CH_2CH_2CH_3$) ppm; ms: m/e 248 (M^+), 231 (M^+-OH); uv (95% ethanol): λ max 217 (log ε 4.24), 239 (4.32), 273 (3.95) nm.

Anal. Calcd. for $C_{10}H_{14}Cl_2N_2O$: C, 48.21; H, 5.66; N, 11.24. Found: C, 48.03; H, 5.47; N, 11.50.

2,5-Dichloro-3,6-dipropylpyrazine 1,4-Dioxide.

This compound was obtained as colorless needles (ethanol), m.p. 147-149°; pmr (deuteriochloroform): δ 1.10 (6H, t, J = 8 Hz, $CH_2CH_2CH_3$), 1.76 (4H, m, J = 8 Hz, $CH_2CH_2CH_3$), 3.13 (4H, t, J = 8 Hz, $CH_2CH_2CH_3$) ppm; ms: m/e 264 (M^+), 247 (M^+-OH); uv (95% ethanol): λ max 216 (log ε 4.21), 254 (4.47), 313 (4.25) nm.

Anal. Calcd. for $C_{10}H_{14}Cl_2N_2O_2$: C, 45.30; H, 5.32; N, 10.57. Found: C, 45.54; H, 5.41; N, 10.35.

Compound **2k**.

This compound was obtained as colorless needles (methanol), m.p. 144°; pmr (deuteriochloroform): δ 1.24 (6H, d, J = 7 Hz, $CH(CH_3)_2$), 1.39 (6H, d, J = 7 Hz, $CH(CH_3)_2$), 3.38 (1H, m, J = 7 Hz, $CH(CH_3)_2$), 3.87 (1H, m, J = 7 Hz, $CH(CH_3)_2$) ppm; ms: m/e 248 (M^+), 231 (M^+-OH); uv (95% ethanol): λ max 216 (log ε 4.18), 239 (4.27), 275 (3.88) nm.

Anal. Calcd. for $C_{10}H_{14}Cl_2N_2O$: C, 48.21; H, 5.66; N, 11.24. Found: C, 48.32; H, 5.48; N, 11.51.

2,5-Dichloro-3,6-diisopropylpyrazine 1,4-Dioxide.

This compound was obtained as colorless prisms (benzene), m.p. 250-253° dec.; pmr (deuteriochloroform): δ 1.48 (12H, d, J = 8 Hz, $CH(CH_3)_2$), 3.95 (2H, m, J = 8 Hz, $CH(CH_3)_2$) ppm; ms: m/e 264 (M^+), 247 (M^+-OH); uv (95% ethanol): λ max 215 (log ε 4.12), 254 (4.38), 316 (4.16) nm.

Anal. Calcd. for $C_{10}H_{14}Cl_2N_2O_2$: C, 45.30; H, 5.32; N, 10.56. Found: C, 45.20; H, 5.26; N, 10.60.

3) General Procedure for Alkaline Hydrolysis of 2-Chloropyrazine 1-Oxides.

A solution of a 2-chloropyrazine 1-oxide (100 mmoles) dissolved in 20% potassium hydroxide (200 ml.) or in a mixture of ethanol (250 ml.) and 20% potassium hydroxide (250 ml.) was refluxed for 3 hours. After acidification, the solvent was distilled off under a reduced pressure and the residue was extracted with chloroform. The chloroform layer was worked up as usual.

Compound **3c**.

This compound was obtained as pale yellow prisms (ethanol), m.p. 113.5-116.5°; ir (chloroform): 1620 (C=O) cm^{-1}; pmr (deuteriochloroform): δ 0.94 (3H, t, J = 8 Hz, $CH_2CH_2CH_3$), 0.98 (3H, t, J = 8 Hz, $CH_2CH_2CH_3$), 1.74 (4H, m, $CH_2CH_2CH_3$), 2.72 (2H, t, J = 8 Hz, $CH_2CH_2CH_3$), 2.80 (2H, t, J = 8 Hz, $CH_2CH_2CH_3$), 7.26 (1H, s, pyrazine H) ppm; ms: m/e 196 (M^+), 179 (M^+-OH); uv (95% ethanol): λ max 230 (log ε 4.25), 334 (3.96) nm.

Anal. Calcd. for $C_{10}H_{16}N_2O_2$: C, 61.20; H, 8.22; N, 14.28. Found: C, 61.42; H, 8.39; N, 14.54.

Compound **3d**.

This compound was obtained as colorless prisms (hexane), m.p. 74-76°; ir (potassium bromide): 1610 (C=O) cm^{-1}; pmr (deuteriochloroform): δ 1.30 (12H, m, $CH(CH_3)_2$), 3.37 (2H, m, $CH(CH_3)_2$), 7.37 (1H, s, pyrazine H) ppm; ms: m/e 196 (M^+), 179 (M^+-OH); uv (95% ethanol): λ max 234 (log ε

3.97), 326 (3.91) nm.

Anal. Calcd. for $C_{10}H_{16}N_2O_2$: C, 61.20; H, 8.22; N, 14.28. Found: C, 61.15; H, 8.46; N, 14.53.

Compound **3j**.

This compound was obtained as colorless needles (hexane), m.p. 97-99°; ir (potassium bromide): 1630 (C=O) cm^{-1}; pmr (deuteriochloroform): δ 1.02 (3H, t, J = 8 Hz, $CH_2CH_2CH_3$), 1.08 (3H, t, J = 8 Hz, $CH_2CH_2CH_3$), 2.76 (4H, m, $CH_2CH_2CH_3$), 2.92 (4H, m, $CH_2CH_2CH_3$), 8.59 (1H, s, OH) ppm; ms: m/e 230 (M^+), 213 (M^+-OH); uv (95% ethanol): λ max 210 (log ε 3.95), 242 (4.10), 342 (3.91) nm.

Anal. Calcd. for $C_{10}H_{15}ClN_2O_2$: C, 52.06; H, 6.55; N, 12.14. Found: C, 52.08; H, 6.61; N, 12.18.

Compound **3k**.

This compound was obtained as colorless needles (hexane), m.p. 120-121°; ir (potassium bromide): 1635 (C=O) cm^{-1}; pmr (deuteriochloroform): δ 1.26 (6H, d, J = 8 Hz, $CH(CH_3)_2$), 1.45 (6H, d, J = 8 Hz, $CH(CH_3)_2$), 3.36 (1H, m, J = 8 Hz, $CH(CH_3)_2$), 3.65 (1H, m, J = 8 Hz, $CH(CH_3)_2$), 6.60 (1H, broad s, OH) ppm; ms: m/e 230 (M^+), 213 (M^+-OH); uv (95% ethanol): λ max 210 (log ε 3.95), 243 (4.01), 339 (3.92) nm.

Anal. Calcd. for $C_{10}H_{15}ClN_2O_2$: C, 52.06; H, 6.55; N, 12.14. Found: C, 52.05; H, 6.61; N, 12.26.

Compound **3l**.

This compound was obtained as colorless needles (hexane), m.p. 121-122°; ir (potassium bromide): 1630 (C=O) cm^{-1}; pmr (deuteriochloroform): δ 0.96 (6H, d, J = 7 Hz, $CH_2CH(CH_3)_2$), 1.03 (6H, d, J = 7 Hz, $CH_2CH(CH_3)_2$), 2.20 (2H, m, $CH_2CH(CH_3)_2$), 2.70 (2H, d, J = 7 Hz, $CH_2CH(CH_3)_2$), 2.83 (2H, d, J = 7 Hz, $CH_2CH(CH_3)_2$) ppm; ms: m/e 258 (M^+), 241 (M^+-OH); uv (95% ethanol): λ max 208 (log ε 4.01), 244 (4.09), 345 (3.94) nm.

Anal. Calcd. for $C_{12}H_{19}ClN_2O_2$: C, 55.70; H, 7.40; N, 10.83. Found: C, 55.45; H, 7.21; N, 11.12.

4) General Procedure for Reduction of 2-Hydroxypyrazine 1,4-Dioxides with Titanium Trichloride.

To a solution of a 2-hydroxypyrazine 1,4-dioxide (0.5 mmole) dissolved in absolute tetrahydrofuran (20 ml.), titanium trichloride (1 mmole) was added and stirred for 2 hours at 30° or 50° in a stream of nitrogen gas. The reaction mixture was treated with water (20 ml.) and tetrahydrofuran was distilled off *in vacuo*. The residual solution was made alkaline with 2*N* sodium hydroxide. After removing the precipitates by filtration, the filtrate was acidified with 2*N* hydrochloric acid and extracted with methylene chloride. The extract was worked up as usual and the products were purified by column chromatography over silica gel (Wakogel C-200) using a mixture of benzene and chloroform as eluant.

Compound **5f**.

This compound was obtained as pale yellow needles (methanol), m.p. 270° dec.; ir (potassium bromide): 1590 (C=O) cm^{-1}; pmr (DMSO-d_6): δ 2.25 (3H, s, CH_3), 7.36 (5H, m, benzene H), 7.52 (1H, m, pyrazine H) ppm; ms: m/e 218 (M^+), 201 (M^+-OH); uv (95% ethanol): λ max 237 (log ε 4.27), 299 (3.76), 367 (3.94) nm.

Anal. Calcd. for $C_{11}H_{10}N_2O_3$: C, 60.54; H, 4.62; N, 12.84. Found: C, 60.38; H, 4.56; N, 12.73.

5) Reaction of 2,3-Diphenylpyrazine 1,4-Dioxide (**6**) with Phosphoryl Chloride.

A mixture of **6** (1.06 g., 4 mmoles) and phosphoryl chloride (20 ml.) was refluxed for 1 hour, poured into ice water, made alkaline with potassium carbonate, and extracted with methylene chloride. The organic layer was worked up usually to give a pale yellow solid (1.15 g.), which was chromatographed on silica gel (Wakogel C-200, 34 g.) and eluted with hexane, benzene, chloroform, and acetone, successively, to give **7** (0.664 g., 55%) and **8** (0.408 g., 36%).

Compound **7**.

This compound was obtained as colorless needles (hexane), m.p. 190-191° [lit. (21) m.p. 182-183°].

Compound **8**.

This compound was obtained as colorless prisms (ethanol), m.p. 201-203°; pmr (deuteriochloroform): δ 7.27 (5H, s, benzene H), 7.33 (5H, s, benzene H), 8.69 (1H, s, pyrazine H) ppm; ms: m/e 282 (M^+), 265 (M^+-OH); uv (95% ethanol): λ max 207 (log ε 4.29), 227 (4.27), 266 (4.44) nm.

Anal. Calcd. for $C_{16}H_{11}ClN_2O$: C, 67.97; H, 3.92; N, 9.91. Found: C, 67.80; H, 3.79; N, 9.89.

6) 2-Hydroxy-5,6-diphenylpyrazine 1-Oxide (**9**).

A solution of **8** (0.142 g., 0.5 mmole) dissolved in a mixture of ethanol (10 ml.) and 10% sodium hydroxide (2 ml.) was refluxed for 3 hours and worked up as described in Experimental procedure 3, to give **9** (0.140 g., 100%), which was recrystallized from ethanol to furnish colorless needles, m.p. 258°; ir (potassium bromide): 1645 (C=O) cm^{-1}; pmr (DMSO-d_6): δ 7.13 (5H, s, benzene H), 7.34 (5H, s, benzene H), 8.28 (1H, s, pyrazine H) ppm; ms: m/e 264 (M^+), 248 (M^+-O); uv (95% ethanol): λ max 204 (log ε 4.34), 267 (4.11), 352 (3.82) nm.

Anal. Calcd. for $C_{16}H_{12}N_2O_2$: C, 72.71; H, 4.58; N, 10.60. Found: C, 72.70; H, 4.61; N, 10.45.

Acknowledgement.

The authors are indebted to Mr. Y. Shida, Mr. S. Suzuki, Mrs. C. Sakuma, and Miss K. Matsuda, who performed the microanalytical and spectral determinations reported.

REFERENCES AND NOTES

(1) A. R. Katritzky and A. J. Boulton, "Advances in Heterocyclic Chemistry", Academic Press, New York, N.Y., Vol. 14, 1972, p. 99.

(2) P. G. Sammes, "Fortschritte der Chemie Organischer Naturstoffe", Vol. 32, 1975, p. 51.

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

(4) H. Gainer, M. Kokorudz and W. K. Langdon, *J. Org. Chem.*, **26**, 2360 (1961).

(5) A. Ohta, *Chem. Pharm. Bull.*, **16**, 1160 (1968).

(6) A. Ohta, Y. Akita and M. Hara, *ibid.*, **27**, 2027 (1979).

(7) S. Sugiura, S. Inoue, T. Kishi and T. Goto, *Yakugaku Zasshi*, **89**, 1646 (1969).

(8) P. J. Lont and H. C. Van Der Plas, *Rec. Trav. Chim.*, **92**, 449 (1973).

(9) C. Sannie, *Bull. Soc. Chim. France*, **9**, 487 (1942).

(10) C. E. Mixan and R. G. Pews, *J. Org. Chem.*, **42**, 1869 (1977).

(11) K. W. Blake and P. G. Sammes, *J. Chem. Soc. C*, 1070 (1970).

(12) A. Ohta, T. Ohwada, C. Ueno, M. Sumita, S. Masano, Y. Akita and T. Watanabe, *Chem. Pharm. Bull.*, **27**, 1378 (1979).

(13) N. Sato, *J. Org. Chem.*, **43**, 3367 (1978).

(14) A. Ohta, *Chem. Pharm. Bull.*, **12**, 125 (1964).

(15) D. W. C. Ramsay and F. S. Spring, *J. Chem. Soc.*, 3409 (1950).

(16) R. G. Micetich and J. C. MacDonald, *ibid.*, 1507 (1964).

(17) G. Dunn, J. A. Elvidge, G. T. Newbold, D. W. C. Ramsay, F. S. Spring and W. Sweeny, *ibid.*, 2707 (1949).

(18) A. Ohta, Y. Akita, A. Izumida and I. Suzuki, *Chem. Pharm. Bull.*, **27**, 1316 (1979).

(19) A. Ohta, Y. Akita, K. Takizawa, M. Kurihara, S. Masano and T. Watanabe, *ibid.*, **26**, 2046 (1978).

(20) J. K. Landquist, *J. Chem. Soc.*, 1885 (1956).

(21) G. Karmas and P. E. Spoerri, *J. Am. Chem. Soc.*, **78**, 4071 (1956).