ALKYLATION AND ARYLATION OF PYRAZINES BY ORGANOTIN COMPOUNDS

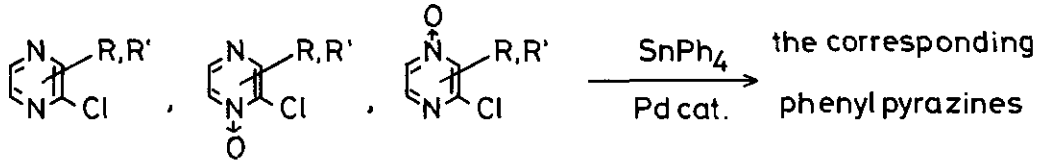
Tokuhiro Watanabe, Kazuhiko Hayashi, Jun Sakurada, Michiyo Ohki, Noriko Takamatsu, Harumi Hirohata, Keiko Takeuchi, Kayo Yuasa and Akihiro Ohta*

Tokyo College of Pharmacy

1432-1 Horinouchi, Hachioji, Tokyo 192-03, Japan

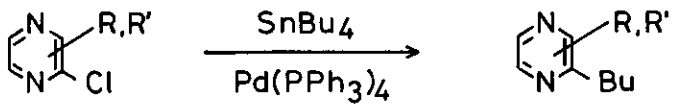
Abstract —— The palladium-catalyzed cross-coupling reactions of chloropyrazines and tetrabutyltin gave butylpyrazines in good yields. By reactions of chloropyrazines with organotin compounds prepared in situ from the Grignard reagents, alkyl and aryl groups were satisfactorily introduced into the pyrazine ring.

Organotin compounds are used for the alkylation and arylation of aromatic compounds[1]. While conducting our previous investigation on the alkylation and arylation of pyrazines, it was found that the phenylation of pyrazines could be achieved by palladium-catalyzed cross-coupling reactions of tetraphenyltin with chloropyrazines[2]. In the present report the butylation of pyrazines with tetrabutyltin, and the alkylation and arylation of pyrazines with organotin compounds, prepared in situ from the Grignard reagents, will be described.



Various chloropyrazines were heated for 5 h with tetrabutyltin in the presence of potassium carbonate and tetrakis(triphenylphosphine)palladium in N,N-dimethylformamide (DMF). The optimum molar ratio of chloropyrazines and tetrabutyltin was found to be 1:1. The results of the above reaction are summarized in Table 1. Judging from the results, organotin compounds appear useful not only for the phenylation but also alkylation of pyrazines.

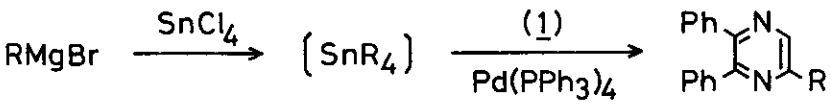
Table 1. Reaction of Chloropyrazines with Tetrabutyltin



R,R	Yield (%)
5,6-diphenyl (1)[3]	82
3,6-diethyl (2)[4]	73
3,6-diisopropyl (3)[5]	42

Grignard reagents are known to be quite suitable for the alkylation and arylation of aromatic rings[6]. However, in reactions between Griganrd reagents and chloropyrazines, both cross-coupling and substitution take place, leading to the formation of a mixture of various products[7]. Thus, in the present study, an attempt was made to carry out coupling reactions of chloropyrazines with organotin compounds prepared in situ from Grignard reagents and tin(IV) chloride[8].
The catalysts used were palladium acetate and tetrakis(triphenylphosphine)-palladium; solvents used : hexamethylphosphoramide, tetrahydrofuran (THF) and DMF; bases used: potassium carbonate and potassium acetate. The optimum molar ratio of tin(IV) chloride and chloropyrazines was found to be 1:1. The reactions were carried out under the conditions specified in the Experimental section. The results of the reaction of 2-chloro-5,6-diphenylpyrazine (1)[3] and 2-chloro-3,6-diisopropylpyrazine (3)[4] with various organotin compounds were satisfactory and are given in Tables 2 and 3.

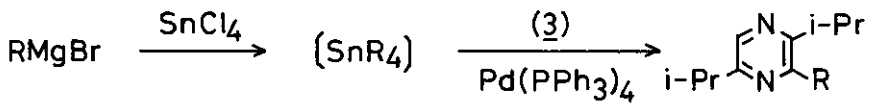
Table 2. Reaction of 2-Chloro-5,6-diphenylpyrazine (1) with Various Organotin Compounds



R	Reaction time (h)	Yield[a] (%)
o-MePh	5	53
m-MePh	2	87
p-MePh	2	88
p-MeOPh	2	87
p-ClPh	2	52
C_5H_{11}	5	80
C_8H_{17}	2	83

a: Based on (1).

Table 3. Reaction of 2-Chloro-3,6-diisopropylpyrazine (3) with Various Organotin Compounds

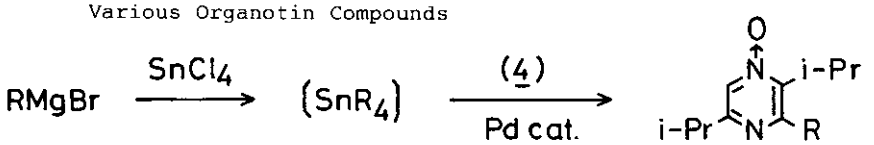


R	Reaction time (h)	Yield[a] (%)
o-MePh	5	10
m-MePh	2	59
p-MePh	2	80
p-MeOPh	5	65
p-ClPh	5	67
C_5H_{11}	5	40
C_8H_{17}	5	66

a: Based on (3).

From the results of the reaction of 2-chloro-3,6-diisopropylpyrazine 4-oxide (4)[9] with various organotin compounds tetrakis(triphenylphosphine)palladium was found suitable for arylation and palladium acetate for alkylation, as shown in Table 4.

Table 4. Reaction of 2-Chloro-3,6-diisopropylpyrazine 4-Oxide (4) with Various Organotin Compounds

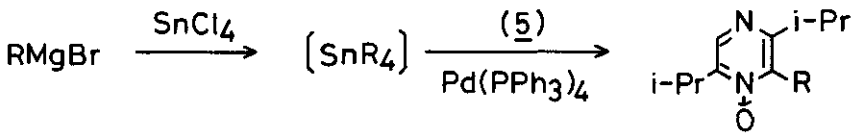


R	Pd cat.	Reaction time (h)	Yield[a] (%)
p-MePh	$Pd(PPh_3)_4$	5	81
p-MeOPh	〃	2	66
p-ClPh	〃	5	55
C_5H_{11}	$Pd(OAc)_2$	18	37
C_8H_{17}	〃	18	43

a: Based on (4).

The pentylation and octylation of 2-chloro-3,6-diisopropylpyrazine 1-oxide (5)[5] using organotin compounds were unsuccessful even with a variety of palladium catalysts.

Table 5. Reaction of 2-Chloro-3,6-diisopropylpyrazine 1-Oxide (5) with Various Organotin Compounds



R	Reaction time (h)	Yield[a] (%)
p-MePh	5	50
p-MeOPh	2	52
p-ClPh	7	29

a: Based on (5).

Grignard reagents, though quite suitable for the alkylation and arylation of aromatic rings, are of little use for the purpose in the case of pyrazines, as described before. Organotin compounds, however, are adequate for the latter purpose. Not many organotin compounds are available on the market and thus the effective method we devised for the preparation of alkyl- and arylpyrazines was shown to be quite useful.

EXPERIMENTAL

No correction was made for melting and boiling points. To obtain ms and ^{1}H-nmr spectral data, a Hitachi M-80 spectrometer, and a Varian EM-390 ($CDCl_3$/TMS) or a Brucker AM-400 ($CDCl_3$/$CHCl_3$), respectively, were used. For liquid chromatography silica gel (230-400 mesh, Merck A.G.) was used as the packing material.

General Procedure for Conducting Reactions of Chloropyrazines with Tetrabutyltin: A mixture of a chloropyrazine (2 mmol), $Pd(PPh_3)_4$ (116 mg, 0.1 mmol), K_2CO_3 (414 mg, 3 mmol), and $SnBu_4$ (694 mg, 2 mmol) in dry DMF (10 ml) was heated under reflux for 5 h. Following removal of the solvent by distillation under reduced pressure, the residue was triturated with water and extracted with Et_2O. The crude products were purified by medium pressure liquid chromatography using a mixture of hexane and AcOEt as the developing solvent.

2-Butyl-5,6-diphenylpyrazine: colorless oil; bp 169-171°C/2 torr; ms: m/z 288 (M^+), 246 (M^+-CH_2=$CHCH_3$); ^{1}H-nmr: δ 0.98 (t, J = 7.5 Hz, 3H, $(CH_2)_3\underline{CH_3}$), 1.23-2.03 (m, 4H, $CH_2(\underline{CH_2})_2CH_3$), 2.90 (t, J = 7.5 Hz, 2H, $\underline{CH_2}(CH_2)_2CH_3$), 7.10-7.60 (m, 10H, benzene H), 8.43 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{20}H_{20}N_2$: C, 83.30; H, 6.99; N, 9.71. Found: C, 83.25; H, 6.90; N, 9.95.

2-Butyl-3,6-diethylpyrazine: colorless oil; bp 92-95°C/2 torr; ms: m/z 192 (M^+), 150 (M^+-CH_2=$CHCH_3$); ^{1}H-nmr: δ 0.93 (t, J = 7.0 Hz, 3H, $(CH_2)_3C\underline{H}_3$), 1.13-1.93 (m, 4H, $CH_2(C\underline{H}_2)_2CH_3$), 1.27 (t, J = 7.5 Hz, 6H, 2 x $CH_2C\underline{H}_3$), 2.70 (t, J = 7.0 Hz, 2H, $C\underline{H}_2(CH_2)_2CH_3$), 2.81 (q, J = 7.5 Hz, 4H, 2 x $C\underline{H}_2CH_3$), 8.17 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{12}H_{20}N_2$: C, 74.95; H, 10.48; N, 14.57. Found: C, 74.68; H, 10.50; N, 14.43.

2-Butyl-3,6-diisopropylpyrazine: colorless oil; bp 87-89°C/2 torr; ms: m/z 220 (M^+), 178 (M^+-CH_2=$CHCH_3$); ^{1}H-nmr: δ 0.90 (t, J = 6.6 Hz, 3H, $(CH_2)_3C\underline{H}_3$), 1.20 (d, J = 6.6 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.23 (d, J = 6.6 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.10-1.90 (m, 4H, $CH_2(C\underline{H}_2)_2CH_3$), 2.77 (t, J = 6.6 Hz, 2H, $C\underline{H}_2(CH_2)_2CH_3$), 2.82-3.36 (m, 2H, 2 x $C\underline{H}(CH_3)_2$), 8.25 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{14}H_{24}N_2$: C, 76.31; H, 10.98; N, 12.71. Found: C, 76.02; H, 10.95; N, 12.66.

General Procedure for Conducting Cross-coupling Reactions of Chloropyrazines and their N-Oxides with Organotin Compounds Prepared in situ from Grignard Reagents: To a THF (10 ml) solution of a Grignard reagent prepared from Mg (146 mg, 6 mmol) and an alkyl or aryl bromide (6.6 mmol), $SnCl_4$ (260 mg, 1 mmol) was added, followed by refluxing for 1 h. The solvent was removed by distillation in vacuo, and a chloropyrazine or its N-oxide (1 mmol), a palladium catalyst (0.05 mmol), K_2CO_3 (207 mg, 1.5 mmol for reaction of 2-chloro-5,6-diphenylpyrazine and 414 mg, 3 mmol in other cases) and DMF (5 ml) were added to the residue. The reaction mixture was then refluxed for 2-18 h under an argon stream. After the solvent was removed in vacuo, the residue was triturated with water and extracted with Et_2O. The crude products were purified as described above.

2-(2-Methylphenyl)-5,6-diphenylpyrazine: colorless plates (from cyclohexane); mp 158-159°C; ms: m/z 322 (M^+); ^{1}H-nmr; δ 2.53 (s, 3H, CH_3), 7.20-7.63 (m, 14H, benzene H), 8.73 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{23}H_{18}N_2$: C, 85.68; H, 5.63; N, 8.69. Found: C, 85.73; H, 5.64; N, 8.62.

2-(3-Methylphenyl)-5,6-diphenylpyrazine: colorless needles (from hexane); mp 146-147°C; ms: m/z 322 (M^+); ^{1}H-nmr; δ 2.43 (s, 3H, CH_3), 7.13-7.67 (m, 12H, benzene H), 7.80-8.00 (m, 2H, benzene H), 8.97 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{23}H_{18}N_2$: C, 85.68; H, 5.63; N, 8.69. Found: C, 85.53; H, 5.67; N, 8.58.

2-(4-Methylphenyl)-5,6-diphenylpyrazine: colorless needles (from hexane); mp 123-124°C; ms: m/z 322 (M^+); ^{1}H-nmr: δ 2.42 (s, 3H, CH_3), 7.17-7.33 (m, 12H, benzene H), 8.05 (d, J = 8.0 Hz, 2H, benzene H), 9.00 (s, 1H, pyrazine H) ppm;

Anal. Calcd for $C_{23}H_{18}N_2$: C, 85.68; H, 5.63; N, 8.69. Found: C, 85.53; H, 5.63; N, 8.54.

2-(4-Methoxyphenyl)-5,6-diphenylpyrazine: colorless plates (from MeOH); mp 171-172°C; ms: m/z 338 (M^+); ^{1}H-nmr: δ 3.87 (s, 3H, OCH_3), 7.05 (d, J = 9.0 Hz, 2H, benzene H), 7.20-7.67 (m, 10H, benzene H), 8.13 (d, J = 9.0 Hz, 2H, benzene H), 9.00 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{23}H_{18}N_2O$: C, 81.63; H, 5.36; N, 8.28. Found: C, 81.69; H, 5.41; N, 8.27.

2-(4-Chlorophenyl)-5,6-diphenylpyrazine: colorless needles (from hexane); mp 196-198°C; ms: m/z 342 (M^+); ^{1}H-nmr: δ 7.23-7.63 (m, 12H, benzene H), 8.10 (d, J = 9.0 Hz, 2H, benzene H), 9.00 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{22}H_{15}ClN_2$: C, 77.07; H, 4.41; N, 8.17. Found: C, 77.14; H, 4.34; N, 8.12.

2-Pentyl-5,6-diphenylpyrazine: colorless oil; bp 165-170°C/0.07 torr; ms: m/z 302 (M^+), 301 (M^+-H), 246 (M^+-CH_2=$CHCH_2CH_3$); ^{1}H-nmr: δ 0.93 (t, J = 6.9 Hz, 3H, $(CH_2)_4C\underline{H}_3$), 1.37-1.45 (m, 4H, $CH_2CH_2(C\underline{H}_2)_2CH_3$), 1.80-1.88 (m, 2H, $CH_2C\underline{H}_2(CH_2)_2CH_3$), 2.91 (t, J = 6.9 Hz, 2H, $C\underline{H}_2(CH_2)_3CH_3$), 7.26-7.46 (m, 10H, benzene H), 8.46 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{21}H_{22}N_2$: C, 83.40; H, 7.33; N, 9.26. Found: C, 83.37; H, 7.37; N, 9.37.

2-Octyl-5,6-diphenylpyrazine: colorless oil; bp 180-187°C/0.07 torr; ms: m/z: 344 (M^+), 343 (M^+-H), 246 (M^+-CH_2=$CH(CH_2)_4CH_3$); ^{1}H-nmr: δ 0.89 (t, J = 7.5 Hz, 3H, $(CH_2)_7C\underline{H}_3$), 1.25-1.47 (m, 10H, $CH_2CH_2(C\underline{H}_2)_5CH_3$), 1.79-1.87 (m, 2H, $CH_2C\underline{H}_2(CH_2)_5CH_3$), 2.97 (t, J = 6.9 Hz, 2H, $C\underline{H}_2(CH_2)_6CH_3$), 7.26-7.45 (m, 10H, benzene H), 8.46 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{24}H_{28}N_2$: C, 83.67; H, 8.19; N, 8.13. Found: C, 83.61; H, 8.21; N, 8.27.

3,6-Diisopropyl-2-(2-methylphenyl)pyrazine: colorless needles (from MeOH-H_2O); mp 65-66°C; ms: m/z 254 (M^+), 253 (M^+-H), 239 (M^+-CH_3); ^{1}H-nmr: δ 1.17 (d, J = 6.6 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.33 (d, J = 6.6 Hz, 6H, $CH(C\underline{H}_3)_2$), 2.10 (s, 3H, CH_3), 2.72-3.32 (m, 2H, 2 x $C\underline{H}(CH_3)_2$), 7.07-7.53 (m, 4H, benzene H), 8.47 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{17}H_{22}N_2$: C, 80.27; H, 8.72; N, 11.01. Found: C, 80.43; H, 8.68; N, 10.87.

3,6-Diisopropyl-2-(3-methylphenyl)pyrazine: colorless oil; bp 135-140°C/3 torr; ms: m/z 254 (M^+), 253 (M^+-H), 239 (M^+-CH_3); ^{1}H-nmr: δ 1.25 (d, J = 6.6 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.33 (d, J = 6.6 Hz, 6H, $CH(C\underline{H}_3)_2$), 2.38 (s, 3H, CH_3), 2.88-3.54 (m, 2H, 2 x $C\underline{H}(CH_3)_2$), 7.07-7.48 (m, 4H, benzene H), 8.40 (s, 1H, pyrazine H) ppm;

Anal. Calcd for $C_{17}H_{22}N_2$: C, 80.27; H, 8.72; N, 11.01. Found: C, 80.38; H, 8.81; N, 11.00.

3,6-Diisopropyl-2-(4-methylphenyl)pyrazine: colorless oil; bp 142-145°C/1 torr, mp 37-38°C; ms: m/z 254 (M^+), 253 (M^+-H), 239 (M^+-CH_3); ^{1}H-nmr: δ 1.23 (d, J = 6.6 HZ, 6H, $CH(C\underline{H}_3)_2$), 1.35 (d, J = 6.6 Hz, 6H, $CH(C\underline{H}_3)_2$), 2.43 (s, 3H, CH_3), 2.90-3.57 (m, 2H, 2 x $C\underline{H}(CH_3)_2$), 7.28 (d, J = 9.0 Hz, 2H, benzene H), 7.45 (d, J = 9.0 Hz, 2H, benzene H), 8.43 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{17}H_{22}N_2$: C, 80.27; H, 8.72; N, 11.01. Found: C, 80.38; H, 8.75; N, 11.05.

3,6-Diisopropyl-2-(4-methoxyphenyl)pyrazine: colorless oil; bp 152-157°C/3 torr; ms: m/z 270 (M^+), 269 (M^+-H), 255 (M^+-CH_3), 239 (M^+-OCH_3); ^{1}H-nmr: δ 1.23 (d, J = 6.6 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.33 (d, J = 6.6 Hz, 6H, $CH(C\underline{H}_3)_2$), 2.87-3.55 (m, 2H, 2 x $C\underline{H}(CH_3)_2$), 3.83 (s, 3H, OCH_3), 6.95 (d, J = 9.0 Hz, 2H, benzene H), 7.43 (d, J = 9.0 Hz, 2H, benzene H), 8.50 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{17}H_{22}N_2O$: C, 75.52; H, 8.20; N, 10.36. Found: C, 75.72; H, 8.34; N, 10.39.

2-(4-Chlorophenyl)-3,6-diisopropylpyrazine: colorless oil; bp 138-145°C/3 torr; ms: m/z 274 (M^+); ^{1}H-nmr: δ 1.23 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.33 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 2.93-3.38 (m, 2H, 2 x $C\underline{H}(CH_3)_2$), 7.42 (s, 4H, benzene H), 8.40 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{16}H_{19}ClN_2$: C, 69.93; H, 6.97; N, 10.19. Found: C, 69.75; H, 6.99; N, 10.21.

3,6-Diisopropyl-2-pentylpyrazine: colorless oil; bp 105-108°C/3 torr; ms: m/z 234 (M^+), 178 (M^+-CH_2=$CHCH_2CH_3$); ^{1}H-nmr: δ 0.91 (t, J = 6.9 Hz, 3H, $(CH_2)_4C\underline{H}_3$), 1.27 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.30 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.33-1.40 (m, 4H, $CH_2CH_2(C\underline{H}_2)_2CH_3$), 1.66-1.72 (m, 2H, $CH_2C\underline{H}_2(CH_2)_2CH_3$), 2.80 (t, J = 6.9 Hz, 2H, $C\underline{H}_2(CH_2)_3CH_3$), 2.98-3.05 (m, 1H, $C\underline{H}(CH_3)_2$), 3.21-3.28 (m, 1H, $C\underline{H}(CH_3)_2$), 8.23 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{15}H_{26}N_2$: C, 76.86; H, 11.18; N, 11.95. Found: C, 76.80; H, 11.06; N, 11.97.

3,6-Diisopropyl-2-octylpyrazine: colorless oil; bp 145-150°C/4 torr; ms: m/z 276 (M^+), 178 (M^+-CH_2=$CH(CH_2)_4CH_3$); ^{1}H-nmr: δ 0.88 (t, J = 6.9 Hz, 3H, $(CH_2)_7C\underline{H}_3$), 1.27 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.30 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.23-1.39 (m, 10H, $CH_2CH_2(C\underline{H}_2)_5CH_3$), 1.65-1.73 (m, 2H, $CH_2C\underline{H}_2(CH_2)_5CH_3$), 2.80 (t, J = 6.9 Hz, 2H, $C\underline{H}_2(CH_2)_6CH_3$), 2.98-3.05 (m, 1H, $C\underline{H}(CH_3)_2$), 3.21-3.28 (m, 1H, $C\underline{H}(CH_3)_2$), 8.23 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{18}H_{32}N_2$: C, 78.20; H, 11.67; N, 10.13. Found: C, 78.11; H, 11.57; N, 10.15.

3,6-Diisopropyl-2-(4-methylphenyl)pyrazine 4-Oxide: colorless plates (from hexane); mp 107-109°C; ms: m/z 270 (M^+), 253 (M^+-OH); ^{1}H-nmr: δ 1.30 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.40 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 2.43 (s, 3H, CH_3), 2.81-3.61 (m, 1H, 2 x $C\underline{H}(CH_3)_2$), 7.37 (m, 4H, benzene H), 7.98 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{17}H_{22}N_2O$: C, 75.52; H, 8.20; N, 10.36. Found: C, 75.59; H, 8.17; N, 10.27.

3,6-Diisopropyl-2-(4-methoxyphenyl)pyrazine 4-Oxide: colorless needles (from hexane); mp 97-98°C; ms: m/z 286 (M^+), 269 (M^+-OH); ^{1}H-nmr: δ 1.30 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.40 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 2.75-3.59 (m, 2H, 2 x $C\underline{H}(CH_3)_2$), 3.83 (s, 3H, OCH_3), 6.95 (d, J = 9.0 Hz, 2H, benzene H), 7.37 (d, J = 9.0 Hz, 2H, benzene H), 7.90 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{17}H_{22}N_2O_2$: C, 71.30; H, 7.74; N, 9.78. Found: C, 71.53; H, 7.73; N, 9.52.

2-(4-Chlorophenyl)-3,6-diisopropylpyrazine 4-Oxide: colorless prisms (from hexane); mp 98-101°C; ms: m/z 290 (M^+), 273 (M^+-OH); ^{1}H-nmr: δ 1.28 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.37 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 2.75-3.50 (m, 2H, 2 x $C\underline{H}(CH_3)_2$), 7.38 (m, 4H, benzene H), 7.92 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{16}H_{19}ClN_2O$: C, 66.09; H, 6.59; N, 9.63. Found: C, 65.80; H, 6.58; N, 9.54.

3,6-Diisopropyl-2-pentylpyrazine 4-Oxide: colorless oil; bp 120-124°C/3 torr; ms: m/z 250 (M^+), 233 (M^+-OH), 194 (M^+-CH_2=$CHCH_2CH_3$); ^{1}H-nmr: δ 0.91 (t, J = 6.9 Hz, 3H, $(CH_2)_4C\underline{H}_3$), 1.27 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.36-1.39 (m, 4H, $CH_2CH_2(C\underline{H}_2)_2CH_3$), 1.45 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.65-1.69 (m, 2H, $CH_2C\underline{H}_2(CH_2)_2CH_3$), 2.80 (t, J = 6.9 Hz, 2H, $C\underline{H}_2(CH_2)_3CH_3$), 2.87-2.94 (m, 1H, $C\underline{H}(CH_3)_2$), 3.46 (broad s, 1H, $C\underline{H}(CH_3)_2$), 7.82 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{15}H_{26}N_2O$: C, 71.95; H, 10.47; N, 11.19. Found: C, 71.65; H, 10.49; N, 10.97.

3,6-Diisopropyl-2-octylpyrazine 4-Oxide: colorless oil; bp 160-163°C/3 torr; ms: m/z 292 (M^+), 275 (M^+-OH), 194 (M^+-CH_2=$CH(CH_2)_4CH_3$); ^{1}H-nmr: δ 0.88 (t, J = 6.9 Hz, 3H, $(CH_2)_7C\underline{H}_3$), 1.27 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.26-1.38 (m, 10H, $CH_2CH_2(C\underline{H}_2)_5CH_3$), 1.45 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.64-1.68 (m, 2H, $CH_2C\underline{H}_2(CH_2)_5CH_3$), 2.80 (t, J = 6.9 Hz, 2H, $C\underline{H}_2(CH_2)_6CH_3$), 2.87-2.94 (m, 1H, $C\underline{H}(CH_3)_2$), 3.46 (broad s, 1H, $C\underline{H}(CH_3)_2$), 7.82 (s, 1H, pyrazine H) ppm; Anal. Calcd for $C_{18}H_{32}N_2O$: C, 73.92; H, 11.03; N, 9.58. Found: C, 74.07; H, 11.07; N, 9.51.

3,6-Diisopropyl-2-(4-methylphenyl)pyrazine 1-Oxide: colorless needles (from hexane); mp 160-161°C; ms: m/z 270 (M^+), 253 (M^+-OH); ^{1}H-nmr: δ 1.17 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 1.33 (d, J = 6.9 Hz, 6H, $CH(C\underline{H}_3)_2$), 2.40 (s, 3H, CH_3),

2.68-3.02 (m, 1H, C<u>H</u>$(CH_3)_2$), 3.40-3.73 (m, 1H, C<u>H</u>$(CH_3)_2$), 7.16 (d, J = 9.0 Hz, 2H, benzene H), 7.27 (d, J = 9.0 Hz, 2H, benzene H), 8.37 (s, 1H, pyrazine H) ppm; <u>Anal</u>. Calcd for $C_{17}H_{22}N_2O$: C, 75.52; H, 8.20; N, 10.36. Found: C, 75.26; H, 8.20; N, 10.61.

<u>3,6-Diisopropyl-2-(4-methoxyphenyl)pyrazine 1-Oxide</u>: colorless needles (from hexane); mp 141-142°C; ms: m/z 286 (M^+), 269 (M^+-OH); ^{1}H-nmr: δ 1.18 (d, J = 6.9 Hz, 6H, CH(C<u>H</u>$_3)_2$), 1.35 (d, J = 6.9 Hz, 6H, CH(C<u>H</u>$_3)_2$), 2.71-3.16 (m, 1H, C<u>H</u>$(CH_3)_2$), 3.40-3.85 (m, 1H, C<u>H</u>$(CH_3)_2$), 3.88 (s, 3H, OCH_3), 7.08 (d, J = 9.0 Hz, 2H, benzene H), 7.32 (d, J = 9.0 Hz, 2H, benzene H), 8.47 (s, 1H, pyrazine H) ppm; <u>Anal</u>. Calcd for $C_{17}H_{22}N_2O_2$: C, 71.30; H, 7.74; N, 9.78. Found: C, 71.17; H, 7.77; N, 9.56.

<u>2-(4-Chlorophenyl)-3,6-diisopropylpyrazine 1-Oxide</u>: colorless plates (from hexane); mp 126-129°C; ms: m/z 290 (M^+), 273 (M^+-OH); ^{1}H-nmr: δ 1.17 (d, J = 6.9 Hz, 6H, CH(C<u>H</u>$_3)_2$), 1.33 (d, J = 6.9 Hz, 6H, CH(C<u>H</u>$_3)_2$), 2.60-3.05 (m, 1H, C<u>H</u>$(CH_3)_2$), 3.35-3.80 (m, 1H, C<u>H</u>$(CH_3)_2$), 7.27 (d, J = 9.0 Hz, 2H, benzene H), 7.52 (d, J = 9.0 Hz, 2H, benzene H), 8.43 (s, 1H, pyrazine H) ppm; <u>Anal</u>. Calcd for $C_{16}H_{19}ClN_2O$: C, 66.09; H, 6.59; N, 9.63. Found: C, 66.33; H, 6.60; N, 9.65.

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