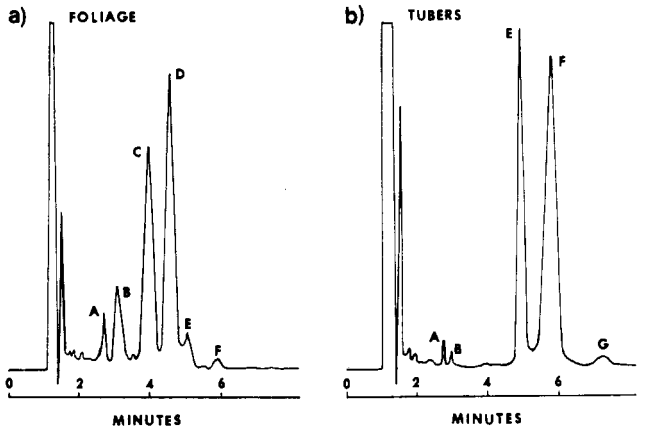


Figure 2. HPLC separation of glycoalkaloids in the foliage and tubers of high-leptine PI 458310-1: (a) foliar glycoalkaloids; (b) tuber glycoalkaloids (greened tubers). Peaks: A = leptinine II; B = leptinine I; C = leptine II; D = leptine I; E = α-solanine; F = α-chaconine; G = β-chaconine.

dition, with the HPLC method of analysis, the relative concentration of each glycoalkaloid present in the ammonia-precipitated extract can be estimated.

It remains to be determined whether the gene(s) for acetylating solanidine will be expressed in *S. chacoense* × *S. tuberosum* hybrids. The low frequency of high-leptine sibs among the 720 in our *S. chacoense* sample possibly indicates that recessive gene(s) control the high levels of leptine synthesis. Even if the ability to synthesize high leptine levels such as the 100 mg % that causes adults and larvae to cease feeding (Kuhn and Low, 1961c; Struckow and Low, 1961) cannot be transferred to *S. tuberosum*, the reported potency of leptine I is so high that considerably lower levels might still partially deter larval and adult feeding. A report on the CPB resistance of the six *S. chacoense* clones in Table II will be published subsequently.

ACKNOWLEDGMENT

We express our appreciation to S. F. Osman, ERRC, Philadelphia, PA, for advice on the chemistry of the leptines and the GC/MS analyses.

LITERATURE CITED

Buhr, H.; Toball, R.; Schreiber, K. *Entomol. Exptl. Appl.* **1958**, *1*, 209.
Bushway, R. J.; Wilson, A. M.; Bushway, A. A. *Am. Potato J.* **1980**, *57*, 561.
Deahl, K. L.; Young, R. J.; Sinden, S. L. *Am. Potato J.* **1973**, *50*, 248.
Gregory, P.; Sinden, S. L.; Osman, S. F.; Tingey, W. M.; Chessin, D. A. *J. Agric. Food Chem.* **1981**, *29*, 1212.
Heftman, E. *Lloydia* **1967**, *30*, 209.
King, R. R. *J. Assoc. Off. Anal. Chem.* **1980**, *63*, 1226.
Kuhn, R.; Low, I. *Chem. Ber.* **1961a**, *94*, 1088.
Kuhn, R.; Low, I. *Chem. Ber.* **1961b**, *94*, 1096.
Kuhn, R.; Low, I. *Tagungsber. Deut. Akad. Landwirtschaftswiss.* **1961c**, *27*, 7.
Morris, S. C.; Lee, T. H. *J. Chromatogr.* **1981**, *219*, 403.
Osman, S. F.; Sinden, S. L. *J. Agric. Food Chem.* **1977**, *25*, 955.
Sanford, L. L.; Sinden, S. L. *Am. Potato J.* **1972**, *49*, 209.
Sanford, L. L.; Ladd, T. L.; Sinden, S. L.; Cantelo, W. W. *Am. Potato J.* **1984**, *61*, 405.
Schreiber, K. In "The Alkaloids"; Manske, R. H. F., Ed.; Academic Press: New York, 1968; Vol. X, Chapter 1.
Schwarze, P. *Zuchter* **1962**, *32*, 155.
Schwarze, P. *Zuchter* **1963**, *33*, 275.
Shih, M.-J.; Kuc, J. *Phytochemistry* **1974**, *13*, 997.
Sinden. S. L.; Webb, R. E. *Am. Potato J.* **1972**, *49*, 334.
Sinden, S. L.; Sanford, L. L.; Osman, S. F. *Am. Potato J.* **1980**, *57*, 331.
Sinden, S. L.; Sanford, L. L. *Am. Potato J.* **1981**, *58*, 305.
Sinden, S. L.; Sanford, L. L.; Webb, R. E. *Am. Potato J.* **1984**, *61*, 141.
Struckow, B.; Low, I. *Entomol.* Expt. *Appl.* **1961**, *4*, 133.
Tingey, W. M. *Am. Potato J.* **1984**, *61*, 157.
Torka, M. *Am. Potato J.* **1950**, *27*, 263.
Varma, R.; Varma R. S.; Wardi, A. H. *J. Chromatogr.* **1973**, *77*, 222.
Zitnak, A.; Johnston, G. R. *Am. Potato J.* **1970**, *47*, 256.

Received for review July 22, 1985. Revised manuscript received November 4, 1985. Accepted January 21, 1986. Reference to a brand or firm name does not constitute endorsement by the U.S. Department of Agriculture over others of a similar nature not mentioned.

Synthesis of Alkoxy-, (Alkylthio)-, Phenoxy-, and (Phenylthio)pyrazines and Their Olfactive Properties

Hideki Masuda and Satoru Mihara*

The following series of 22 new pyrazines have been synthesized: two 5-alkyl-2-methoxy-3-methylpyrazines, four 5-alkyl-2-ethoxy-3-methylpyrazines, four 5-alkyl-3-methyl-2-phenoxypyrazines, three 5-alkyl-3-methyl-2-(methylthio)pyrazines, five 5-alkyl-2-(ethylthio)-3-methylpyrazines, and four 5-alkyl-3-methyl-2-(phenylthio)pyrazines. The IR, NMR, and mass spectra of these pyrazines were measured. $M^+ - SH$ peaks were observed for most of the mass spectra of (methylthio)- and (ethylthio)pyrazines. Odor descriptions and odor threshold values of a number of these pyrazines are presented and compared with each other.

Because of the characteristic flavors that possess roasted or smoky odors and low threshold values, alkoxy- and (alkylthio)pyrazines have been widely used as flavor ingredients (Maga, 1982). In 1969 (a,b) Buttery et al. reported the isolation of 2-isobutyl-3-methoxypyrazine from green peppers. The extremely potent odor was shown to be a character-impact compound of bell peppers with an

Ogawa & Company, Limited, 6-32-9 Akabanenishi Kita-Ku, Tokyo 115, Japan.

0021-8561/86/1434-0377$01.50/0

Table I. Yields, Boiling Points, and Precursors of New Pyrazines (I)

no.	pyrazine (I) R^1	pyrazine (I) R^2	yield,[a] %	bp, °C (mmHg)	precursor for 5-subst
1	OCH_3	$CH(CH_3)_2$	69	61 (2)	MeONa
2	OCH_3	$CH(CH_3)C_2H_5$	63	89 (7)	MeONa
3	OC_2H_5	$CH(CH_3)_2$	65	64 (1)	EtONa
4	OC_2H_5	$CH(CH_3)C_2H_5$	72	85 (3)	EtONa
5	OC_2H_5	$CH_2CH(CH_3)C_2H_5$	68	106 (4)	EtONa
6	OC_2H_5	$CH_2CH(CH_3)C_3H_7$	69	104 (3)	EtONa
7	OC_6H_5	$CH(CH_3)_2$	42	135 (2)	PhONa
8	OC_6H_5	$CH(CH_3)C_2H_5$	50	145 (3)	PhONa
9	OC_6H_5	$CH_2CH(CH_3)C_2H_5$	62	141 (1)	PhONa
10	OC_6H_5	$CH_2CH(CH_3)C_3H_7$	57	154 (2)	PhONa
11	SCH_3	$CH(CH_3)_2$	90	107 (7)	MeSNa
12	SCH_3	$CH(CH_3)C_2H_5$	91	100 (2)	MeSNa
13	SCH_3	$CH_2CH(CH_3)C_2H_5$	81	115 (0.5)	MeSNa
14	SC_2H_5	$CH(CH_3)_2$	93	94 (2)	EtSNa
15	SC_2H_5	$CH(CH_3)C_2H_5$	86	96 (1)	EtSNa
16	SC_2H_5	$CH_2CH(CH_3)_2$	76	99 (1)	EtSNa
17	SC_2H_5	$CH_2CH(CH_3)C_2H_5$	78	112 (1)	EtSNa
18	SC_2H_5	$CH_2CH(CH_3)C_3H_7$	84	120 (1)	EtSNa
19	SC_6H_5	$CH(CH_3)_2$	82	135 (1)	PhSNa
20	SC_6H_5	$CH(CH_3)C_2H_5$	79	120 (2)	PhSNa
21	SC_6H_5	$CH_2CH(CH_3)C_2H_5$	68	158 (1)	PhSNa
22	SC_6H_5	$CH_2CH(CH_3)C_3H_7$	71	167 (1)	PhSNa

[a] Relative to the quantity of the corresponding chloropyrazine used.

Table II. Spectral Data of New Pyrazines

no.	IR (neat), cm^{-1}	NMR ($CDCl_3$), δ	MS, m/z (%)
1	2870, 1580, 1550, 1450, 1370, 1250, 1180, 1030, 990, 890	1.28 (6 H, d, J = 7 Hz, $CH(CH_3)_2$), 2.40 (3 H, s, $ArCH_3$), 2.93 (1 H, septet, J = 7 Hz, $CH(CH_3)_2$), 3.92 (3 H, s, OCH_3), 7.78 (1 H, s, ring H)	166 (100), 151 (83), 138 (54), 132 (30), 119 (60), 108 (18), 94 (20), 82 (22), 78 (24), 67 (17), 55 (20), 42 (26)
2	2870, 1580, 1550, 1445, 1370, 1230, 1170, 1030, 980, 880	0.80 (3 H, t, J = 7 Hz, CH_2CH_3), 1.23 (3 H, d, J = 7 Hz, $CHCH_3$), 1.4–2.0 (2 H, m, CH_2CH_3), 2.40 (3 H, s, $ArCH_3$), 2.60 (1 H, septet, J = 7 Hz, $CHCH_3$), 3.89 (3 H, s, OCH_3), 7.77 (1 H, s, ring H)	180 (40), 165 (50), 152 (100), 138 (37), 118 (48), 109 (16), 94 (10), 78 (16)
3	2870, 1580, 1550, 1475, 1455, 1420, 1380, 1345, 1250, 1180, 1040, 1000, 890	1.26 (3 H, d, J = 7 Hz, $CH(CH_3)_2$), 1.40 (3 H, t, J = 7 Hz, OCH_2CH_3), 2.40 (3 H, s, $ArCH_3$), 2.93 (1 H, septet, J = 7 Hz, $CH(CH_3)_2$), 4.40 (2 H, q, J = 7 Hz, OCH_2CH_3), 7.80 (1 H, s, ring H)	180 (50), 165 (68), 152 (100), 137 (63), 124 (28), 121 (30), 119 (28), 109 (65), 68 (18), 42 (16)
4	2870, 1580, 1550, 1470, 1455, 1420, 1380, 1345, 1240, 1175, 1040, 890	0.83 (3 H, t, J = 7 Hz, CH_2CH_3), 1.23 (3 H, d, J = 7 Hz, $CHCH_3$), 1.38 (3 H, t, J = 7 Hz, OCH_2CH_3), 1.4–2.0((2 H, m, CH_2CH_3), 2.3–2.8 (1 H, m, $CHCH_2$), 2.40 (3 H, s, $ArCH_3$), 4.33 (2 H, q, J = 7 Hz, OCH_2CH_3), 7.78 (1 H, s, ring H)	194 (50), 179 (54), 166 (100), 151 (21), 138 (40), 137 (50), 109 (10)
5	2870, 1580, 1545, 1450, 1410, 1380, 1340, 1170, 1040, 890	0.87 (3 H, d, J = 7 Hz, $CHCH_3$), 0.89 (3 H, t, J = 7 Hz, CH_2CH_3), 1.1–1.5 (2 H, m, CH_2CH_3), 1.37 (3 H, t, J = 7 Hz, OCH_2CH_3) 1.7–2.1 (1 H, m, $CHCH_3$), 2.39 (3 H, s, $ArCH_3$), 2.4–2.9 (2 H, m, $ArCH_2$), 4.37 (2 H, q, J = 7 Hz, OCH_2CH_3), 7.73 (1 H, s, ring H)	208 (24), 193 (18), 179 (16), 165 (10), 152 (100), 124 (88), 101 (20)
6	2870, 1580, 1555, 1460, 1420, 1380, 1350, 1170, 1040, 890	0.87 (3 H, d, J = Hz, $CHCH_3$), 0.88 (3 H, t, J = 7 Hz, CH_2CH_3), 1.1–1.5 (4 H, m, $(CH_2)_2CH_3$), 1.7–2.1 (1 H, m, $CHCH_3$), 2.37 (3 H, t, J = 7 Hz, OCH_2CH_3), 2.4–2.9 (2 H, m, $ArCH_2$), 4.35 (2 H, q, J = 7 Hz, OCH_2CH_3), 7.72 (1 H, s, ring H)	222 (31), 207 (11), 193 (42), 179 (13), 165 (25), 152 (99), 124 (100), 95 (28), 80 (6), 55 (7), 43 (26)
7	3030, 1590, 1540, 1490, 1370, 1240, 1210, 1190, 1170, 1000, 750, 690	1.15 (6 H, d, J = 7 Hz, $CH(CH_3)_2$), 2.53 (3 H, s, $ArCH_3$), 2.86 (1 H, septet, J = 7 Hz, $CH(CH_3)_2$), 6.9–7.5 (5 H, m, OC_6H_5), 7.90 (1 H, s, pyrazine ring H)	228 (100), 213 (22), 200 (8), 185 (100), 135 (10)
8	3030, 1590, 1535, 1490, 1370, 1230, 1200, 1160, 740, 680	0.77 (3 H, t, J = 7 Hz, CH_2CH_3), 1.10 (3 H, d, J = 7 Hz, $CHCH_3$), 1.3–1.8 (2 H, m, CH_2CH_3), 2.3–2.9 (1 H, m, $CHCH_3$), 2.53 (3 H, s, $ArCH_3$), 6.9–7.5 (5 H, m, OC_6H_5), 7.96 (1 H, s, pyrazine ring H)	242 (54), 227 (32), 214 (100), 200 (26), 185 (40)
9	3030, 1600, 1540, 1490, 1460, 1380, 1210, 1170, 900, 840, 760, 690	0.82 (3 H, d, J = 7 Hz, $CHCH_3$), 0.83 (3 H, t, J = 7 Hz, CH_2CH_3), 1.0–1.5 (2 H, m, CH_2CH_3), 1.6–2.1 (1 H, m, $CHCH_3$), 2.4–2.8 (2 H, m, $ArCH_2$), 2.56 (3 H, s, $ArCH_3$), 6.8–7.5 (5 H, m, OC_6H_5), 7.89 (1 H, s, pyrazine ring H)	256 (2), 241 (4), 227 (3), 200 (100), 171 (2)

Table II (Continued)

no.	IR (neat), cm^{-1}	NMR ($CDCl_3$), δ	MS, m/z (%)
10	3030, 1590, 1540, 1490, 1460, 1370, 1210, 1170, 1155, 1020, 760, 690	0.80 (3 H, d, J = 7 Hz, $CHCH_3$), 0.82 (3 H, t, J = 7 Hz, CH_2CH_3), 1.1–1.5 (4 H, m, $(CH_2)_2CH_3$), 1.5–2.1 (1 H, m, $CHCH_3$), 2.3–2.7 (2 H, m, $ArCH_2$), 2.53 (3 H, s, $ArCH_3$), 6.9–7.5 (5 H, m, OC_6H_5), 7.90 (1 H, s, pyrazine ring H)	270 (4), 241 (7), 227 (2), 200 (100), 171 (1)
11	2870, 1560, 1530, 1475, 1440, 1380, 1340, 1300, 1180, 1100, 990, 920	1.30 (6 H, d, J = 7 Hz, $CH(CH_3)_2$), 2.40 (3 H, s, $ArCH_3$), 2.53 (3 H, s, SCH_3), 3.00 (1 H, m, $CH(CH_3)_2$), 7.90 (1 H, s, ring H)	182 (100), 167 (56), 149 (70), 132 (28), 121 (30), 119 (28), 92 (10), 67 (12), 43 (18)
12	2870, 1560, 1520, 1460, 1440, 1380, 1340, 1310, 1180, 1100, 985, 915	0.93 (3 H, t, J = 7 Hz, CH_2CH_3), 1.30 (3 H, d, J = 7 Hz, $CHCH_3$), 1.4–1.9 (2 H, m, CH_2CH_3), 2.43 (3 H, s, $ArCH_3$), 2.52 (3 H, s, SCH_3), 2.77 (1 H, m, $CHCH_3$), 7.90 (1 H, s, ring H)	196 (91), 181 (50), 168 (100), 167 (30), 163 (30), 154 (22), 119 (20)
13	2870, 1560, 1520, 1460, 1440, 1380, 1330, 1310, 1170, 1100, 985	0.89 (3 H, d, J = 7 Hz, $CHCH_3$), 1.02 (3 H, t, J = 7 Hz, CH_2CH_3), 1.1–1.5 (2 H, m, CH_2CH_3), 1.6–2.2 (1 H, m, $CHCH_3$), 2.47 (3 H, s, $ArCH_3$), 2.5–2.9 (2 H, m, $ArCH_2$), 2.56 (3 H, s, SCH_3), 7.96 (1 H, s, ring H)	210 (16), 195 (8), 181 (3), 154 (100), 106 (8)
14	2870, 1560, 1530, 1470, 1440, 1380, 1335, 1180, 1100, 1080, 980	1.33 (3 H, t, J = 7 Hz, SCH_2CH_3), 1.35 (6 H, d, J = 7 Hz, $CH(CH_3)_2$), 2.40 (3 H, s, $ArCH_3$), 3.10 (1 H, septet, J = 7 Hz, $CH(CH_3)_2$), 3.17 (2 H, q, J = 7 Hz, SCH_2CH_3), 7.90 (1 H, s, ring H)	196 (69), 181 (26), 168 (25), 163 (100), 153 (12), 136 (16), 121 (17)
15	2870, 1530, 1460, 1440, 1380, 1315, 1180, 1100, 980, 915	0.93 (3 H, t, J = 7 Hz, CH_2CH_3), 1.28 (3 H, d, J = 7 Hz, $CHCH_3$), 1.38 (3 H, t, J = 7 Hz, SCH_2CH_3), 1.5–2.1 (2 H, m, CH_2CH_3), 2.41 (3 H, s, $ArCH_3$), 2.5–3.0 (1 H, m, $CHCH_3$), 3.18 (2 H, q, J = 7 Hz, SCH_2CH_3), 7.88 (1 H, s, ring H)	210 (91), 195 (51), 182 (79), 177 (100), 154 (50), 148 (30), 121 (28)
16	2860, 1550, 1520, 1440, 1375, 1320, 1165, 1100, 980	0.92 (6 H, d, J = 7 Hz, $CH(CH_3)_2$), 1.33 (3 H, t, J = 7 Hz, SCH_2CH_3), 1.6–2.4 (1 H, m, $CH(CH_3)_2$), 2.40 (3 H, s, $ArCH_3$), 2.55 (2 H, d, J = 7 Hz, $ArCH_2$), 3.16 (2 H, q, J = 7 Hz, SCH_2CH_3), 7.83 (1 H, s, ring H)	210 (82), 195 (30), 177 (60), 168 (100), 150 (10), 140 (37), 134 (22), 107 (18)
17	2870, 1560, 1530, 1450, 1380, 1335, 1320, 1180, 1105, 985	0.89 (3 H, d, J = 7 Hz, $CHCH_3$), 0.92 (3 H, t, J = 7 Hz, CH_2CH_3), 1.37 (3 H, t, J = 7 Hz, SCH_2CH_3), 1.5–2.3 (3 H, m, $CHCH_2CH_3$), 2.42 (3 H, s, $ArCH_3$), 2.43 (1 H, dd, J = 13, 7.5 Hz, $ArCHH$), 2.75 (1 H, dd, J = 13, 6 Hz, $ArCHH$), 3.20 (2 H, q, J = 7 Hz, SCH_2CH_2), (1 H, s, ring H)	224 (43), 209 (13), 191 (28), 168 (100), 140 (26), 136 (18), 107 (10)
18	2870, 1560, 1530, 1440, 1380, 1330, 1170, 1100, 980	0.88 (3 H, t, J = Hz, CH_2CH_3), 0.89 (3 H, d, J = 7 Hz, $CHCH_3$), 1.35 (3 H, t, J = 7 Hz, SCH_2CH_3), 1.6–2.3 (5 H, m, $CHCH_3(CH_2)_2CH_3$), 2.43 (1 H, dd, J = 13, 7.5 Hz, $ArCHH$), 2.73 (1 H, dd, J = 13, 6 Hz, $ArCHH$), 3.18 (2 H, q, J = 7 Hz, SCH_2CH_3), 7.87 (1 H, s, ring H)	238 (22), 223 (2), 209 (16), 205 (20), 195 (6), 168 (100), 140 (10)
19	3030, 1585, 1520, 1480, 1440, 1380, 1330, 1300, 1170, 1090, 980, 750, 690	1.03 (6 H, d, J = 7 Hz, $CH(CH_3)_2$), 2.51 (3 H, s, $ArCH_3$), 2.73 (1 H, m, $CH(CH_3)_2$), 7.0–7.6 (5 H, m, SC_6H_5), 7.97 (1 H, s, pyrazine ring H)	244 (100), 229 (78), 216 (30), 185 (4), 135 (10), 119 (4)
20	3030, 1580, 1520, 1475, 1440, 1375, 1300, 1170, 1080, 980, 900, 750, 690	0.69 (3 H, t, J = 7 Hz, CH_2CH_3), 0.90 (3 H, d, J = 7 Hz, $CHCH_3$), 1.2–1.7 (2 H, m, CH_2CH_3), 2.4–2.8 (1 H, m, $CHCH_3$), 2.45 (3 H, s, $ArCH_3$), 7.2–7.6 (5 H, m, SC_6H_5), 7.90 (1 H, s, pyrazine ring H)	258 (38), 243 (32), 230 (100), 216 (18), 119 (2)
21	3030, 1580, 1520, 1440, 1380, 1330, 1170, 1085, 740, 690	0.72 (3 H, d, J = 7 Hz, $CHCH_3$), 0.83 (3 H, t, J = 7 Hz, CH_2CH_3), 1.0–1.4 (2 H, m, CH_2CH_3), 1.4–2.0 (1 H, m, $CHCH_3$), 2.3–2.8 (2 H, m, $ArCH_2$), 2.52 (3 H, s, $ArCH_3$), 7.0–7.7 (5 H, m, SC_6H_5), 7.98 (1 H, s, pyrazine ring H)	272 (10), 257 (7), 243 (7), 216 (100), 172 (1), 106 (2)
22	3030, 1580, 1520, 1480, 1440, 1380, 1320, 1300, 1170, 1080, 980, 750, 690	0.73 (3 H, d, J = 7 Hz, $CHCH_3$), 0.89 (3 H, t, J = 7 Hz, CH_2CH_3), 1.0–1.5 (4 H, m, $(CH_2)_2CH_3$), 1.5–2.0 (1 H, m, $CHCH_3$), 2.3–2.9 (2 H, m, $ArCH_2$), 2.53 (3 H, s, $ArCH_3$), 7.2–7.7 (5 H, m, SC_6H_5), 7.98 (1 H, s, pyrazine ring H)	286 (8), 257 (5), 243 (5), 216 (100), 106 (1)

odor threshold of 2 parts/10^{12} parts of water.

The presence of the trisubstituted alkoxypyrazines such as 2-methoxy-3-isopropyl-5-methylpyrazine and 3-*sec*-butyl-2-methoxy-5-methylpyrazine in galbanum oil (Burrell et al., 1970) and Ginseng Radix (Iwabuchi et al., 1984) has been reported.

2-Methoxy-3-isopropyl-5-methylpyrazine and 3-*sec*-butyl-2-methoxy-5-methylpyrazine, which have green and floral odors, have low threshold values of 0.05 and 2.0 ppb, respectively. Therefore, they are quite effective in flavor contribution even in trace quantities.

Masuda et al. (1980, 1981) reported a new synthetic method of pyrazines including 5-alkyl-2,3-dimethylpyrazines, alkoxypyrazines, a phenoxypyrazine, (alkylthio)pyrazines, and a (phenylthio)pyrazine.

In this report, we have synthesized other representatives of the trisubstituted alkoxypyrazines for an olfactive study. Odor descriptions were given. We measured the odor

Table III. Odor Descriptions of Substituted Pyrazines (I)

R^2	R¹						
	CH_3	OCH_3	OC_2H_5	OC_6H_5	SCH_3	SC_2H_5	SC_6H_5
H	nutty, roasted, sweet	nutty, roasted, sweet	nutty, roasted, weakly green, earthy		nutty, sweet, weakly green		
$CH(CH_3)_2$	sweet, maple-like, brown	weakly chemical, sour	brown, chemical, green, vegetable, earthy	vegetable, green, asparagus-like, green pepper like	petrolic, charcoal-like, phenolic, weakly floral	oily, petrolic, rubber, charcoal-like	musky, cosmetic, weakly green
$CH(CH_3)C_2H_5$	herb, medicine-like, brown	chemical, petrolic	weakly green, burdock-like	sweet, mild, weakly earthy	oily, chemical	sharp, green, oily, burdock-like	sandalwood-like, weakly cosmetic
$CH_2CH(CH_3)_2$	brown, mild, woody	burdock-like, ginseng-like, weakly green	sweet, weakly green	green, earthy, burdock-like	burdock-like, green, vegetable	chemical, petrolic	green, burdock-like, nutty
$CH_2CH(CH_3)C_2H_5$	sweet, brown, nutty	burdock-like, weakly green	green, burdock-like, green beans like	weak, sweet, fruity	metallic, burdock-like	bitter, rubber, cresol-like	musky, sandlewood-like cosmetic
$CH_2CH(CH_3)C_3H_7$		vegetable, green beans like, green	green, burdock-like, vegetable, asparagus-like	green, waxy, green beans like, sweet	green, earthy, green beans like	green, burdock-like, sweet	floral, citrusy, weakly green, sweet

thresholds of the obtained pyrazines in this paper and some pyrazines that were synthesized by Masuda et al. (1980, 1981) and Kitamura and Shibamoto (1981).

EXPERIMENTAL SECTION

Materials. All starting chemicals were obtained from reliable commercial sources and used without further purification. IR, NMR, and mass spectral data were obtained on a Jasco IR-S, a JNM-PMX 60, and a Hitachi Model RMU-6M, respectively.

Synthesis of 2,3-Dimethylpyrazine. This was synthesized by the methods described by Akiyama et al. (1978).

Synthesis of 5-Alkyl-2,3-dimethylpyrazines. The procedure used for the synthesis of these compounds was the same as that described previously (Masuda et al., 1980; Kitamura and Shibamoto, 1981).

Synthesis of 2-Alkoxy-5-alkyl-3-methylpyrazines, 5-Alkyl-3-methyl-2-phenoxypyrazines, 5-Alkyl-2-(alkylthio)-3-methylpyrazines, and 5-Alkyl-3-methyl-2-(phenylthio)pyrazines. These compounds were prepared by the method described by Masuda et al. (1981).

Synthesis of 2-Methoxy-3-methylpyrazine, 2-Ethoxy-3-methylpyrazine, and 2-Methyl-3-(methylthio)pyrazine. 5,6-Dihydro-3-methyl-2(1*H*)-pyrazinone was obtained by the method described by Masuda et al. (1981). This compound (30 g, 0.27 mol) and MnO_2 (48.8 g, 0.56 mol) were added in 32 g of methanol. KOH (19.4 g) in a 40 g of methanol solution was dropped into the above mixture. This mixture was refluxed for 2 h. The reaction mixture was filtered and the filtrate concentrated to a 100-g weight on a rotary flash evaporator. NH_4Cl (25 g) in a 50 g of aqueous solution was added to the above solution. The solution was extracted with two 50-g portions of chloroform, and the extract was dried over anhydrous sodium sulfate. 3-Methyl-2(1*H*)-pyrazinone (11.8 g) was obtained by recrystallization from benzene in 40% yield. It had the following spectra: IR (Nujol) (cm^{-1}) 1670, 1650, 1540, 1460, 1370, 1240, 1220, 810; NMR ($CDCl_3$) δ 2.49 (3 H, s, CH_3), 7.25 (1 H, d, J = 7 Hz, ring H at 6-position), 7.40 (1 H, d, J = 7 Hz, ring H at 5-position), 9.6 (1 H, br s, NH); MS, m/z (%) 100 (100, M^+), 82 (56), 81 (50), 55 (10), 54 (12), 42 (10).

3-Methyl-2(1*H*)-pyrazinone was converted to 2-chloro-3-methylpyrazine, which was subsequently reacted with sodium methoxide, sodium ethoxide, and sodium thiomethoxide to obtain the desired 2-methoxy-3-methyl-, 2-ethoxy-3-methyl-, and 2-methyl-3-(methylthio)pyrazine, respectively.

Sensory Evaluation. Threshold values for the pyrazines were determined by the "$^2/_5$ test" (selecting the same two out of five samples) employed by Amoore et al. (1970). The water solution (20 ± 1 °C) was measured (20 mL) into clean 50-mL glass cups. If the compound was detectable at a certain level, it was tested until a level was reached where the compound was no longer detectable. The concentration of pyrazines was decreased by a factor of $1/10^{1/2}$. The odor thresholds were a geometrical average of the seven panelists responses.

The panelists (seven males) ranged in age from approximately 22 to 29 years of age. They had extensive experience and proven reliability in odor judgements.

The odor characteristics of the pyrazines were evaluated at about 100 times higher concentrations than the thresholds.

All judgement were conducted in a room equipped with individual booths maintained at a temperature of 23 ± 1 °C and 60% relative humidity by means of air conditioner. The sessions were conducted in midmorning of every day.

Table IV. Odor Thresholds[a] of Substituted Pyrazines (I)

R^2	R^1 = CH_3	OCH_3	OC_2H_5	OC_6H_5	SCH_3	SC_2H_5	SC_6H_5
H	400[b]	3[b,d]	0.8		4		
	2500[c]	4[e]					
$CH(CH_3)_2$	530	26	120	370	16	85	160
$CH(CH_3)C_2H_5$	680	32	12	72	19	61	61
$CH_2CH(CH_3)_2$	770	0.18	16	320	15	32	100
$CH_2CH(CH_3)C_2H_5$	3200	0.01	6	120	0.01	2.5	56
$CH_2CH(CH_3)C_3H_7$		1.2	3	140	12	56	160

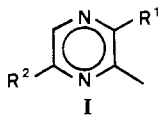
[a] Threshold in ppb parts of water. [b] Calabretta, 1975. [c] Guadagni et al., 1972. [d] Calabretta, 1978. [e] Seifert et al., 1970.

RESULTS AND DISCUSSION

The yields and boiling points of the new pyrazines are shown in Table I. The spectral data of these pyrazines are listed in Table II. The mass spectra of alkylpyrazine derivatives showed similar systematic fragmentations starting from McLafferty rearrangement and γ-cleavage (Iwabuchi et al., 1984; Kitamura and Shibamoto, 1981). $M^+ - SH$ peaks were observed for most of the (methylthio)- and (ethylthio)pyrazines.

$M^+ - OC_6H_5$ and $M^+ - SC_6H_5$ peaks were present in some of the mass spectra of the phenoxy- and (phenylthio)pyrazines, respectively.

The odor descriptions of substituted pyrazines (I) are listed in Table III. A comparison of the odor descriptions



I

leads us to the following remarks: 2-Substituted 3-methylpyrazines (I, R^2 = H) and 5-alkyl-2,3-dimethylpyrazines (I, $R^1 = CH_3$) have nutty and/or brown notes. 5-Alkyl-3-methyl-2-(phenylthio)pyrazines (I, $R^1 = SC_6H_5$) have cosmetic or floral odors except for 5-isobutyl-3-methyl-2-(phenylthio)pyrazine. Most other pyrazines have more or less green odors. The lower alkyl-substituted pyrazines (I, $R^2 = CH(CH_3)_2$ and $CH(CH_3)C_2H_5$) tend to have more chemical or oily odors, while the higher substituted pyrazines (I, $R^2 = CH_2CH(CH_3)_2$, $CH_2CH(CH_3)C_2H_5$, $CH_2CH(CH_3)C_3H_7$) have more burdock-like and/or green notes. Table IV lists the odor threshold data of a number of substituted pyrazines collected from literature and our own measurements. In general, the influence of alkyl substituents at R^2 on the odor thresholds increases with a decreasing molecular weight of R^1 except for 2,3-dimethylpyrazines. Replacement of the methyl group at R^1 in compound I by an alkoxy, phenoxy, alkylthio, and phenylthio group resulted in a decrease in odor thresholds. 2-Methoxy-3-methyl-5-(2-methylbutyl)pyrazine and 3-methyl-5-(2-methylbutyl)-2-(methylthio)pyrazine (**13**) are the most potent odorants of the pyrazines shown in Table IV. On the other hand, the odor potency of 2,3-dimethyl-5-(2-methylbutyl)pyrazine is much lower (about $10^5\times$). The order of decreasing odor thresholds is as given in the following: $R^1 = OCH_3, SCH_3 \leq R^1 = OC_2H_5, SC_2H_5 < R^1 = OC_6H_5, SC_6H_5 < R^1 = CH_3$. This could be attributed to hydrogen-bond formation resulting from the O or S atom of these groups (R^1) (Calabretta, 1978).

In connection with the measurements of the threshold of methoxy-disubstituted pyrazines, Parliment and Epstein (1973) and Seifert et al. (1972) proposed that one side of the ring must be unsubstituted to obtain extremely potent odorants. Our measurements are in agreement with the supposition when a isopropyl or 1-methylpropyl group is introduced at the 5-position of the pyrazine ring (compare 5-isopropyl-2-methoxy-3-methylpyrazine and 2-methoxy-3-methyl-5-(1-methylpropyl)pyrazine with 2-methoxy-3-methylpyrazine). But, the reverse was found here for the higher alkyl-substituted pyrazines (see 5-isobutyl-2-methoxy-3-methylpyrazine, 2-methoxy-3-methyl-5-(2-methylbutyl)pyrazine, and 2-methoxy-3-methyl-5-(2-methylpentyl)pyrazine. In 5-alkyl-3-methyl-2-(methylthio)pyrazines (I, $R^1 = SCH_3$), there is a similar tendency toward the substituent effect on the threshold values. It appears that the oxygen of the methoxy, ethoxy, and phenoxy groups can be replaced by sulfur with a quantitative (odor thresholds, see Table IV) but not qualitative change in character (odor descriptions, see Table III).

Registry No. 1, 38346-76-8; 2, 99784-13-1; 3, 99784-14-2; 4, 99784-15-3; 5, 99784-16-4; 6, 99784-17-5; 7, 99784-18-6; 8, 99784-19-7; 9, 99784-20-0; 10, 99784-21-1; 11, 99784-22-2; 12, 99784-23-3; 13, 99784-24-4; 14, 99784-25-5; 15, 99784-26-6; 16, 99784-27-7; 17, 99784-28-8; 18, 99784-29-9; 19, 99784-30-2; 20, 99784-31-3; 21, 99784-32-4; 22, 99784-33-5; I (R^1 = Me, R^2 = H), 5910-89-4; I (R^1 = OMe, R^2 = H), 2847-30-5; I (R^1 = OEt, R^2 = H), 32737-14-7; I (R^1 = SMe, R^2 = H), 2882-20-4; I (R^1 = Me, R^2 = Pr-*i*), 40790-21-4; I (R^1 = Me, R^2 = Bu-*s*), 32263-00-6; I (R^1 = OMe, R^2 = Bu-*i*), 78246-20-5; I (R^1 = OEt, R^2 = Bu-*i*), 78246-14-7; I (R^1 = OPh, R^2 = Bu-*i*), 78246-16-9; I (R^1 = SPh, R^2 = Bu-*i*), 78246-19-2; I (R^1 = Me, R^2 = Bu-*i*), 54410-83-2; I (R^1 = SMe, R^2 = Bu-*i*), 78246-17-0; I (R^1 = Me, $R^2 = CH_2CH(CH_3)C_2H_5$), 75492-01-2; I (R^1 = OMe, $R^2 = CH_2CH(CH_3)C_2H_5$), 78246-21-6; I (R^1 = OMe, $R^2 = CH_2CH(CH_3)C_3H_7$), 78261-14-0; I (R^1 = Cl, R^2 = H), 95-58-9; I (R^1 = SMe, $R^2 = CH_2CH(CH_3)C_3H_7$), 78246-18-1; 5,6-dihydro-3-methyl-2(1*H*)-pyrazinone, 69849-58-7; 3-methyl-2(1*H*)-pyrazinone, 19838-07-4.

LITERATURE CITED

Akiyama, T.; Enomoto, Y.; Shibamoto, T. *J. Agric. Food Chem.* **1978**, *26*, 1176.

Amoore, J. E.; Venstrom, D.; Davis, A. R. *Percept Motor Skills* **1968**, *26*, 143.

Amoore, J. E. "Molecular Basis of Odor"; Charles C. Thomas: Springfield, 1970; pp 16–25.

Burrell, J. W. K.; Lucas, R. A.; Michalkiewicz, D. M.; Riezebos, G. *Chem. Ind. (London)* **1970**, 1409.

Buttery, R. G.; Seifert, R. M.; Guadagni, D. G.; Ling, L. C. *J. Agric. Food Chem.* **1969a**, *17*, 1322.

Buttery, R. G.; Seifert, R. M.; Lundin, R. E.; Guadagni, D. G.; Ling, L. C. *Chem. Ind. (London)* **1969b**, 490.

Calabretta, P. J. *Cosmetics Perfumery* **1975**, *90*, 74.

Calabretta, P. J. *Perfumer Flavorist* **1978**, *3*, 33.

Guadagni, D. G.; Buttery, R. G.; Turnbaugh, J. G. *J. Sci. Food Agric.* **1972**, *23*, 1435.

Iwabuchi, H.; Yoshikura, M.; Obata, S.; Kamisako, W. *Yakugaku Zasshi* **1984**, *104*, 951.

Kitamura, K.; Shibamoto, T. *J. Agric. Food Chem.* **1981**, *29*, 188.

Maga, J. A. *CRC Crit. Rev. Food Sci. Nutr.* **1982**, *16*, 1.

Masuda, H.; Tanaka, M.; Akiyama, T.; Shibamoto, T. *J. Agric. Food Chem.* **1980**, *28*, 244.

Masuda, H.; Yoshida, M.; Shibamoto, T. *J. Agric. Food Chem.* **1981**, *29*, 944.

Parliment, T. H.; Epstein, M. F. *J. Agric. Food Chem.* **1973**, *21*, 714.

Seifert, R. M.; Buttery, R. G.; Guadagni, D. G.; Black, D. R.; Harris, J. G. *J. Agric. Food Chem.* **1970**, *18*, 246.

Seifert, R. M.; Buttery, R. G.; Guadagni, D. G.; Black, D. R.; Harris, J. G. *J. Agric. Food Chem.* **1972**, *20*, 135.

Received for review July 10, 1985. Accepted October 25, 1985.