Chatterjee, A.; Dutta, C. P. *Tetrahedron* **1967**, *23*, 1769–1781.
Concon, J. M.; Swerczek, T. W.; Newburg, D. S. *Nutr. Cancer* **1979**, *1*, 22–26.
Dallacker, F.; Schubert, J. *Chem. Ber.* **1975**, *108*, 95–108.
DeCleyn, R.; Verzele, M. *Bull. Soc. Chim. Belg.* **1975**, *84*, 435–438.
DeFeoand, R. J.; Strickler, P. D. *J. Org. Chem.* **1963**, *28*, 2915–2917.
Gedye, R. N.; Nechvatal, A. *J. Chem. Soc.* **1964**, 5925–5929.
Grewe, R.; Greist, W.; Neumann, H.; Kersten, H. *Chem. Ber.* **1970**, *103*, 3752–3770, and references cited therein.
Loder, J. W.; Moorhouse, A.; Russel, G. V. *Aust. J. Chem.* **1969**, *22*, 1531–1538.
Lurik, B. B.; Kamennov, N. A.; Volkov, Y. P. *Khim.-Farm. Zh.* **1971**, *5*, 15–17.
Normant, H.; Feugeas, C. *C. R. Hebd. Seances Acad. Sci.* **1964**, *258*, 2846–2848.
Posner, T.; Rohde, K. *Chem. Ber.* **1910**, *43*, 2665–2676.
Rügheimer, L. *Chem. Ber.* **1882**, *15*, 1390–1391.
Shulgin, A. T. *Bull. Narc.* **1973**, *25*, 59–74.
Singh, J.; Dhar, K. L.; Atal, C. K. *Tetrahedron Lett.* **1969**, 4975–4978.
Su, H. C. F.; Horvat, R. *J. Agric. Food Chem.* **1981**, *29*, 115–118, and references cited therein.
Tsuboi, S.; Takeda, A. *Tetrahedron Lett.* **1979**, 1043–1044.
Yang, K. W.; Cannon, J. G.; Rose, J. G. *Tetrahedron Lett.* **1970**, 1791–1794.
Yazawa, H.; Tanaka, K.; Kariyone, K. *Tetrahedron Lett.* **1974**, 3995–3996.

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Synthesis of New Pyrazines for Flavor Use

Hideki Masuda, Misaku Yoshida, and Takayuki Shibamoto*

Ten newly synthesized pyrazines, some of which possessed a licorice–woody (isobutylquinoline-like) odor, showed very low odor thresholds (0.2–1.0 ppm in an ethyl alcohol solution). This indicates that these pyrazines have high potential use as flavor ingredients. Eight 5-alkyl-3-methyl-2(1*H*)-pyrazinones were synthesized from 3-methyl-5,6-dihydro-2(1*H*)-pyrazinone, which was prepared from the reaction of methyl pyruvate and ethylenediamine, with aldehydes or ketones. Some pyrazinones synthesized were derived to 2-chloropyrazine derivatives, which were subsequently reacted with sodium alkylate, sodium phenolate, sodium thioalkylate, and sodium thiophenylate to obtain the desired alkoxy-, phenoxy-, (alkylthio)-, and (phenylthio)pyrazines, respectively. The spectral data (IR; NMR; MS) of 8 pyrazinones and 10 new pyrazines are also reported.

Alkoxypyrazines are found in various foods: in coffee beans (Vitzthum et al., 1975), cooked potato (Nursten and Sheen, 1974), green peas (Murray et al., 1976), grape (Bayonove et al., 1975), cooked beets (Parliment et al., 1977), roasted almond (Takei and Yamanishi, 1974), and galbanum oil (Bramwell et al., 1969).

Because of the characteristic flavor and low threshold values (Seifert et al., 1970; Parliment and Epstein, 1973), alkoxy- and (alkylthio)pyrazines have been widely used as flavor ingredients. 2-Methoxy-3-methylpyrazine is used to create a fondant and an ice cream flavor (Firmenich et al., 1967). 2,5-Dimethyl-3-(methylthio)pyrazine is applied to make coffee and sugar syrup flavors (Winter et al., 1972).

Alkoxypyrazines have been synthesized by a condensation reaction of an α-amino amide and an α-dicarbonyl compound via a 2-pyrazinone intermediate (Jones, 1949; Karmas and Spoerri, 1952; Seifert et al., 1972). Because α-amino amides are not readily available, only limited quantities of alkoxypyrazines can be produced by this method.

Masuda et al. (1980) synthesized 5-substituted 3,5-dimethylpyrazines by the reaction of 2,3-dimethyl-5,6-dihydropyrazine, which was obtained from the condensation of diacetyl and ethylenediamine, and aldehydes or ketones using the method reported by Shibamoto et al. (1979).

Department of Environmental Toxicology, University of California, Davis, Davis, California 95616 (T.S.), and Ogawa & Co., Ltd., 1-12-3 Niitaka, Yodogawa-Ku, Osaka, Japan (H.M. and M.Y).

This study reports a new method for synthesizing pyrazines including alkoxypyrazines, a phenoxypyrazine, (alkylthio)pyrazines, and a (phenylthio)pyrazine.

EXPERIMENTAL SECTION

Synthesis of 3-Methyl-5,6-dihydro-2(1*H*)-pyrazinone (1). Fifteen grams (0.25 mol) of ethylenediamine was dissolved in 80 mL of methylene chloride in a 200-mL Erlenmeyer flask. To the ice-cooled solution, 20 g (0.20 mol) of methyl pyruvate was slowly added over a 3-h period under constant stirring. The reaction mixture was extracted with 800 mL of methylene chloride. The extract was washed with saturated sodium chloride solution, dried over anhydrous sodium sulfate, and concentrated under vacuum. The residual solid was recrystallized from benzene. Colorless needles (16.5 g) were identified by NMR, IR, and MS as 3-methyl-5,6-dihydro-2(1*H*)-pyrazinone.

Synthesis of 5-Isobutyl-3-methyl-2(1*H*)-pyrazinone (2). An excess amount of isobutyl aldehyde (43.7 g, 0.61 mol) was added to a methanol solution (30 mL) of compound 1 (14.2 g, 0.13 mol). The reaction mixture was cooled in an ice bath and stirred for 30 min. A methanol solution (80 mL) of potassium (18 g, 0.28 mol) was added dropwise to the above cooled reaction mixture over a 30-min period. The reaction mixture was brought to room temperature in ~1 h. The solution was then refluxed for 2 h. After the solvent was evaporated to dryness, 60 mL of water and 30 mL of ethyl acetate were added to the residue. Ammonium chloride (80 g) was added to the above aqueous layer. The solution was then extracted with

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Table I. Yields, Melting Points, and Precursors of Pyrazinones Synthesized

pyrazinone	yield, %	mp, °C	precursor for 5 substituent
1, 3-methyl-5,6-dihydro-2(1*H*)-pyrazinone	75	98–101	
2, 5-isobutyl-3-methyl-2(1*H*)-pyrazinone	65	108–109	$(CH_3)_2CHCHO$
3, 5-(2-methylbutyl)-3-methyl-2(1*H*)-pyrazinone	52	104–105	$CH_3CH_2CH(CH_3)CHO$
4, 5-isopentyl-3-methyl-2(1*H*)-pyrazinone	39	124–125	$(CH_3)_2CHCH_2CHO$
5, 5-(2-methylpentyl)-3-methyl-2(1*H*)-pyrazinone	49	102–104	$CH_3CH_2CH_2CH(CH_3)CHO$
6, 5-(ethylbutyl)-3-methyl-2(1*H*)-pyrazinone	40	106–107	$(CH_3CH_2)_2CHCHO$
7, 5-isopropyl-3-methyl-2(1*H*)-pyrazinone	22	129–131	$(CH_3)_2CO$
8, 5-(1-methylpropyl)-3-methyl-2(1*H*)-pyrazinone	17	75–76	$CH_3CH_2COCH_3$

Table II. Spectral Data of Pyrazinones

pyrazinone	IR (Nujol), cm^{-1}	NMR (Me_2SO-d_6)	MS, *m/e* (%)
1	1680, 1630	δ 2.02 (3 H, t,[a] J = 1.6 Hz, $-CH_3$), 3.1–3.3 (2 H, m, $-CH_2$), 3.4–3.6 (2 H, m, $-CH_2$), 8.17 (1 H, broad s, N*H*)	112 (45), 84 (36), 83 (25), 69 (30), 55 (100)
2	1650, 1620, 815, 780	δ 0.86 [6 H, d, J = 6.4 Hz, $-CH(CH_3)_2$], 1.7–2.1 [1 H, m, $-CH(CH_3)_2$], 2.21 (3 H, s, $-CH_3$, 2.29 (2 H, d, J = 7.8 Hz, $-CH_2-$), 6.99 (1 H, s, olefin), 12.04 (1 H, br s, N*H*)	166 (33), 151 (9), 124 (100), 106 (8), 95 (50)
3	1650, 1620, 820, 790	δ 0.80 (3 H, d, J = 6.8 Hz, $-CHCH_3$), 0.84 (3 H, t, J = 7.8 Hz, $-CH_2CH_3$), 0.9–1.4 (2 H, m, $-CH_2CH_3$), 1.5–1.8 (1 H, m, $-CH$), 2.21 (3 H, s, $-CH_3$), 2.1–2.4 (2 H, AB, $-CH_2CH$), 6.99 (1 *H*, s, olefin), 12.02 (1 H, br s, N*H*)	180 (12), 165 (2), 124 (100), 95 (18)
4	1650, 1620, 850, 830, 780	δ 0.88 [6 H, d, J = 5.9 Hz, $-CH(CH_3)_2$], 1.3–1.6 (3 H, m, $-CH_2CH$), 2.21 (3 H, s, $-CH_3$), 2.39 (2 H, t, $-CH_2$), 7.02 (1 H, s, olefin), 12.04 (1 H, br s, N*H*)	180 (10), 165 (2), 137 (7), 124 (100), 95 (28), 83 (2)
5	1650, 1620, 830, 790	δ 0.80 (3 H, d, J = 6.4 Hz, $-CHCH_3$), 0.85 (3 H, t, J = 5.9 Hz, $-CH_2CH_3$), 0.9–1.5 (4 H, m, $-CH_2CH_2-$), 1.7–1.9 (1 H, m, $-CHCH_3$), 2.21 (3 H, s, $-CH_3$), 2.1–2.4 (2 H, AB, $-CH_2CH$), 6.98 (1 H, s, olefin), 12.03 (1 H, br s, N*H*)	194 (12), 151 (4), 124 (100), 95 (12)
6	1650, 1620, 830, 790	δ 0.83 (6 H, t, J = 7.4 Hz, $-CH_2CH_3$), 1.1–1.5 (2 H, m, $-CH_2CH_3$), 1.6–1.9 (1 H, m, $-CH$), 2.2–2.4 (2 H, AB, $-CH_2-$), 2.21 (3 H, 3, $-CH_3$), 6.98 (1 H, s, olefin), 12.04 (1 H, br s, N*H*)	194 (10), 151 (5), 124 (100), 95 (11)
7	1650, 1620, 830, 790	δ 1.19 [6 H, d, J = 6.8 Hz, $-CH(CH_3)_2$], 2.22 (3 H, s, $-CH_3$), 2.72 (1 H, m, C*H*), 7.04 (1 H, s, olefin), 11.98 (1 H, br s, N*H*)	162 (100), 137 (88), 124 (50), 119 (48), 109 (98)
8	1650, 1620, 780	δ 0.78 (3 H, t, J = 7.3 Hz, $-CH_2CH_3$), 1.17 (3 H, d, J = 6.8 Hz, $-CHCH_3$), 1.4–1.8 (2 H, m, $-CHCH_2CH_3$), 2.22 (3 H, s, $-CH_3$), 2.3–2.5 (1 H, m, $-CH$), 7.04 (1 H, s, olefine), 11.96 (1 H, br s, N*H*)	166 (60), 151 (28), 138 (100), 137 (50), 124 (43), 119 (24), 109 (65), 68 (12)

[a] The multiplicity of methyl protons on compound 1 is due to the long-range spin coupling from the proton on a carbon which is attached to an azomethine group (imino carbon or imino nitrogen; Weygand et al., 1964; Weinberger and Greenhalgh, 1963; Staab et al., 1965).

Table III. Yields, Boiling Points, Precursors, Odor Descriptions, and Odor Thresholds of New Pyrazines

pyrazine	pyrazinone intermediate	yield,[a] %	bp, °C/ mmHg	precursor for 2 substituent	odor descriptions	odor threshold in ethyl alcohol, ppm
I, 5-isobutyl-2-methoxy-3-methylpyrazine	2	75	125/15	CH_3ONa	licorice-woody	0.7
II, 5-(2-methylbutyl)-2-methoxy-3-methylpyrazine	3	74	142/8	CH_3ONa	licorice-woody with slightly green odor	1
III, 5-isopentyl-2-methoxy-3-methylpyrazine	4	72	95/4	CH_3ONa	licorice-woody with walnut-like odor	1
IV, 5-(2-methylpentyl)-2-methoxy-3-methylpyrazine	5	70	105/3	CH_3ONa	burdock, bellpepper odor	0.5
V, 2-ethoxy-5-isobutyl-3-methylpyrazine	2	89		C_2H_5ONa	burdock-like brownish odor with slightly bellpepper and galbanum green odor	0.2
VI, 5-isobutyl-2-isopropoxy-3-methylpyrazine	2	90		$(CH_3)_2CHONa$	licorice-woody odor with walnut-like odor	1
VII, 5-isobutyl-3-methyl-2-phenoxypyrazine	2	92		PhONa	bellpepper, cacao bean odor	1
VIII, 5-isobutyl-3-methyl-2-(methylthio)pyrazine	2	69	106/5	CH_3SNa	licorice-woody odor with walnut-like odor	0.8
IX, 5-(2-methylpentyl)-3-methyl-2-(methylthio)pyrazine	5	51	125/3	CH_3SNa	burdock-like odor with slightly earthy odor	1
X, 5-isobutyl-3-methyl-2-(phenylthio)pyrazine	2	98		PhSNa	nutty, macademia-like odor	0.7

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

Table IV. Spectral Data of New Pyrazines

pyrazine	IR (neat), cm^{-1}	NMR ($CDCl_3$)	MS, *m/e* (%)
I	2850, 1580, 1550, 1445, 1370, 1180, 1040, 990.	δ 0.93 [6 H, d, J = 6.6 Hz, $-CH(CH_3)_2$], 1.8-2.3 (1 H, m, C*H*), 2.42 (3 H, s, $-CH_3$), 2.51 (2 H, d, J = 7.1 Hz, $-CH_2CH$), 3.95 (3 H, s, $-OCH_3$), 7.79 (1 H, s, ring *H*)	180 (56), 165 (45), 139 (30), 138 (100), 137 (23), 123 (23), 106 (14), 95 (12)
II	2850, 1580, 1550, 1455, 1370, 1180, 1040, 990	δ 0.88 (3 H, d, J = 6.4 Hz, $-CHCH_3$), 0.91 (3 H, t, J = 7.3 Hz, $-CHCH_3$), 1.0-1.5 (2 H, m, $-CH_2CH_3$), 1.7-2.1 (1 H, m, $-CHCH_3$), 2.42 (3 H, s, $-CH_3$), 2.4-2.7 (2 H, m, $-CH_2-$), 3.95 (3 H, s, $-OCH_3$), 7.80 (1 H, s, ring *H*)	194 (56), 179 (40), 165 (32), 152 (16), 139 (56), 138 (100), 137 (36), 123 (42), 106 (26), 95 (35)
III	2850, 1580, 1550, 1455, 1370, 1180, 1040, 990	δ 0.95 [6 H, d, J = 6.1 Hz, $-CH(CH_3)_2$], 1.4-1.7 (3 H, m, $-CHCH_2CH$), 2.41 (3 H, s, $-CH_3$), 2.65 (2 H, t, J = 6.8 Hz, $-CH_2CH_2CH$), 3.95 (3 H, s, $-OCH$), 7.82 (1 H, s, ring *H*)	194 (10), 179 (12), 151 (15), 139 (30), 138 (100), 137 (12), 123 (18), 106 (8), 95 (10)
IV	2850, 1550, 1455, 1370, 1180, 1040, 990	δ 0.87 (3 H, d, J = 6.6 Hz, $-CHCH_3$), 0.88 (3 H, t, J = 6.0 Hz, $-CH_2CH_3$), 1.1-1.5 (4 H, m, $-CHCH_2CH_2CH$), 1.8-2.1 (1 H, m, $-CH_2CHCH_2$), 2.42 (3 H, s, $-CH_3$), 2.4-2.6 (2 H, m, $-CH_2CH$), 3.95 (3 H, s, $-OCH_3$), 7.79 (1 H, s, ring *H*)	208 (38), 193 (30), 179 (40), 165 (38), 151 (18), 139 (51), 138 (100), 137 (28), 123 (36), 106 (20), 95 (25)
V	2850, 1580, 1550, 1450, 1410, 1380, 1340, 1170, 1040, 990, 790	δ 0.93 [6 H, d, J = 7.0 Hz, $-CH(CH_3)_2$], 1.37 (3 H, t, J = 7.0 Hz, $-CH_2CH_3$), 1.8-2.1 [1 H, m, $-CH_2CH(CH_3)_2$], 2.40 (3 H, s, $-CH_3$), 2.47 [2H, d, J = 7.0 Hz, $-CH_2CH(CH_3)_2$], 4.33 (2 H, q, J = 7.0 Hz, $-CH_2CH_3$), 7.74 (1 H, s, ring *H*)	194 (40), 179 (25), 165 (10), 152 (100), 124 (73), 95 (15)
VI	2850, 1540, 1450, 1400, 1380, 1370, 1335, 1320, 1170, 1020, 920, 780	δ 0.93 [6 H, d, J = 7.0 Hz, $-CH(CH_3)_2$], 1.33 [6 H, d, J = 7.0 Hz, $-OCH(CH_3)_2$], 1.8-2.1 [1 H, m, $-CH_2CH(CH_3)_2$], 2.38 (3 H, s, $-CH_3$), 2.45 [2 H, d, J = 7.0 Hz, $-CH_2CH(CH_3)_2$], 5.27 [1 H, m, $-OCH-(CH_3)_2$], 7.70 (1 H, s, ring *H*)	208 (19), 166 (27), 151 (12), 124 (100), 95 (15)
VII	3030, 1590, 1540, 1490, 1380, 1370, 1210, 1265, 760, 690	δ 0.84 [6 H, d, J = 7.0 Hz, $-CH(CH_3)_2$], 1.7-2.2 [1 H, m, $-CH_2CH(CH_3)_2$], 2.40 [2 H, d, J = 7.0 Hz, $-CH_2CH(CH_3)_2$], 2.56 (3 H, s, $-CH_3$), 6.9-7.5 (5H, m, $-C_6H_5$), 7.90 (1 H, s, ring *H*)	242 (28), 227 (12), 200 (100), 171 (20)
VIII	1560, 1520, 1470, 1440, 1390, 1380, 1330, 1320, 1170, 1100, 980	δ 0.94 [6 H, d, J = 6.6 Hz, $-CH(CH_3)_2$], 0.9-2.3 [1 H, m, $-CH_2CH(CH_3)_2$], 2.45 (3 H, s, $-SCH_3$ or $-CH_3$), 2.55 (3 H, s, $-CH_3$ or $-SCH_3$), 2.58 (2 H, d, J = 6.6 Hz, $-CH_2CH$), 7.90 (1 H, s, ring *H*)	196 (75), 181 (41), 163 (30), 154 (100), 120 (20), 106 (32)
IX	1550, 1520, 1470, 1440, 1380, 1330, 1310, 1170, 1090, 980	δ 0.88 (3 H, d, J = 6.6 Hz, $-CH_2CH(CH_3)$, 0.89 (3 H, t, 1.1-1.5 (2 H, m, $-CHCH_2-CH_3$), 1.8-2.1 (1 H, m, $-CH_2CH$), 2.3-2.8 (2 H, m, $-CH_2$), 2.46 (3 H, $-SCH_3$ or $-CH_3$), 2.55 (3 H, s, $-CH_3$ or $-SCH_3$), 7.90 (1 H, s, ring *H*)	226 (36), 209 (16), 195 (30), 181 (16), 154 (100), 120 (8), 106 (16)
X	3030, 1580, 1520, 1480, 1470, 1440, 1380, 1320, 1290, 1170, 1080, 740, 690	δ 0.76 [6 H, d, J = 7.0 Hz, $-CH(CH_3)_2$], 1.4-2.1 [1 H, m, $-CH_2CH(CH_3)_2$], 2.35 [2 H, d, J = 7.0 Hz, $-CH_2CH(CH_3)$], 2.50 (3 H, s, $-CH_3$), 7.0-7.5 (5 H, m, $-C_6H_5$), 7.83 (1 H, s, ring *H*)	258 (70), 242 (31), 216 (100), 106 (13), 80 (10), 79 (10)

200 mL of ethyl acetate. The solvent was removed from the extract and a residual solid was recrystallized from hexane. Colorless needles (13.6 g) were obtained and identified by NMR, IR, and MS as 5-isobutyl-3-methyl-2(1*H*)-pyrazinone.

All other 5-alkyl-3-methyl-2(1*H*)-pyrazinones (3–8) were synthesized by the method described above (the pecursors of the 5 substituents are listed in Table I).

Synthesis of 5-Isobutyl-2-methoxy-3-methylpyrazine (I). Compound **2** (36 g, 0.22 mol) and phosphorus oxychloride (55 g, 0.36 mol) were dissolved in 50 mL of toluene. The solution was refluxed for 4.5 h. Ice-cooled water (100 mL) was then gradually added to the reaction mixture. The pH of the reaction mixture was adjusted to 8 with $NaHCO_3$. After the insoluble material was filtered off, the filtrate was concentrated under vacuum. The oily residue (23.5 g) was further distilled in vacuo to give 2-chloro-5-isobutyl-3-methylpyrazine (13.2 g). This chloro derivative was dissolved in a 30-mL methanol solution of sodium methylate (28%). The methanol solution was refluxed for 3.5 h. The solvent was removed by distillation and the residual liquid was extracted with ethyl ether. The ethyl ether solution was dried over anhydrous sodium sulfate and ethyl ether was distilled off. The crude oil obtained (13.4 g) was purified by fractional distillation in vacuo. The desired 5-isobutyl-2-methoxy-3-methylpyrazine (10.8 g) was obtained in 75.2% (relative to the quantity of **2**) yield.

All other alkoxypyrazines (II–VI) were synthesized by the method described above except that an ethanol–sodium ethylate solution and a 2-propanol–sodium isopropylate solution were used for the ethoxy derivative (V) and the isopropyl derivative (VI).

Synthesis of 5-Alkyl-3-methyl-2-(methylthio)-pyrazines (VIII and IX). These compounds were synthesized following the procedure for alkoxypyrazines, ex-

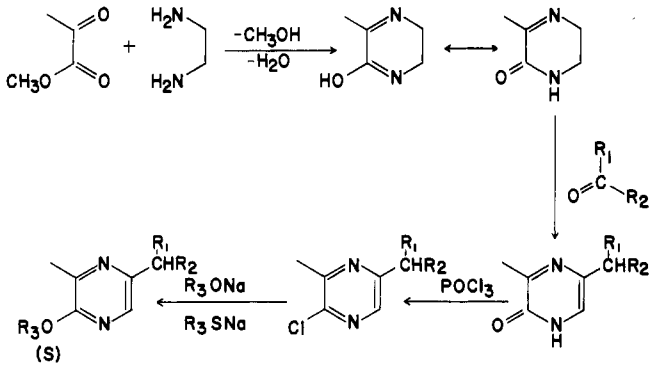

Figure 1. Overall reaction scheme for the synthesis of new pyrazines.

cept that the methanol solution of sodium methylate was replaced with an aqueous solution of sodium thiomethylate.

Synthesis of 5-Isobutyl-3-methyl-2-phenoxypyrazine (VII). A sodium metal (250 mg, 10.9 mol) was dissolved in 5 mL of phenol and the excess phenol was removed in vacuo. 2-Chloro-5-isobutyl-3-methylpyrazine (500 mg, 2.7×10^{-3} mol) in a 25 mL of *N,N*-dimethylformamide (DMF) solution was added to the above residual sodium phenolate, and the solution was refluxed for 6 h. DMF was removed in vacuo and the residue was dissolved into 100 mL of ethyl ether. The ether solution was washed with brine water (10 mL), and the ethyl ether phase was dried with sodium metal and concentrated in vacuo to give crude oil (1.71 g). The crude oil was purified with preparative thin-layer chromatography (ethyl acetate–chloroform (1:6) as a developing agent) to give 605 mg of 5-isobutyl-3-methyl-2-phenoxypyrazine (VII), the structure of which was confirmed by NMR, IR, and MS.

5-Isobutyl-3-methyl-2-(phenylthio)pyrazine (X) was synthesized by the procedure described above from 2-chloro-5-isobutyl-3-methylpyrazine with sodium thiophenolate.

RESULTS AND DISCUSSION

The yields and melting points of pyrazinones synthesized are shown in Table I. The spectral data of pyrazinones are listed in Table II. The synthesis of pyrazinones 2–8 has not been reported prior to this study. The synthesis of 1 has been reported previously (Carr et al., 1962). They reported, however, a fairly low yield (10%) compared with the method developed in this study (75%). The new pyrazines synthesized and their odor descriptions are shown in Table III. Odor thresholds were measured in an aqueous ethanol solution. Each sample was added into 1% ethanol solution, and then each ethanol solution was diluted with distilled water successively until no odor was detected. The five perfumers, who have at least 5 years experience in perfume compounding, evaluated the threshold. The average value of five results for each compound is presented in Table III. The spectral data of the new pyrazines are presented in Table IV. The overall reaction scheme for the synthesis of new pyrazines is shown in Figure 1.

The reaction mechanism from dihydropyrazinone to 5-substituted pyrazinone was proposed previously (Shibamoto et al., 1979). In this step, a carbanion on the 5 position, which is formed by a base, performs a nucleophilic attack on a carbonyl carbon atom of an aldehyde or a ketone. The 5-substituted pyrazines are formed following dehydration and isomerization. When carbanion is formed on pyrazinone, the negative charge will be conjugated with the carbonyl group on the 2 position (Cram and Guthrie, 1966) and leave the 6 position uncharged. Consequently, a carbonyl carbon atom will attack the 5 position exclusively.

In the case of the synthesis of compounds VII and X, the objective phenoxypyrazine or (phenylthio)pyrazine did not form in the phenol and thiophenol solutions, respectively. Sodium phenolate or thiophenylate was, therefore, prepared beforehand, and the reaction with a chloro derivative was performed in a DMF solution. Phenoxypyrazine and (phenylthio)pyrazine were synthesized in high yields (92 and 98%, respectively) by this method.

The pyrazinones obtained in this study can be used to synthesize alkoxy-, phenoxy-, (alkylthio)-, and (phenylthio)pyrazines, which possess very interesting licorice-like flavors (Table III).

This method is potentially useful for synthesis of flavor materials.

LITERATURE CITED

Bayonove, C.; Cordonnier, R.; Dubois, P. *C. R. Hebd. Seances Acad. Sci., Ser. D* **1975**, *281*, 75.
Bramwell, A. F.; Burrell, J. W. K.; Riezebos, G. *Tetrahedron Lett.* **1969**, 3215.
Carr, A. A., Jr.; Tilford, C. H.; Kuhn, W. L. U.S. Patent 3056784, 1962.
Cram. D. J.; Guthrie, R. D. *J. Am. Chem. Soc.* **1966**, *88*, 5760.
Firmenich, R.; Firmenich, G.; Firmenich, R. E. British Patent 1061734, 1967.
Jones, R. G. *J. Am. Chem. Soc.* **1949**, *71*, 78.
Karmas, G.; Spoerri, P. E. *J. Am. Chem. Soc.* **1952**, *74*, 1580.
Masuda, H.; Tanaka, M.; Akiyama, T.; Shibamoto, T. *J. Agric. Food Chem.* **1980**, *28*, 244.
Murray, D. D.; Shipton, J.; Whitfield, F. B.; Fank, B.; Last, J. H. *J. Sci. Food Agric.* **1976**, *27*, 1093.
Nursten, H. E.; Sheen, M. R. *J. Sci. Food Agric.* **1974**, *25*, 643.
Parliment, T. H.; Epstein, M. F. *J. Agric. Food Chem.* **1973**, *21*, 714.
Parliment, T. H.; Kolor, M. G.; Maing, Y. *J. Food Sci.* **1977**, *42*, 1592.
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.
Shibamoto, T.; Akiyama; T.; Sakaguchi, M.; Enomoto, Y.; Masuda, H. *J. Agric. Food Chem.* **1979**, *27*, 1027.
Staab, H. A.; Vögtle, F.; Mannschreck, A. *Tetrahedron Lett.* **1965**, 679.
Takei, Y.; Yamanishi, T. *Agric. Biol. Chem.* **1974**, *38*, 2329.
Vitzthum, O. G.; Werkhoff, P.; Ablanque, E. *Colloq. Int. Chim. Cafes Verts, Torrefies Leurs Deriv.*, [*C. R.*] **1975**, *7*, 115.
Weinberger, M. A.; Greenhalgh, R. *Can. J. Chem.* **1963**, *41*, 1038.
Weygand, F.; Steglich, W.; Mayer, D.; von Philipsborn, W. *Chem. Ber.* **1964**, *97*, 2023.
Winter, M.; Gautschi, F.; Flament, I.; Stoll, M.; Goldman, I. M. U.S. Patent 3702253, 1972.

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