Synthesis and Herbicidal Activity of 6-Phenyl-5-Propylamino-2-Pyrazinecarbonitriles and Related Compounds

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6-Phenyl- and 5-phenyl-2-pyrazinecarbonitriles with or without a propylamino group at the 3-, 5- or 6-position of the pyrazine ring were prepared together with some related compounds from the corresponding 2,3-pyrazinedicarbonitriles. Their herbicidal activities against barnyardgrass and broadleaf weeds were examined in pot tests. The 6-phenyl-2-pyrazinecarbonitriles were relatively potent compared with the 5-phenyl derivatives. Moreover, the presence of a propylamino group at the 5-position of the 6-phenyl-2-pyrazinecarbonitriles was closely related to an increase in activity.

2,3-Pyrazinedicarbonitrile derivatives are of interest as a potential synthetic intermediate for a variety of biologically active compounds in addition to their own fungicidal or herbicidal activities. Previously, it has been reported that some 6-phenyl-5-propylamino-2,3-pyrazinedicarbonitriles possess marked herbicidal activity against barnyardgrass in a pre-emergence test, and it was demonstrated that the hydrophobic and steric properties of substituents at the 6-position of the pyrazine ring play an important role in determining the potency of the activity.

In order to obtain further information on the structure-activity relationships of these compounds, the chemical modification of the cyano groups on the pyrazine ring was planned. This paper describes the preparation of the mono carbonitrile derivatives and some related compounds from the corresponding 2,3-dicarbonitrile derivatives in addition to their herbicidal activities.

Hydrolysis of 5-phenyl-2,3-pyrazinedicarbonitrile 1 with a mole equivalent of sodium hydroxide in water at 95~100°C for 3 hr, followed by subsequent chromatographic separation of the reaction mixture over silica gel gave 3-carbamoyl-5-phenyl-2-pyrazinecarboxylic acid 2 and 3-carbamoyl-6-phenyl-2-pyrazinecarboxylic acid 3 in 46% and 14% yields, respectively. Other minor products were not further examined. Decarboxylation of 2 in o-dichlorobenzene gave 6-phenyl-2-pyrazinecarboxamide 4, which was further converted to 6-phenyl-2-carbonitrile 6 by treatment with phosphoryl chlorode.
Similarly, 3 gave 5-phenyl-2-pyrazinecarboxamide 5, which in turn gave 5-phenyl-2-pyrazinecarbonitrile 7.

The structures of 6 and 7 were assigned on the basis of their NMR data. It is known that the pyrazine ring proton coupling constants of 2-substituted 6-phenylpyrazines are in the range of 0~0.6 Hz, whereas those of 2-substituted 5-phenylpyrazines are in the range of 1.1~1.8 Hz. In fact, the NMR spectrum of 7 showed the characteristic coupling constant (1.5 Hz) of the 3, 6 ring protons, whereas that of 6 showed the characteristic coupling constant (0.0 Hz) of the 3, 5 ring protons.

Hydrolysis of 6-phenyl-5-propylamino-2,3-pyrazinedicarbonitrile 8 with a mole equivalent of sodium hydroxide in water at 95~100°C for 4 hr gave at least three products, which were detected by TLC. Decarboxylation of the resulting crude mixture in o-dichlorobenzene, followed by treatment with phosphoryl chloride gave a mixture of 6-phenyl-5-propylamino-2-pyrazinecarbonitrile 9, 5-phenyl-6-propylamino-2-pyrazinecarbonitrile 10 and other products. Subsequent chromatographic separation of the mixture over silica gel gave 9 and 10 in 18 and 3% yields from 8, respectively. The other products were not isolated.

Compounds 9 and 10 were differentiated by their NMR spectra. The NMR signals of 9 and 10 at the lowest field were assigned to the hydrogen at the 3-position of the pyrazine ring (9 = 8.23 ppm, 10 = 8.16 ppm). The electron-donating propylamino group at the 6-position heightened the chemical shift of the proton at the 3-position of 10. In addition, the IR spectrum of the cyano group in 10 shows an absorption band at 2240 cm⁻¹, whereas that of 9 appears at 2220 cm⁻¹. The latter absorption

![Scheme 2.](image)

**Table I. Spectral Data of 5-Propylamino-6-phenylpyrazines**

<table>
<thead>
<tr>
<th>No.</th>
<th>R¹</th>
<th>R²</th>
<th>X</th>
<th>δ ppm (CDCl₃)</th>
<th>UV λ max% EtOH nm (log ε)</th>
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</thead>
<tbody>
<tr>
<td>8</td>
<td>CN</td>
<td>CN</td>
<td>H</td>
<td>245 (3.98)</td>
<td>272 (3.99) 308 (4.26) 370 (3.88)</td>
</tr>
<tr>
<td>11</td>
<td>CN</td>
<td>CN</td>
<td>Me</td>
<td>247 (3.99)</td>
<td>275 (4.08) 307 (4.29) 366 (3.92)</td>
</tr>
<tr>
<td>12</td>
<td>CN</td>
<td>CN</td>
<td>Cl</td>
<td>250 (4.06)</td>
<td>265 (4.00) 305 (4.31) 374 (3.85)</td>
</tr>
<tr>
<td>13</td>
<td>CN</td>
<td>CN</td>
<td>F</td>
<td>250 (4.04)</td>
<td>265 (4.04) 305 (4.28) 367 (3.88)</td>
</tr>
<tr>
<td>9</td>
<td>CN</td>
<td>H</td>
<td>H</td>
<td>8.23</td>
<td>232 (4.05) 288 (4.32) 347 (3.99)</td>
</tr>
<tr>
<td>14</td>
<td>CN</td>
<td>H</td>
<td>Me</td>
<td>8.24</td>
<td>232 (4.06) 288 (4.33) 347 (4.00)</td>
</tr>
<tr>
<td>15</td>
<td>CN</td>
<td>H</td>
<td>Cl</td>
<td>8.29</td>
<td>238 (4.08) 289 (4.33) 350 (4.01)</td>
</tr>
<tr>
<td>16</td>
<td>CN</td>
<td>H</td>
<td>F</td>
<td>8.30</td>
<td>235 (4.09) 288 (4.37) 349 (4.01)</td>
</tr>
<tr>
<td>10</td>
<td>H</td>
<td>CN</td>
<td>H</td>
<td>8.16</td>
<td>243 (3.86) 270 (4.07) 368 (3.87)</td>
</tr>
<tr>
<td>17</td>
<td>H</td>
<td>CN</td>
<td>Me</td>
<td>8.12</td>
<td>245 (3.86) 271 (4.08) 367 (3.89)</td>
</tr>
<tr>
<td>18</td>
<td>H</td>
<td>CN</td>
<td>Cl</td>
<td>8.13</td>
<td>245 (3.88) 269 (4.00) 373 (3.83)</td>
</tr>
</tbody>
</table>

* Chemical shift of pyrazine ring proton.
Herbicidal 2,3-Pyrazinedicarbonitriles. Part IV.

Band appears at the lower wave number owing to the effect of the electron-donating propylamino group at the p-position.

Similarly, compounds 11, 12 and 13 gave the corresponding 6-phenyl-2-pyrazinecarbonitriles 14, 15 and 16 and 5-phenyl derivatives 17 and 18. The isomer of 16 was not isolated. As shown in Table I, the electronic spectra of the 6-phenyl derivatives showed characteristic absorption bands at 232~238 and 288~289 nm. On the other hand, those of the 5-phenyl derivatives showed characteristic absorption bands at 243~245 and 269~271 nm.

To obtain further information on the hydrolysis of the pyrazinedicarbonitrile compounds, hydrolysis of 12 was investigated in detail. Treatment of 12 with concentrated sulfuric acid gave the 2,3-pyrazinedicarboxamide 19 in a 73% yield. Treatment of 12 with a large excess of sodium hydroxide in water under reflux for 5 hr gave the 2,3-pyrazinedicarboxylic acid 20 in an 83% yield.

On the other hand, the reaction of 12 with hydrogen peroxide in the presence of sodium molybdate caused selective hydrolysis to give the 3-cyano-2-pyrazinecarboxamide 21 in a 77% yield. The reaction of 12 with sodium alcoholate at room temperature also gave selectively the corresponding mono imidate derivatives (22 or 23). The resulting 22 and 23 readily converted to the corresponding alkyl ester derivatives 24 and 25, which were then converted to 21 by treatment with ammonia water.

Hydrolysis of 21 with aqueous sodium carbonate gave the 3-carbamoyl-2-pyrazinecarboxylic acid 26 in a 94% yield. Decarboxylation of 26 in o-dichlorobenzene gave the 2-pyrazinecarboxamide 27, which was readily converted to the 2-pyrazinecarbonitrile 15 by treatment with phosphoryl chloride. Hydrolysis of 27 with an excess amount of sodium hydroxide in water gave the 2-pyrazinecarboxylic acid 28.

As shown in Table II, the electron-donating propylamino group on the pyrazine ring shifted the IR absorption of the carbonyl group at the p-position to the lower wave number. The absorption pattern of the electronic spectra of compounds listed in Table II was similar to that of 15.

6-Phenyl-3-propylamino-2-pyrazinecarbonitrile 29 and 5-phenyl-3-propylamino-2-pyrazinecarbonitrile 30 were prepared in a similar way to that employed by Hirano et al. Compound I was allowed to react with an excess amount of propylamine at room temperature without a solvent. Subsequent chromatographic separation of the reaction mix-
Table II. Spectral Data of 5-Propylamino-6-(m-chlorophenyl)pyrazines

<table>
<thead>
<tr>
<th>No.</th>
<th>R¹</th>
<th>R²</th>
<th>IR ν max (C=O) cm⁻¹</th>
<th>UV λ max% EtOH nm (log e)</th>
</tr>
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<tbody>
<tr>
<td>21</td>
<td>CN</td>
<td>CONH₂</td>
<td>1695</td>
<td>245 (4.02) 303 (4.23) 364 (3.77)</td>
</tr>
<tr>
<td>24</td>
<td>CN</td>
<td>COOMe</td>
<td>1730</td>
<td>250 (4.10) 305 (4.29) 367 (3.85)</td>
</tr>
<tr>
<td>25</td>
<td>CN</td>
<td>COOEt</td>
<td>1730</td>
<td>248 (4.09) 304 (4.28) 365 (3.87)</td>
</tr>
<tr>
<td>19</td>
<td>CONH₂</td>
<td>CONH₂</td>
<td>1660</td>
<td>240 (3.99) 295 (4.13) 353 (3.85)</td>
</tr>
<tr>
<td>26</td>
<td>CONH₂</td>
<td>COOH</td>
<td>1640</td>
<td>240 (4.11) 297 (4.24) 351 (4.02)</td>
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<tr>
<td>27</td>
<td>CONH₂</td>
<td>H</td>
<td>1650</td>
<td>239 (4.06) 293 (4.29) 349 (4.05)</td>
</tr>
<tr>
<td>20</td>
<td>COOH</td>
<td>COOH</td>
<td>1680</td>
<td>241 (3.97) 298 (4.13) 350 (3.79)</td>
</tr>
<tr>
<td>28</td>
<td>COOH</td>
<td>H</td>
<td>1680</td>
<td>240 (4.02) 292 (4.24) 346 (3.95)</td>
</tr>
</tbody>
</table>

Scheme 4.

The herbicidal activities of these pyrazine derivatives were examined according to the method of Yoneyama et al.¹⁷ against barnyardgrass (Echinochloa crus-galli) and broadleaf weeds (Rotala indica and Monochoria vaginalis). As shown in Table III, 6-phenyl-2-pyrazinecarbonitriles with or without a propylamino group on the pyrazine ring were relatively potent compared with the 5-phenyl derivatives. Among the 6-phenyl derivatives, the 5-propylamino compounds (9, 14, 15 and 16) were highly effective in controlling these plants at a dosage of 20 g/are but less active than the corresponding dicarbonitriles, 8, 11, 12 and 13, at a dosage of 5 g/are.¹¹ Other 6-phenyl-5-propylamino-2-pyrazinecarbonitriles (21 ~25 and 31) possessed various degrees of activity against these plants at a dosage of 20 g/are. On the other hand, compounds 2 ~5, 19, 20, 26 ~28 and 32, which do not have a cyano group on the pyrazine ring, were inactive at a dosage of 200 g/are. These results
indicate that the structure of the 6-phenyl-5-
propylamino-2-pyrazinecarbonitrile moiety is 
important for high herbicidal activity.

EXPERIMENTAL

Melting points were determined on a Yanagimoto 
micro-melting apparatus and were uncorrected. IR spectra 
were recorded on a Hitachi 260-10 spectrometer. NMR 
spectra were recorded on a Hitachi R-24 (60 MHz) spec-
trometer with TMS as an internal standard. UV spectra 
were determined on a Hitachi 323 spectrometer.

**3-Carbamoyl-5-phenyl-2-pyrazinecarboxylic acid 2 and 3-carbamoyl-6-phenyl-2-pyrazinecarboxylic acid 3.** A mixture of 1 (1.03 g, 5 mmol) and 0.1 N sodium hydroxide (50 ml) was stirred at 95~100°C for 3 hr and then cooled to room temperature. After filtration, the filtrate was acidified with concentrated hydrochloric acid at pH 2. The precipitate was collected by filtration and extracted with benzene (100 ml). The extract was washed with water, dried over anhydrous magnesium sulfate, and evaporated to dryness. Chromatography of the residue on silica gel (50 g) and elution with benzene gave 0.17 g (14%) of 3, mp 220~240°C dec. (ethanol). IR ν\textsuperscript{KBr} cm\textsuperscript{-1}: 3480, 3350 (NH), 3100~2600 br (OH), 1700, 1665 (C=O). Anal. Found: C, 66.50; H, 4.77; N, 20.76. Calcd. for C\textsubscript{12}H\textsubscript{9}N\textsubscript{3}O: C, 66.32; H, 4.55; N, 21.09%. Similarly, 0.98 g (4 mmol) of 2 gave 0.20 g (20%) of 4, mp 190~195°C dec. (ethanol). IR ν\textsuperscript{KBr} cm\textsuperscript{-1}: 3400, 3320 (NH), 1660 (C=O). Anal. Found: C, 66.05; H, 4.70; N, 21.00. Calcd. for C\textsubscript{11}H\textsubscript{9}N\textsubscript{3}O: C, 66.32; H, 4.55; N, 21.09%. 

**6-Phenyl-2-pyrazinecarboxamide 4 and 5-phenyl-2-
pyrazinecarboxamide 5.** A mixture of 2 (0.98 g, 4 mmol) 
and o-dichlorobenzene (10 ml) was refluxed for 2 hr and 
allowed to stand overnight at room temperature. The 
precipitated product was collected by filtration to give 0.25 g (32%) of 4, mp 268~269°C dec. (ethanol). IR ν\textsuperscript{KBr} cm\textsuperscript{-1}: 3410, 3250 (NH), 1660 (C=O). Anal. Found: C, 66.50; H, 4.77; N, 20.76. Calcd. for C\textsubscript{12}H\textsubscript{9}N\textsubscript{3}O: C, 66.32; H, 4.55; N, 21.09%. Similarly, 0.98 g (4 mmol) of 3 gave 0.20 g (20%) of 5, mp 270~273°C dec. (ethanol). IR ν\textsuperscript{KBr} cm\textsuperscript{-1}: 3400, 3320 (NH), 1660 (C=O). Anal. Found: C, 66.05; H, 4.70; N, 21.00. Calcd. for C\textsubscript{11}H\textsubscript{9}N\textsubscript{3}O: C, 66.32; H, 4.55; N, 21.09%. 

**6-Phenyl-2-pyrazinecarbonitrile 6 and 5-phenyl-2-
pyrazinecarbonitrile 7.** A mixture of 4 (0.30 g, 1.5 mmol) 
and phosphoryl chloride (30 ml) was refluxed for 5 hr and 
evaporated to dryness. The residue was extracted with 
chloroform, and the extract was washed with water. After 
evaporation, the crude product was recrystallized from 
hexane to give 0.20 g (74%) of 6, mp 93~94°C (hexane). IR ν\textsuperscript{KBr} cm\textsuperscript{-1}: 2240 (C=O). NMR δ ppm (CDCl\textsubscript{3}): 9.17 (s, 1H), 8.76 (s, 1H), 8.10~7.90 (m, 2H), 7.55~7.40 (m, 3H). UV λ\textsuperscript{max} \textsuperscript{EtOH} nm (log ε): 261 (4.18), 308 (3.96). Anal. Found: C, 72.85; H, 3.91; N, 21.09%. Similarly, 0.30 g (1.5 mmol) of 5 gave 0.19 g (65%) of 7, mp 133~136°C (hexane). IR ν\textsuperscript{KBr} cm\textsuperscript{-1}: 2245 (C=O). NMR δ ppm (CDCl\textsubscript{3}): 9.10 (d, 1H, J=1.5 Hz), 8.90 (d, 1H, J=1.5 Hz), 8.10~7.90 (m, 2H), 7.55~7.40 (m, 3H). UV λ\textsuperscript{max} \textsuperscript{EtOH} nm (log ε): 243 (3.91), 266 (4.07), 308 (4.29). Anal. Found: C, 72.85; H, 3.91; N, 21.09%.
4.00; N, 23.25. Calcd. for C_{11}H_{13}N_{3}O: C, 72.92; H, 3.89; N, 23.19%.

5-Propylamino-6-phenyl-2-pyrazinecarbonitrile 9 and 6-propylamino-5-phenyl-2-pyrazinecarbonitrile 10. A mixture of 8 (13.2 g, 0.05 mol) and 1 N sodium hydroxide (200 ml) was stirred at 95~100°C for 4 hr. After cooling to room temperature, any insoluble matter was removed by filtration, and the filtrate was acidified with 6 N hydrochloric acid and allowed to stand at 0°C overnight. The precipitate was collected by filtration, dried under reduced pressure, and dissolved in o-dichlorobenzene (100 ml). The solution was refluxed for 3 hr and evaporated to dryness. Phosphoryl chloride (50 g) was added to the residue, and the resulting solution was refluxed for 2 hr. After evaporation, the resulting solid was washed with water, dried under reduced pressure, and chromatographed on silica gel (100 g) with elution by hexane-benzene (1:1) to give 0.56 g (5%) of 9. mp 99~100°C (hexane). IR νKBr cm⁻¹: 3270 (NH), 1540, 1495 (C=N). NMR δ ppm (CDCl₃): 8.11 (s, 1H), 7.46 (m, 4H), 5.20 (br, 1H), 3.39 (q, 2H), 1.65 (sec, 2H), 0.93 (t, 3H). Anal. Found: C, 73.33; H, 5.90; N, 23.77. Calcd. for C₁₅H₁₆N₄: C, 70.33; H, 5.90; N, 23.77.

Further elution with benzene–hexane (1:1) gave 2.13 g (19%) of 9. mp 80~81.5°C (hexane). IR νKBr cm⁻¹: 3370 (NH), 2240 (C=N). NMR δ ppm (CDCl₃): 8.23 (s, 1H), 7.46 (m, 4H), 5.58 (br, 1H), 3.40 (q, 2H), 1.62 (sec, 2H), 0.92 (t, 3H). Anal. Found: C, 70.80; H, 6.02; N, 23.51%. Further elution with benzene–hexane (1:1) gave 2.13 g (19%) of 9. IR νKBr cm⁻¹: 3380 (NH), 2240 (C=N). NMR δ ppm (CDCl₃): 8.11 (s, 1H), 7.46 (m, 4H), 5.58 (br, 1H), 3.40 (q, 2H), 1.62 (sec, 2H), 0.92 (t, 3H). Anal. Found: C, 70.80; H, 6.02; N, 23.51%.

In the same manner as described above, 11 gave 15 (18%) and 18 (3%); 15, mp 83~84°C (hexane). IR νKBr cm⁻¹: 3380 (NH), 2230 (C≡N). Anal. Found: C, 62.00; H, 5.02; N, 20.44. Calcd. for C₁₄H₁₁N₃: C, 61.65; H, 4.80; N, 23.51.

15 was stirred at room temperature for 2 hr. The precipitated product was collected by filtration and recrystallized from water to give 0.53 g (83%) of 16. mp 170~171°C. IR νKBr cm⁻¹: 3470, 3400, 3300~3500 (NH), 1680 (C≡O). Anal. Found: C, 53.70; H, 4.04; N, 12.30. Calcd. for C₁₅H₁₄N₃O₄: C, 53.66; H, 4.20; N, 12.52%.

5-Propylamino-6-(m-chlorophenyl)-2,3-pyrazinedicarboxylic acid 20. A mixture of 12 (2.98 g, 0.01 mol) and 4 N sodium hydroxide (100 ml) was stirred at 95~100°C for 5 hr and cooled to room temperature. After filtration, the filtrate was acidified with concentrated hydrochloric acid at pH 2. The precipitated product was collected by filtration and recrystallized from toluene to give 6.13 g (95%) of 22. mp 161~163°C. IR νKBr cm⁻¹: 3480, 3400, 3300~3500 (NH), 1695 (C≡O). Anal. Found: C, 57.27; H, 4.60; N, 22.00. Calcd. for C₁₅H₁₄N₃O₄Cl: C, 57.06; H, 4.47; N, 22.18%.

Methyl 3-cyano-6-propylamino-5-(m-chlorophenyl)-2-pyrazinecarboxylate 24. A mixture of sodium molybdate (0.13 g, 0.63 mmol) in 30% aqueous hydrogen peroxide (7.7 ml, 67.8 mmol) and ethanol (20 ml) was added to a stirred solution of 12 (4.05 g, 13.6 mmol) in ethanol (150 ml). The reaction mixture was stirred at 40°C for 2 hr and then allowed to stand at room temperature. The precipitated product was collected by filtration and washed with cool ethanol to give 3.31 g (77%) of 21. mp 233~234°C (ethanol). IR νKBr cm⁻¹: 3470, 3400, 3300~3500 (NH), 2230 (C≡N), 1695 (C≡O). Anal. Found: C, 57.27; H, 4.60; N, 22.00. Calcd. for C₁₅H₁₄N₃O₄Cl: C, 57.06; H, 4.47; N, 22.18%.

Methyl 3-cyano-6-propylamino-5-(m-chlorophenyl)-2-pyrazinecarboximidate 22. A solution of sodium methoxide in methanol was prepared from sodium (0.49 g, 21 mmol) and methanol (40 ml). To this solution was added 5.95 g (20 mmol) of 12, and the reaction mixture was stirred at room temperature for 2 hr. The precipitated product was collected by filtration and recrystallized from toluene to give 6.13 g (95%) of 22. mp 161~163°C. dec. IR νKBr cm⁻¹: 3470, 3405, 3300~3500 (NH), 2230 (C≡N), 1640 (C≡O). Anal. Found: C, 58.22; H, 5.13; N, 21.50. Calcd. for C₁₅H₁₄N₃O₄: C, 58.22; H, 4.89; N, 21.24%. In the same manner, treatment of 12 with sodium ethoxide gave 23 in an 88% yield. mp 84~88°C. dec. (toluene). IR νKBr cm⁻¹: 3470, 3340, 3300 (NH), 2230 (C≡N), 1640 (C≡O). Anal. Found: C, 59.15; H, 5.30; N, 20.14. Calcd. for C₁₅H₁₄N₃O₄Cl: C, 59.39; H, 5.28; N, 20.37%.
and 0.2 N hydrochloric acid (30 ml) was stirred at 60°C for 2 hr and cooled to room temperature. The precipitated product was collected by filtration, washed with water, and recrystallized from toluene to give 0.94 g (94%) of 24. mp 124 ~ 126°C. IR vKBr cm⁻¹: 3430 (NH), 2320 (C=N), 1730 (C=O). Anal. Found: C, 57.85; H, 4.60; N, 17.02. Calcd. for C₁₄H₁₄N₃O₂C₁: C, 57.64; H, 4.84; N, 14.40%.

In the same manner, 23 gave 25 in a 94% yield. mp 102°C (toluene–hexane). IR vKBr cm⁻¹: 3380 (NH), 2320 (C=N), 1730 (C=O). Anal. Found: C, 59.10; H, 5.00; N, 16.04. Caled. for C₁₅H₁₅N₄O₃C₁: C, 53.82; H, 4.52; N, 16.74%.

A mixture of 24 (1.65 g, 5 mmol) and 28% ammonia water (10 ml) was stirred at room temperature for 1 hr and allowed to stand overnight. The precipitate was collected by filtration, washed with water, and dried to give 1.20 g (72%) of 21.

3-Carbamoyl-6-propylamino-5-(m-chlorophenyl)-2-pyrazinecarboxylic acid 26. A mixture of 21 (3.16 g, 12 ml) and ethanol (30 ml) was stirred at 80°C for 10 hr, allowed to stand overnight. The precipitate was collected by filtration, washed with water, and recrystallized from toluene to give 0.61 g (76%) of 28. mp 189 ~ 191°C. IR vKBrcm⁻¹: 3480, 3320, 3080 (NH, OH), 1705, 1640 (C=O). Anal. Found: C, 59.10; H, 5.00; N, 17.02. Calcd. for C₁₇H₂₁N₅: C, 69.12; H, 7.17; N, 23.71%.

5-Propylamino-6-(m-chlorophenyl)-2-pyrazinecarboxamide 27. In the same manner as described for 4, 1.00 g (3 mmol) of 26 gave 0.30 g (40%) of 27. mp 175 ~ 177°C (toluene). IR vKBr cm⁻¹: 3460, 3390, 3200 (NH, OH), 1650 (C=O). Anal. Found: C, 57.74; H, 5.50; N, 19.51. Calcd. for C₁₅H₁₄N₄O₂Cl: C, 57.83; H, 5.20; N, 19.27%. In the same manner as described for 6, 1.00 g (3.4 mmol) of 27 gave 0.79 g (85%) of 15.

3-Propylamino-6-phenyl-2-pyrazinecarbonitrile 29 and 3-propylamino-5-phenyl-2-pyrazinecarbonitrile 30. A mixture of 1 (5.00 g, 24 mmol) and propylamine (50 ml) was stirred at room temperature for 10 min and evaporated. The residue was dissolved in benzene (100 ml). The solution was washed with water, dried over anhydrous magnesium sulfate and evaporated. The crude product was chromatographed on silica gel (50 g) and eluted with benzene to give 0.80 g (14%) of 29. mp 137 ~ 138°C (toluene–hexane). IR vKBr cm⁻¹: 3445 (NH), 2240 (C=N). NMR δ ppm (CDCl₃): 8.60 (s, 1H), 7.75 ~ 7.35 (m, 5H), 5.40 (br, 1H), 3.45 (q, 2H), 1.66 (sec, 2H), 0.96 (t, 3H). Anal. Found: C, 70.70; H, 5.75; N, 23.54. Calcd. for C₁₄H₁₄N₄: C, 70.57; H, 5.92; N, 23.51%.

3,5-Bis(propylamino)-6-phenyl-2-pyrazinecarbonitrile 31. A mixture of 8 (25.0 g, 0.095 mol) and propylamine (80 ml) was stirred at room temperature for 16 hr and evaporated to dryness. The residue was chromatographed on silica gel (150 g) and eluted with benzene to give 15.8 g of 8 and 7.5 g (27%) of 31. mp 102 ~ 103°C (ethanol). IR vKBrcm⁻¹: 3350 (NH), 2200 (C=N). NMR δ ppm (CDCl₃): 8.34 (s, 1H), 8.02 ~ 7.55 (m, 5H), 5.40 (br, 1H), 3.56 (q, 2H), 1.71 (sec, 2H), 1.03 (t, 3H). Anal. Found: C, 70.82; H, 5.90; N, 23.27. Calcd. for C₁₇H₂₃N₅O: C, 70.57; H, 5.92; N, 23.51%.

3,5-Bis(propylamino)-6-phenyl-2-pyrazinecarboxamide 32. A solution of 31 (1.00 g, 3.4 mmol) in ethanol (10 ml) and 5N sodium hydroxide (10 ml) was stirred at 95 ~100°C for 3 hr, cooled to room temperature, and extracted with toluene (50 ml x 4). The extract was evaporated to give 0.82 g (80%) of 32. mp 142 ~ 143°C (toluene). IR vKBrcm⁻¹: 3500, 3375, 3300 (NH), 1630 (C=O). Anal. Found: C, 65.32; H, 7.30; N, 22.14. Calcd. for C₁₇H₂₃N₅O: C, 65.15; H, 7.40; N, 22.35%.

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REFERENCES
