

Tokuhiro Watanabe, Ikuko Ueda, Naomi Hayakawa, Yasuo Kondo,
Hiroko Adachi, Akiko Iwasaki, Shizuko Kawamata, Fumiko Mentori,
Miyuki Ichikawa, Kayo Yuasa and Akihiro Ohta*

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

Teruo Kurihara and Hiroshi Miyamae

Faculty of Sciences, Josai University, 1-1 Keyakidai,
Sakado, Saitama 350-02, Japan

Received September 27, 1989

2,3-Dichloro- and 2,5-dichloropyrazines were treated with sodium azide. The former gave diazidopyrazines and the latter, monoazidomonochloropyrazines. Pyrolysis of 2,3-diazidopyrazines resulted the production of 1,2-dicyanoiminoethanes and that of 2-azido-5-chloropyrazines, chloroimidazoles.

J. Heterocyclic Chem., **27**, 711 (1990).

The ring transformation of azidopyrazines to imidazoles was studied in detail [1]. The authors have also reported the pyrolytic transformation of azidopyrazines to the corresponding imidazoles [2] and considered the formation of 4-membered ring compounds from 2,3- and 2,5-diazidopyrazines to occur through the elimination of 2 equivalents of nitrogen. Actually, however, reactions of 2,3-diazidopyrazines were found to give 1,2-dicyanoiminoethanes

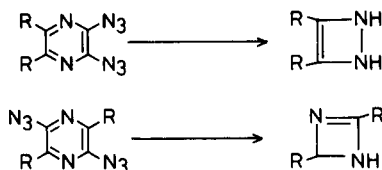


Figure 1. Possible reactions of diazidopyrazines.

and attempts to synthesize 2,5-diazidopyrazines were unsuccessful.

In the present study, the preparation of 1,4-dioxides **1a-e** of 2,3-bis(*p*-chlorophenyl)-, 2,3-bis(*p*-bromophenyl)-, 2,3-

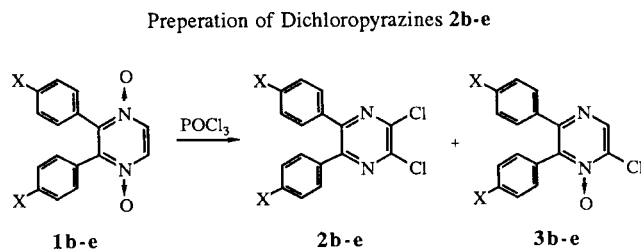
bis(*p*-methylphenyl)- and 2,3-bis(*p*-methoxyphenyl)pyrazines was carried out in the same manner as that previously reported [3]. That is, **1a** [4] was reacted with phosphoryl chloride to give 2,3-dichloro-5,6-diphenylpyrazine (**2a**) [5] and 2-chloro-5,6-diphenylpyrazine 1-oxide (**3a**) [3]. Under the same reaction conditions, pyrazine 1,4-dioxides **1b-e** [6] gave the corresponding 2,3-dichloropyrazines **2b-e** and 2-chloropyrazine 1-oxides **3b-e** which could be easily separated from each other by column chromatography. The results are shown in Table I.

By stirring a suspension of **2a-e** and sodium azide in *N,N*-dimethylformamide, the desired 2,3-diazidopyrazines **4a-e** were obtained in satisfactory yields, as shown in Table II. The ir spectra of **4a-e**, taken both in chloroform and potassium bromide, indicated the absence of any band due to the azide group. It would thus appear that these 2,3-diazidopyrazines **4a-e** exist in the tetrazole form both in solution and the solid state.

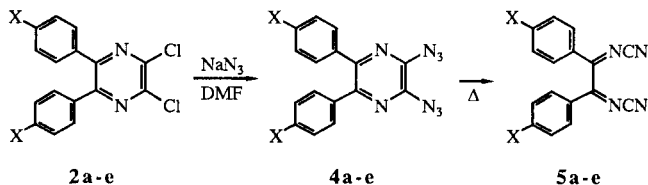
Table II

Transformations of 2,3-Dichloropyrazines **2a-e** to

Cyanoiminoethanes **5a-e**



| Compound | X | Product | Yield (%) | Product | Yield (%) |
|---------------|-----|-----------|-----------|-----------|-----------|
| 1b [6] | Br | 2b | 70 | 3b | 25 |
| 1c [6] | Cl | 2c | 89 | 3c | 10 |
| 1d [6] | Me | 2d | 76 | 3d | 19 |
| 1e [6] | MeO | 2e | 78 | 3e | 20 |



| Compound | X | Product | Yield (%) | Product | Yield (%) |
|-----------|-----|-----------|-----------|-----------|-----------|
| 2a | H | 4a | 82 | 5a | 52 |
| 2b | Br | 4b | 79 | 5b | 62 |
| 2c | Cl | 4c | 86 | 5c | 45 |
| 2d | Me | 4d | 71 | 5d | 56 |
| 2e | MeO | 4e | 73 | 5e | 54 |

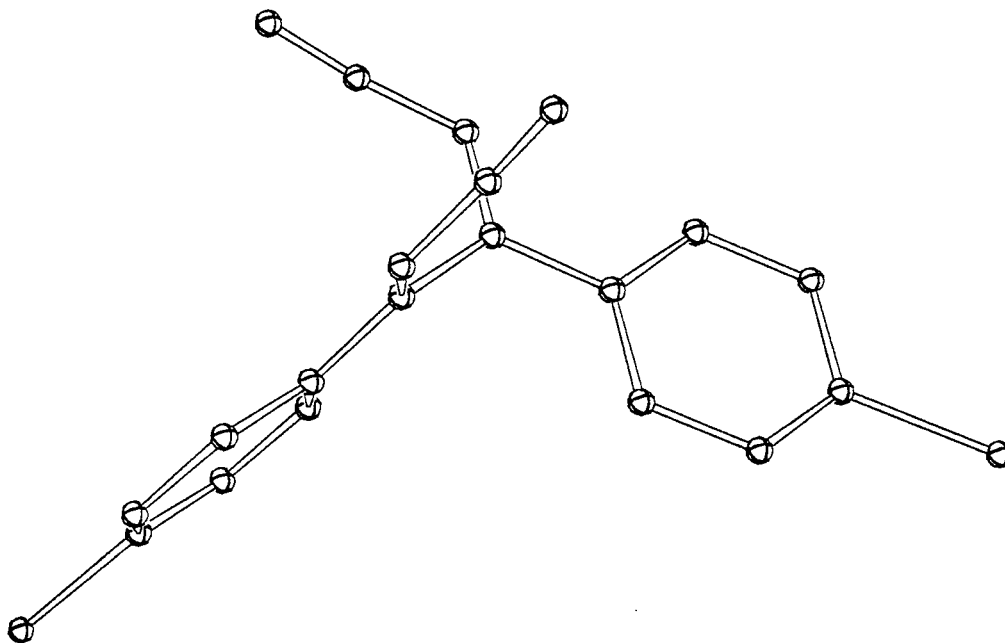


Figure II. X-ray diffraction of 1,2-bis(p-bromophenyl)-1,2-dicyanoiminoethane (**5b**).

Table III

Transformations of 2,5-Dichloropyrazines **6a-f** to Chloroimidazoles **9a-f**

| 6a-f | | $\xrightarrow[\text{DMF}]{\text{NaN}_3}$ | 7a-f | | $\xrightarrow{\Delta}$ | 8a-f | | $\xrightarrow[\text{ref.}]{20\% \text{ KOH}}$ | 9a-f | |
|-----------------|--------------|--|-----------------|-----------|------------------------|-----------------|-----------|---|-----------------|--|
| Compound | R | Product | Yield (%) | Product | Yield (%) | Product | Yield (%) | | | |
| 6a [7] | Me | 7a | 69 | 8a | 80 | 9a | 86 | | | |
| 6b [7] | Et | 7b | 9 | 8b | 39 | 9b | 84 | | | |
| 6c [3] | <i>n</i> -Pr | 7c | 24 | 8c | 77 | 9c | 85 | | | |
| 6d [2] | <i>n</i> -Bu | 7d | 26 | 8d | 68 | 9d | 95 | | | |
| 6e [8] | <i>i</i> -Bu | 7e | 45 | 8e | 89 | 9e | 100 | | | |
| 6f [9] | Ph | 7f | 79 | 8f | 61 | 9f | 79 | | | |

The diazidopyrazines **4a-e** thus obtained were heated in test tubes at 220° to 250° in a metal bath and the products were purified by column chromatography. The ir spectra of all the products showed a strong band at 2150 cm⁻¹ corresponding to a cyano group. The structures of the products could not be determined by spectral analysis and consequently, product **5b** was submitted to X-ray analysis and was found to have the structure shown in Figure II.

An attempt was made to synthesize **5b** from 4,4'-dibromobenzil and cyanamide but without success. The pyrolysis of 2,3-diazidopyrazines was concluded to give 1,2-dicyanoiminoethanes by opening the pyrazine ring.

Reactions of 2,5-dichloropyrazines **6a-f** with sodium azide were also examined. Although compounds **6a-f** were treated with sodium azide under various conditions, the desired 2,5-diazidopyrazines were not obtained, but rather

corresponding monoazidomonochloropyrazines **7a-f** in moderate yields. The ir spectra of **7a-f**, taken in chloroform and a liquid film, showed a weak band near 2150 cm^{-1} due to an azido group. In the ir spectra of solid monoazido-monochloropyrazines, taken in potassium bromide, no band due to the azido group was observed.

These pyrazines **7a-f** were heated at 220° to yield chloro-cyanoimidazoles **8a-f** which were subsequently hydrolyzed under alkaline conditions to give chloroimidazoles **9a-f**. The melting point of **9a** corresponded well with that previously reported [10]. Structure determinations for other chloroimidazoles **9a-f** were essentially in agreement with those proposed. These reactions may prove useful for the preparation of chloroimidazoles.

EXPERIMENTAL

Melting points were recorded on a Yanagimoto micro-melting-point apparatus and for which, no correction was made. The ir spectra were taken on a Shimadzu IR-400 spectrometer, pmr spectra in deuteriochloroform, unless otherwise stated, using a Varian EM-390 with tetramethylsilane as the internal standard. Mass spectra were obtained with a Hitachi M-80B spectrometer. For column chromatography, Wakogel C-200 (Wako Pure Chemical Industry, Ltd., Tokyo) was used as the packing material. Medium-pressure column chromatography was carried out using a UVILOG ALPC-100 as the pump, UVILOG 5IIIa as the UV detector (Oyo-Bunko KiKi Co., Ltd., Tokyo) and Kieselgel 60 (Merck AG, Darmstadt) as the packing material.

General Procedure for Preparation of 2,3-Dichloropyrazines **2b-e**.

The preparation of 2,3-dichloro-5,6-diphenylpyrazine derivatives was achieved under the same conditions as reported for the preparation of 2,3-dichloro-5,6-diphenylpyrazine. The products and yields are shown in Table I.

5,6-Bis(*p*-bromophenyl)-2,3-dichloropyrazine (**2b**).

This compound had the following physical properties, mp 186-187°, pale yellow needles (from hexane); pmr: δ 7.32 (4H, d, J = 9 Hz, benzene H), 7.47 (4H, d, J = 9 Hz, benzene H) ppm; ms: m/z 456 (M^+).

Anal. Calcd. for $C_{16}H_8Br_2Cl_2N_2$: C, 41.87; H, 1.76; N, 6.10. Found: C, 42.14; H, 1.82; N, 6.06.

5,6-Bis(*p*-bromophenyl)-2-chloropyrazine 1-Oxide (**3b**).

This compound had the following physical properties, mp 255-256°, pale yellow needles (from chloroform); pmr: δ 7.05 (2H, d, J = 8 Hz, benzene H), 7.10 (2H, d, J = 8 Hz, benzene H), 7.37 (2H, d, J = 8 Hz, benzene H), 7.47 (2H, d, J = 8 Hz, benzene H), 8.63 (1H, s, pyrazine H) ppm; ms: m/z 438 (M^+).

Anal. Calcd. for $C_{16}H_8Br_2ClN_2O$: C, 43.62; H, 2.06; N, 6.36. Found: C, 43.74; H, 2.02; N, 6.20.

2,3-Dichloro-5,6-bis(*p*-chlorophenyl)pyrazine (**2c**).

This compound had the following physical properties, mp 167-168°, pale yellow needles (from hexane); pmr: δ 7.27 (8H, broad s, benzene H) ppm; ms: m/z 368 (M^+).

Anal. Calcd. for $C_{16}H_8Cl_4N_2$: C, 51.93; H, 2.18; N, 7.57. Found: C, 52.14; H, 2.21; N, 7.58.

2-Chloro-5,6-bis(*p*-chlorophenyl)pyrazine 1-Oxide (**3c**).

This compound had the following physical properties, mp 261-262°, pale yellow needles (from acetone); pmr: δ 7.10-7.23 (8H, m, benzene H), 8.60 (1H, s, pyrazine H) ppm; ms: m/z 350 (M^+).

Anal. Calcd. for $C_{16}H_8Cl_3N_2O$: C, 54.62; H, 2.58; N, 7.97. Found: C, 54.65; H, 2.56; N, 7.93.

2,3-Dichloro-5,6-bis(*p*-methylphenyl)pyrazine (**2d**).

This compound had the following physical properties, mp 135-136°, colorless needles (from hexane); pmr: δ 2.28 (6H, s, 2 x CH_3), 7.13 (8H, q, J = 8 Hz, benzene H) ppm; ms: m/z 328 (M^+), 313 ($M^+ - \text{CH}_3$).

Anal. Calcd. for $C_{18}H_{14}Cl_2N_2$: C, 65.67; H, 4.29; N, 8.51. Found: C, 65.86; H, 4.26; N, 8.50.

2-Chloro-5,6-bis(*p*-methylphenyl)pyrazine 1-Oxide (**3d**).

This compound had the following physical properties, mp 200-201°, colorless needles (from hexane-ethyl acetate); pmr: δ 2.22 (3H, s, CH_3), 2.27 (3H, s, CH_3), 7.00-7.20 (8H, m, benzene H), 8.53 (1H, s, pyrazine H) ppm; ms: m/z 310 (M^+).

Anal. Calcd. for $C_{18}H_{15}ClN_2O$: C, 69.56; H, 4.87; N, 9.01. Found: C, 69.42; H, 4.83; N, 9.02.

2,3-Dichloro-5,6-bis(*p*-methoxyphenyl)pyrazine (**2e**).

This compound had the following physical properties, mp 120-121°, colorless needles (from hexane); pmr: δ 3.77 (6H, s, 2 x OCH_3), 6.83 (4H, d, J = 7.5 Hz, benzene H), 7.43 (4H, d, J = 7.5 Hz, benzene H) ppm; ms: m/z 360 (M^+).

Anal. Calcd. for $C_{18}H_{15}Cl_2N_2O_2$: C, 59.85; H, 3.91; N, 7.76. Found: C, 60.02; H, 3.88; N, 7.79.

2-Chloro-5,6-bis(*p*-methoxyphenyl)pyrazine 1-Oxide (**3e**).

This compound had the following physical properties, mp 197-198°, colorless needles (from methanol); pmr: δ 3.73 (3H, s, OCH_3), 3.78 (3H, s, OCH_3), 6.77 (2H, d, J = 9 Hz, benzene H), 6.87 (2H, d, J = 9 Hz, benzene H), 7.23 (2H, d, J = 9 Hz, benzene H), 7.27 (2H, d, J = 9 Hz, benzene H), 8.63 (1H, s, pyrazine H) ppm; ms: m/z 342 (M^+).

Anal. Calcd. for $C_{18}H_{15}ClN_2O_3$: C, 63.07; H, 4.41; N, 8.17. Found: C, 63.30; H, 4.50; N, 8.30.

General Procedure for Preparation of 2,3-Diazidopyrazines **4a-e**.

A suspension of a 2,3-dichloropyrazine (50 mmoles) and sodium azide (90% purity, 14.50 g, 200 mmoles) in *N,N*-dimethylformamide (100 ml) was stirred at room temperature for 48 hours. The reaction mixture was poured into water and the precipitates were collected by suction to give the crude 2,3-diazidopyrazine as a pale brown crystalline mass. Purification of the crude product was made by column chromatography on silica gel (20 g), eluting with a mixture of hexane and methylene chloride (1:1) and the following recrystallization.

2,3-Diazido-5,6-diphenylpyrazine (**4a**).

This compound had the following physical properties, mp 254-255° dec, yellow needles (from hexane); pmr: δ 7.43 (10H, broad s, benzene H) ppm; ms: m/z 314 (M^+).

Anal. Calcd. for $C_{16}H_{10}N_6$: C, 61.14; H, 3.21; N, 35.65. Found: C, 60.88; H, 3.13; N, 35.69.

2,3-Diazido-5,6-bis(*p*-bromophenyl)pyrazine (**4b**).

This compound had the following physical properties, mp

240-241°, colorless prisms (from hexane); pmr: δ 7.57 (4H, d, J = 9 Hz, benzene H), 7.73 (4H, d, J = 9 Hz, benzene H) ppm; ms: m/z 470 (M⁺).

Anal. Calcd. for C₁₆H₈Br₂N₈: C, 40.70; H, 1.71; N, 23.74. Found: C, 40.58; H, 1.73; N, 23.91.

2,3-Diazido-5,6-bis(*p*-chlorophenyl)pyrazine (4c).

This compound had the following physical properties, mp 247-248° dec, pale yellow needles (from benzene); pmr (acetone-d₆): δ 7.20-7.73 (8H, m, benzene H) ppm; ms: m/z 282 (M⁺).

Anal. Calcd. for C₁₆H₈Cl₂N₈: C, 50.15; H, 2.10; N, 29.24. Found: C, 50.08; H, 2.10; N, 29.15.

2,3-Diazido-5,6-bis(*p*-methylphenyl)pyrazine (4d).

This compound had the following physical properties, mp 211-212° dec, colorless plates (from methanol); pmr: δ 2.47 (6H, s, 2 x CH₃), 7.38 (4H, d, J = 7 Hz, benzene H), 7.80 (4H, d, J = 7 Hz, benzene H) ppm; ms: m/z 342 (M⁺).

Anal. Calcd. for C₁₈H₁₄N₈: C, 63.15; H, 4.12; N, 32.73. Found: C, 63.11; H, 4.03; N, 32.50.

2,3-Diazido-5,6-bis(*p*-methoxyphenyl)pyrazine (4e).

This compound had the following physical properties, mp 217.5-219° dec, yellow needles (from hexane); pmr: δ 3.83 (6H, s, 2 x OCH₃), 6.97 (4H, d, J = 7.5 Hz, benzene H), 7.45 (4H, d, J = 7.5 Hz, benzene H) ppm; ms: m/z 374 (M⁺).

Anal. Calcd. for C₁₈H₁₄N₈O₂: C, 57.75; H, 3.77; N, 29.93. Found: C, 57.65; H, 3.89; N, 29.68.

General Procedure for Pyrolysis of 2,3-Diazidopyrazines 4a-e.

A 2,3-diazido-5,6-diphenylpyrazine (100 mg) was heated in a test tube at 220-250° in a metal bath. The reaction finished in a moment with an explosive generation of nitrogen gas. The crude product was purified by chromatography on silica gel (ca. 1 g), eluting with hexane containing an increasing amount of methylene chloride. Recrystallization of the product gave colorless or slightly yellow crystals.

1,2-Dicyanoimino-1,2-diphenylethane (5a).

This compound had the following physical properties, mp 130-131°, colorless needles (from cyclohexane); ir (potassium bromide): 2150 cm⁻¹ (ν C \equiv N); pmr: δ 7.47-8.17 (10H, m, benzene H) ppm; ms: m/z 258 (M⁺).

Anal. Calcd. for C₁₆H₁₀N₄: C, 74.40; H, 3.90; N, 21.69. Found: C, 74.62; H, 3.85; N, 21.89.

1,2-Bis(*p*-bromophenyl)-1,2-dicyanoiminoethane (5b).

This compound had the following physical properties, mp 268-269°, pale yellow needles (from benzene); ir (potassium bromide): 2150 cm⁻¹ (ν C \equiv N); pmr: δ 7.73 (8H, s, benzene H) ppm; ms: m/z 414 (M⁺).

Anal. Calcd. for C₁₆H₈Br₂N₄: C, 46.18; H, 1.94; N, 13.47. Found: C, 46.48; H, 1.98; N, 13.48.

1,2-Bis(*p*-chlorophenyl)-1,2-dicyanoiminoethane (5c).

This compound had the following physical properties, mp 193-194°, pale yellow needles (from benzene); ir (potassium bromide): 2150 cm⁻¹ (ν C \equiv N); pmr: δ 7.13 (4H, d, J = 8 Hz, benzene H), 7.80 (4H, d, J = 8 Hz, benzene H) ppm; ms: m/z 328 (M⁺).

Anal. Calcd. for C₁₆H₈Cl₂N₄: C, 58.74; H, 2.46; N, 17.13. Found: C, 58.94; H, 2.45; N, 17.13.

1,2-Dicyanoimino-1,2-bis(*p*-methylphenyl)ethane (5d).

This compound had the following physical properties, mp 174-175°, colorless needles (from cyclohexane); ir (potassium bromide): 2150 cm⁻¹ (ν C \equiv N); pmr: δ 2.40 (6H, s, 2 x CH₃), 7.27 (4H, d, J = 8 Hz, benzene H), 7.43 (4H, d, J = 8 Hz, benzene H) ppm; ms: m/z 286 (M⁺).

Anal. Calcd. for C₁₈H₁₄N₄: C, 75.50; H, 4.93; N, 19.57. Found: C, 75.50; H, 5.02; N, 19.35.

1,2-Dicyanoimino-1,2-bis(*p*-methoxyphenyl)ethane (5e).

This compound had the following physical properties, mp 234-235°, yellow plates (from chloroform); ir (potassium bromide): 2150 cm⁻¹ (ν C \equiv N); pmr: δ 3.90 (6H, s, 2 x OCH₃), 6.93 (4H, d, J = 6.5 Hz, benzene H), 7.87 (4H, d, J = 6.5 Hz, benzene H) ppm; ms: m/z 318 (M⁺).

Anal. Calcd. for C₁₈H₁₄N₄O₂: C, 67.91; H, 4.43; N, 17.60. Found: C, 67.91; H, 4.37; N, 17.56.

General Procedure for Reaction of 2,5-Dichloropyrazines 6a-f with Sodium Azide.

A mixture of a dichloropyrazine (20 mmoles) and sodium azide (90% purity, 2.90 g, 40 mmoles) in *N,N*-dimethylformamide (200 ml) was stirred for 5 hours at 100°. After the solvent was removed *in vacuo*, the residue was diluted with water and extracted with methylene chloride or ether. The extract was worked up as usual and the product was purified by silica gel column chromatography (10 g), eluting with hexane containing an increasing amount of ethyl acetate.

2-Azido-5-chloro-3,6-dimethylpyrazine (7a).

This compound had the following physical properties, mp 136-137.5°, colorless plates (from methanol); ir (chloroform): 2140 cm⁻¹ (ν N₃); pmr: δ 3.05 (6H, s, 2 x CH₃) ppm; ms: m/z 183 (M⁺).

Anal. Calcd. for C₆H₈ClN₅: C, 39.25; H, 3.29; N, 38.15. Found: C, 39.23; H, 3.34; N, 37.94.

2-Azido-5-chloro-3,6-diethylpyrazine (7b).

This compound had the following physical properties, bp 118-123°/3 torr, colorless oil; ir (liquid film): 2150 cm⁻¹ (ν N₃); pmr: δ 1.47 (3H, t, J = 7.2 Hz, CH₂CH₃), 1.54 (3H, t, J = 7.2 Hz, CH₂CH₃), 3.41 (2H, q, J = 7.2 Hz, CH₂CH₃), 3.47 (2H, q, J = 7.2 Hz, CH₂CH₃) ppm; ms: m/z 211 (M⁺).

Anal. Calcd. for C₈H₁₀ClN₅: C, 45.40; H, 4.76; N, 33.09. Found: C, 45.21; H, 4.64; N, 33.30.

2-Azido-5-chloro-3,6-dipropylpyrazine (7c).

This compound had the following physical properties, bp 127-134°/2 torr, colorless oil; ir (liquid film): 2160 cm⁻¹ (ν N₃); pmr: δ 1.08 (3H, t, J = 7.2 Hz, (CH₂)₂CH₃), 1.10 (3H, t, J = 7.2 Hz, (CH₂)₂CH₃), 1.72-2.26 (4H, m, 2 x CH₂CH₂CH₃), 3.37 (2H, t, J = 7.2 Hz, CH₂CH₂CH₃), 3.42 (2H, t, J = 7.2 Hz, CH₂CH₂CH₃) ppm; ms: m/z 239 (M⁺).

Anal. Calcd. for C₁₀H₁₄ClN₅: C, 50.10; H, 5.89; N, 29.22. Found: C, 50.16; H, 5.88; N, 29.27.

2-Azido-3,6-dibutyl-5-chloropyrazine (7d).

This compound had the following physical properties, bp 174-179°/2 torr, colorless oil; ir (liquid film): 2130 cm⁻¹ (ν N₃); pmr: δ 0.99 (3H, t, J = 7.4 Hz, (CH₂)₃CH₃), 1.00 (3H, t, J = 7.4 Hz, (CH₂)₃CH₃), 1.46-1.57 (4H, m, 2 x (CH₂)₂CH₂CH₃), 1.79-1.98 (4H, m, 2 x CH₂CH₂CH₂CH₃), 3.40 (2H, t, J = 7.6 Hz, CH₂(CH₂)₂

CH_3), 3.55 (2H, t, $J = 7.6$ Hz, $\text{CH}_2(\text{CH}_2)_2\text{CH}_3$) ppm; ms: m/z 267 (M^+).

Anal. Calcd. for $\text{C}_{12}\text{H}_{18}\text{ClN}_5$: C, 53.83; H, 6.78; N, 26.16. Found: C, 53.11; H, 6.81; N, 25.92.

2-Azido-5-chloro-3,6-diisobutylpyrazine (7e).

This compound had the following physical properties, mp 66-67°, colorless needles (from methanol-water); ir (chloroform): 2130 cm^{-1} (νN_3); pmr: δ 1.04 (6H, d, $J = 6.6$ Hz, $\text{CH}_2\text{CH}(\text{CH}_3)_2$), 1.06 (6H, d, $J = 6.6$ Hz, $\text{CH}_2\text{CH}(\text{CH}_3)_2$), 2.22-2.73 (2H, m, 2 x $\text{CH}_2\text{-CH}(\text{CH}_3)_2$), 3.22 (2H, d, $J = 7.8$ Hz, $\text{CH}_2\text{CH}(\text{CH}_3)_2$), 3.31 (2H, d, $J = 7.8$ Hz, $\text{CH}_2\text{CH}(\text{CH}_3)_2$) ppm; ms: m/z 267 (M^+).

Anal. Calcd. for $\text{C}_{12}\text{H}_{18}\text{ClN}_5$: C, 53.83; H, 6.78; N, 26.16. Found: C, 53.97; H, 6.76; N, 26.39.

2-Azido-5-chloro-3,6-diphenylpyrazine (7f).

This compound had the following physical properties, mp 179-181°, pale yellow prisms (from ethanol); ir (chloroform): 2140 cm^{-1} (νN_3); pmr: δ 7.49-7.87 (8H, m, benzene H), 8.80-9.01 (2H, m, benzene H) ppm; ms: m/z 307 (M^+).

Anal. Calcd. for $\text{C}_{16}\text{H}_{10}\text{ClN}_5$: C, 62.45; H, 3.28; N, 22.76. Found: C, 62.28; H, 3.18; N, 22.65.

General Procedure for Pyrolysis of Monoazido-monochloropyrazines (7a-f).

A monoazidomonochloropyrazine (100 mg) was heated in a test tube at 220° in a metal bath. The reaction finished in a moment with an explosive generation of nitrogen. After being cooled, the product was purified by silica gel column chromatography (5 g), eluting with hexane containing an increasing amount of ethyl acetate.

4-Chloro-1-cyano-2,5-dimethylimidazole (8a).

This compound had the following physical properties, mp 102-103°, colorless needles (from hexane); ir (potassium bromide): 2250 cm^{-1} ($\nu \text{C}\equiv\text{N}$); pmr: δ 2.22 (3H, s, CH_3), 2.43 (3H, s, CH_3) ppm; ms: m/z 155 (M^+).

Anal. Calcd. for $\text{C}_6\text{H}_6\text{ClN}_3$: C, 46.32; H, 3.89; N, 27.01. Found: C, 46.16; H, 3.85; N, 27.02.

4-Chloro-1-cyano-2,5-diethylimidazole (8b).

This compound had the following physical properties, bp 78-82°/2 torr, colorless oil; ir (liquid film): 2250 cm^{-1} ($\nu \text{C}\equiv\text{N}$); pmr: δ 1.28 (3H, t, $J = 7.8$ Hz, CH_2CH_3), 1.35 (3H, t, $J = 7.8$ Hz, CH_2CH_3), 2.73 (2H, q, $J = 7.8$ Hz, CH_2CH_3), 2.84 (2H, q, $J = 7.8$ Hz, CH_2CH_3) ppm; ms: m/z 183 (M^+).

Anal. Calcd. for $\text{C}_8\text{H}_{10}\text{ClN}_3$: C, 52.32; H, 5.49; N, 22.88. Found: C, 52.35; H, 5.49; N, 22.84.

4-Chloro-1-cyano-2,5-dipropylimidazole (8c).

This compound had the following physical properties, bp 102-107°/1 torr, colorless oil; ir (liquid film): 2260 cm^{-1} ($\nu \text{C}\equiv\text{N}$); pmr: δ 0.99 (3H, t, $J = 6.6$ Hz, $(\text{CH}_2)_2\text{CH}_3$), 1.03 (3H, t, $J = 6.6$ Hz, $(\text{CH}_2)_2\text{CH}_3$), 1.47-2.07 (4H, m, 2 x $\text{CH}_2\text{CH}_2\text{CH}_3$), 2.67 (2H, t, $J = 7.8$ Hz, $\text{CH}_2\text{CH}_2\text{CH}_3$), 2.79 (2H, t, $J = 7.8$ Hz, $\text{CH}_2\text{CH}_2\text{CH}_3$) ppm; ms: m/z 211 (M^+).

Anal. Calcd. for $\text{C}_{10}\text{H}_{14}\text{ClN}_3$: C, 56.74; H, 6.67; N, 19.85. Found: C, 56.53; H, 6.61; N, 19.74.

2,5-Dibutyl-4-chloro-1-cyanoimidazole (8d).

This compound had the following physical properties, bp 132-136°/1 torr, colorless oil; ir (liquid film): 2260 cm^{-1} ($\nu \text{C}\equiv\text{N}$);

pmr: δ 0.96 (6H, t, $J = 7.4$ Hz, 2 x $(\text{CH}_2)_3\text{CH}_3$), 1.33-1.47 (4H, m, 2 x $(\text{CH}_2)_2\text{CH}_2\text{CH}_3$), 1.63 (2H, m, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.78 (2H, m, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 2.69 (2H, t, $J = 7.6$ Hz, $\text{CH}_2(\text{CH}_2)_2\text{CH}_3$), 2.81 (2H, t, $J = 7.6$ Hz, $\text{CH}_2(\text{CH}_2)_2\text{CH}_3$) ppm; ms: m/z 239 (M^+).

Anal. Calcd. for $\text{C}_{12}\text{H}_{18}\text{ClN}_3$: C, 60.12; H, 7.57; N, 17.53. Found: C, 60.07; H, 7.65; N, 17.48.

4-Chloro-1-cyano-2,5-diisobutylimidazole (8e).

This compound had the following physical properties, bp 139-146°/3 torr, colorless oil; ir (liquid film): 2260 cm^{-1} ($\nu \text{C}\equiv\text{N}$); pmr: δ 0.97 (6H, d, $J = 6.7$ Hz, $\text{CH}_2\text{CH}(\text{CH}_3)_2$), 1.00 (6H, d, $J = 6.7$ Hz, $\text{CH}_2\text{CH}(\text{CH}_3)_2$), 1.97-2.22 (2H, m, 2 x $\text{CH}_2\text{CH}(\text{CH}_3)_2$), 2.56 (2H, d, $J = 7.4$ Hz, $\text{CH}_2\text{CH}(\text{CH}_3)_2$), 2.69 (2H, d, $J = 7.4$ Hz, $\text{CH}_2\text{CH}(\text{CH}_3)_2$) ppm; ms: m/z 239 (M^+).

Anal. Calcd. for $\text{C}_{12}\text{H}_{18}\text{ClN}_3$: C, 60.12; H, 7.57; N, 17.53. Found: C, 60.06; H, 7.58; N, 17.62.

4-Chloro-1-cyano-2,5-diphenylimidazole (8f).

This compound had the following physical properties, mp 173-175°, colorless needles (from hexane); ir (potassium bromide): 2260 cm^{-1} ($\nu \text{C}\equiv\text{N}$); pmr: δ 7.40-7.70 (8H, m, benzene H), 7.88-8.06 (2H, m, benzene H) ppm; ms: m/z 279 (M^+).

Anal. Calcd. for $\text{C}_{16}\text{H}_{10}\text{ClN}_3$: C, 68.70; H, 3.70; N, 15.02. Found: C, 68.40; H, 3.70; N, 15.05.

General Procedure for Hydrolysis of 4-Chloro-1-cyanoimidazoles (8a-f).

A solution of a 4-chloro-1-cyanoimidazole (1 mmole) in 20% aqueous potassium hydroxide solution (10 ml) was refluxed for 4 hours and then extracted with methylene chloride. When the substrate was not soluble in the alkali solution, a small amount of methanol was added. The extract was worked up as usual and the product was purified by recrystallization or distillation.

4-Chloro-2,5-dimethylimidazole (9a).

This compound had the following physical properties, mp 212-213° (lit 10, mp 209-210°), colorless plates (from acetone); pmr (deuteriomethanol): δ 1.60 (3H, s, CH_3), 1.70 (3H, s, CH_3) ppm; ms: m/z 130 (M^+).

Anal. Calcd. for $\text{C}_5\text{H}_7\text{ClN}_2$: C, 45.99; H, 5.40; N, 21.45. Found: C, 46.07; H, 5.60; N, 21.43.

4-Chloro-2,5-diethylimidazole (9b).

This compound had the following physical properties, mp 124-125° colorless plates (from hexane); pmr: δ 1.16 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 1.22 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 2.57 (2H, q, $J = 7.5$ Hz, CH_2CH_3), 2.65 (2H, q, $J = 7.5$ Hz, CH_2CH_3) ppm; ms: m/z 158 (M^+).

Anal. Calcd. for $\text{C}_7\text{H}_{11}\text{ClN}_2$: C, 53.00; H, 6.99; N, 17.66. Found: C, 52.84; H, 7.18; N, 17.66.

4-Chloro-2,5-dipropylimidazole (9c).

This compound had the following physical properties, bp 166-170°/3 torr, colorless oil; pmr: δ 0.90 (6H, t, $J = 7.2$ Hz, 2 x $(\text{CH}_2)_2\text{CH}_3$), 1.37-1.92 (4H, m, 2 x $\text{CH}_2\text{CH}_2\text{CH}_3$), 2.54 (2H, t, $J = 7.2$ Hz, $\text{CH}_2\text{CH}_2\text{CH}_3$), 2.62 (2H, t, $J = 7.2$ Hz, $\text{CH}_2\text{CH}_2\text{CH}_3$) ppm; ms: m/z 186 (M^+).

Anal. Calcd. for $\text{C}_9\text{H}_{15}\text{ClN}_2$: C, 57.90; H, 8.10; N, 15.01. Found: C, 57.71; H, 8.09; N, 14.86.

2,5-Dibutyl-4-chloroimidazole (9d).

This compound had the following physical properties, bp 185-

190°/3 torr, colorless oil; pmr: δ 0.91 (3H, t, J = 7.3 Hz, (CH₂)₃-CH₃), 0.92 (3H, t, J = 7.3 Hz, (CH₂)₃CH₃), 1.30-1.39 (4H, m, 2 x (CH₂)₂CH₂CH₃), 1.51-1.58 (2H, m, CH₂CH₂CH₂CH₃), 1.63-1.71 (2H, m, CH₂CH₂CH₂CH₃), 2.55 (2H, t, J = 7.6 Hz, CH₂(CH₂)₂-CH₃), 2.62 (2H, t, J = 7.8 Hz, CH₂(CH₂)₂CH₃) ppm; ms: m/z 214 (M⁺).

Anal. Calcd. for C₁₁H₁₉ClN₂: C, 61.52; H, 8.92; N, 13.05. Found: C, 61.39; H, 9.12; N, 13.06.

4-Chloro-2,5-diisobutylimidazole (9e).

This compound had the following physical properties, mp 127-128.5°, colorless prisms (from cyclohexane); pmr: δ 0.92 (6H, d, J = 6.6 Hz, CH₂CH(CH₃)₂), 0.93 (6H, d, J = 6.6 Hz, CH₂CH(CH₃)₂), 1.71 (1H, broad s, NH), 1.82-1.92 (1H, m, CH₂CH(CH₃)₂), 1.97-2.07 (1H, m, CH₂CH(CH₃)₂), 2.43 (2H, d, J = 7.2 Hz, CH₂CH(CH₃)₂), 2.49 (2H, d, J = 7.2 Hz, CH₂CH(CH₃)₂) ppm; ms: m/z 214 (M⁺).

Anal. Calcd. for C₁₁H₁₉ClN₂: C, 61.52; H, 8.92; N, 13.05. Found: C, 61.40; H, 9.16; N, 12.95.

4-Chloro-2,5-diphenylimidazole (9f).

This compound had the following physical properties, mp 228.5-230°, colorless needles (from acetonitrile); pmr (dimethyl sulfoxide-d₆): δ 7.28-7.58 (6H, m, benzene H), 7.70-7.87 (2H, m, benzene H), 7.91-8.08 (2H, m, benzene H) ppm; ms: m/z 254 (M⁺).

Anal. Calcd. for C₁₅H₁₁ClN₂: C, 70.73; H, 4.35; N, 11.00. Found: C, 70.77; H, 4.30; N, 11.14.

Crystal Data for 1,2-Bis(*p*-bromophenyl)-1,2-dicyanoiminoethane (5b).

The crystal data of **5b** were as follows: triclinic with the space group P $\bar{1}$, a = 16.250(8) Å, b = 13.836(5) Å, c = 7.571(2) Å, α = 94.88(5)°, β = 96.02(1)°, γ = 110.38(8)°, V = 1573.39 Å³. A total 4078 independent reflections ($2^\circ < 2\theta < 135^\circ$) was collected with the Rigaku AFC-5 automatic diffractometer, using graphite-monochromatic MoK α radiation. The final R value was 0.061.

REFERENCES AND NOTES

- [1] H. C. Van der Plas, Ring Transformation of Heterocycles, Academic Press Inc, London, 1973.
- [2] T. Watanabe, J. Nishiyama, R. Hirate, K. Uehara, M. Inoue, K. Matsumoto and A. Ohta, *J. Heterocyclic Chem.*, **20**, 1277 (1983).
- [3] A. Ohta, S. Masano, M. Tsutsui, F. Yamamoto, S. Suzuki, H. Makita, H. Tamamura and Y. Akita, *ibid.*, **18**, 555 (1981).
- [4] J. K. Landquist, *J. Chem. Soc.*, 1885 (1956).
- [5] G. Karmas and P. E. Spoerri, *J. Am. Chem. Soc.*, **78**, 4071 (1956).
- [6] A. Ohta, M. Inoue, J. Yamada, Y. Yamada, T. Kurihara and T. Honda, *J. Heterocyclic Chem.*, **21**, 103 (1984).
- [7] A. Ohta, Y. Akita and M. Hara, *Chem. Pharm. Bull.*, **27**, 2027 (1979).
- [8] A. Ohta, *ibid.*, **16**, 1160 (1968).
- [9] A. Ohta, Y. Akita and Y. Nakane, *ibid.*, **27**, 2980 (1979).
- [10] J. L. Imbach, R. Jacquier and A. Romane, *J. Heterocyclic Chem.*, **4**, 451 (1967).