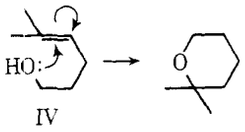
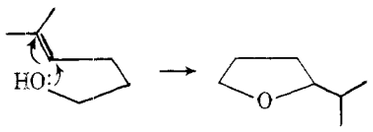
vored. The last step involves cyclization of IV to the tetrahydropyran ring.



(7)

IV

In fact, acid-catalyzed cyclizations of unsaturated alcohols to give either tetrahydropyrans[7,8] or tetrahydrofurans[8,9] are known, and in at least one case unsaturated alcohol has been isolated as an intermediate in the Prins reaction.[4] If unsaturated alcohols are involved, some cyclization is expected to



(8)

occur via a five-membered transition state to give tetrahydrofuran derivatives. The key compound in the case of 5-methylhexanal cyclization would be the presence of 2-isopropyltetrahydrofuran. We found no evidence for this ether among the reaction products. Cyclization appears therefore not to involve olefinic intermediates, and the reaction proceeds mostly via eq 4, analogous to acid-promoted cyclization of 1,5-pentanediol or pentamethylene chlorohydrin which form a tetrahydropyran ring via a cyclic oxonium ion intermediate.[10]

Experimental Section

Preparation of 5-Methylhexanal. About 100 g of 4-methyl-1-pentene (Phillips Petroleum) was carbonylated in benzene solvent (437 g) over 1.0 g of $RhH(CO)(Ph_3P)_3$ catalyst (100 °C, 60 atm, 30 min, $2H_2/CO$) to give 17 g of 5-methylhexanal: bp 80–85 °C (100 mm.Hg) (lit.[11] bp 84 °C at 100 mm); NMR (CCl_4, Me_4Si) 9.5 (s, 1 H, CHO), 2.3 (t, 2 H, CH_2CO, $J \approx 7$ Hz), 1.0–1.8 (m, 5 H, CH_2, CH), and 0.95 (d, 6 H, CH_3, $J \approx 7$ Hz) ppm. The spectrum, however, contained several peaks in the 9.5-ppm region, indicating a purity of only 70%. This is consistent with compositions carried out with $(Co_2(CO)_4)_2$ catalysts.[12,13]

Cyclization of 5-Methylhexanal. In a typical experiment, 9.0 g (0.08 mol) of the above aldehyde was added dropwise, while stirring, to 184 g of 96% sulfuric acid (1.8 mol), maintaining a temperature between 0 and −5 °C. After the addition was completed, the reaction mixture was stirred for 30 min and poured over 500 g of cracked ice. Extraction with ether, followed by washing with water, drying ($MgSO_4$), and distillation gave 3.5 g (39%) of 2,2-dimethyltetrahydropyran: bp 58–60 °C (100 mmHg), $n^{24.5}D$ 1.4245 [lit.[2] bp 119–120 °C (atm), $n^{18}D$ 1.4272]; NMR (CCl_4, Me_4Si) 3.5 (m, 2 H, CH_2O), 1.5 (m, 6 H, CH_2), and 1.1 (s, 6 H, CH_3) ppm, identical to the spectrum of the authentic sample. Aldehydes which did not have a methyl substituent in the δ position were converted to high-boiling resinous materials.

Acknowledgment. We thank Dr. R. C. Williamson for a gift of rhodium carbonylation catalyst.

Registry No.—3,5-Dimethylhexanal, 19796-88-4; 2,2,4-trimethyltetrahydropyran, 7379-08-0; 4-methyl-1-pentene, 691-37-2; 5-methylhexanal, 1860-39-5; 2,2-dimethyltetrahydropyran, 35270-87-2.

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Studies on Pyrazines. 2.[1] Structural Assignment of the Reaction of α-Amino-α-phenylacetonitrile with Chloral or Bromal to *N*-(2,2-Dihaloethenyl)-1-imino-1-phenylacetonitriles

Nobuhiro Sato* and Jiro Adachi

Department of Chemistry, Yokohama City University, Mutsuura-cho, Kanazawa-ku, Yokohama 236, Japan

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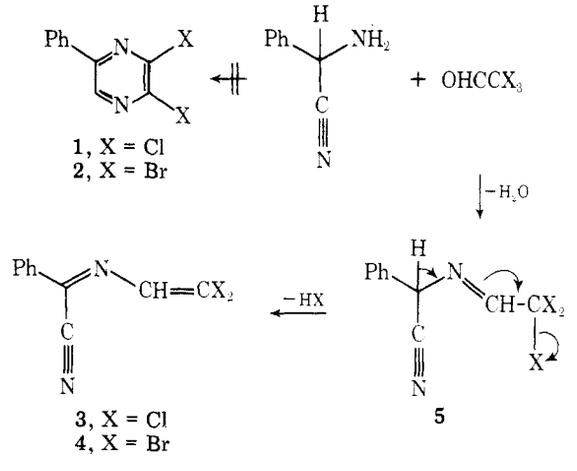
In a previous paper,[1] we reported a preparation of 2,3-dichloro-5-phenylpyrazine (1) by chlorination of 2,3-dihydroxy-5-phenylpyrazine with phosphoryl chloride. In 1915, Minovici and Bente[2] also described compound 1 and its bromo homologue 2 as reaction products of α-amino-α-phenylacetonitrile with chloral and bromal, respectively. We have now found that the dichloro product obtained in this reaction is entirely different (spectra, mixture melting point) from our earlier preparation and have assigned the structures of the Minovici–Bente products as *N*-(2,2-dihaloethenyl)-1-imino-1-phenylacetonitriles 3 and 4.

The NMR spectra contain 1 H singlets at δ 7.78 in 3 and 8.11 in 4. These signals can not be assigned to the ring protons of authentic 2,5-[3] and 2,6-dihalo-3-phenylpyrazines,[4] the latter of which were prepared by halogenation of 2-hydroxy-6-chloro-5-phenylpyrazine. The presence of a conjugated cyano group in the IR spectra at 2210 cm^{-1} in 3 and 2205 cm^{-1} in 4 indicates that 3 and 4 are not dihalopyrazines but acyclic compounds formed on dehydrohalogenation of Schiff base 5



1, X = Cl
2, X = Br

3, X = Cl
4, X = Br

5

prior to the cyclization of dihalopyrazines. The presence of a Ph–C–CN group in 3 and 4 was further confirmed by hydrolytic degradations with concentrated hydrochloric acid to give phenylglyoxalic acid (90–93%) and with 5% ethanolic potassium hydroxide to give benzoic acid (70–75%). Additional evidence for the structure of 3 and 4 was obtained from mass spectra, e.g., for the formation of β,β-dihaloethenium ion, *m/e* 95 and 183, respectively.

The formation of **5**, in contrast to the reaction of α-aminoacetonitrile and chloral which forms an adduct and not a Schiff base,[5] is clearly due to the phenyl group. Similarly,

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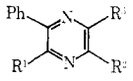
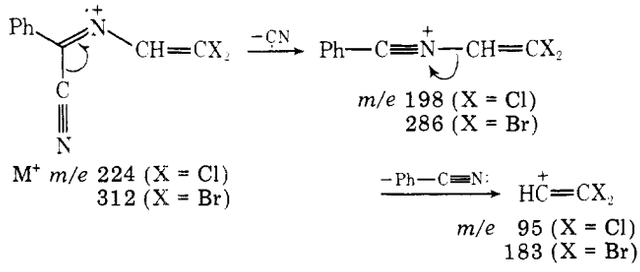
Table I. Preparation and NMR Spectral Data of Dihalopyrazines



	R¹	R²	R³	Registry no.	Type of starting material	Yield, %	Mp, °C (lit. mp, °C)	NMR (ring proton), δ
1	H	Cl	Cl	32493-80-4			(106-107)[1]	8.67
2	H	Br	Br	64163-08-02	Dihydroxy[1]	85[f]	115[a]	8.81
	Cl	H	Cl	64163-09-3	Bromohydroxy[3]	96[g]	58-59[d] (59-60)[3]	8.31
	Br	H	Br	64163-10-6	Bromohydroxy[3]	89[g]	83-84[b] (71-72)[3]	8.39
	Cl	Cl	H	64163-11-7	Chlorohydroxy	93	57-58[e,h]	8.54
	Br	Br	H	64163-12-8	Dichloro	84[g]	66-67[c]	8.65

[a] Anal. Calcd for $C_{10}H_6N_2Br_2$: C, 38.25; H, 1.93; N, 8.92; Br, 50.90. Found: C, 38.45; H, 2.08; N, 9.01; Br, 50.92. [b] Found: C, 38.33; H, 1.87; N, 8.95; Br, 51.09. [c] Found: C, 38.38; H, 1.94; N, 8.95; Br, 50.48. [d] Anal. Calcd for $C_{10}H_6N_2Cl_2$: C, 53.36; H, 2.69; N, 12.45; Cl, 31.15. Found: C, 53.30; H, 2.27; N, 12.34; Cl, 31.34. [e] Found: C, 53.58; H, 2.59; N, 12.44; Cl, 31.56. [f] Recrystallized from *n*-hexane. [g] Recrystallized from ethanol. [h] Bp 122-123 °C (0.1 mm).



3-bromo-4-methylphenylhydrazine reacts with chloral to form the hydrazone,[6] whereas hydrazine gives the adduct *N*-(1-hydroxy-2,2,2-trichloroethyl)hydrazine.[7] This halohydrazone was dehydrochlorinated to form 3-bromo-4-methylbenzeneazo-β,β-dichloroethylene,[6] supporting the transformation of Schiff base **5** to **3** or **4**.

Experimental Section

Melting points were determined in a capillary and are corrected. IR spectra (KBr) were recorded on a Hitachi Model EPI-G3 spectrometer. NMR spectra ($CDCl_3$) were recorded on a JEOL Model JNM-MH-100 instrument with tetramethylsilane as an internal standard. Mass spectra were measured on a Hitachi Model RMU-6L instrument at 70 eV.

General Procedure for Preparation of Dihalopyrazines. These results are summarized in Table I.

A mixture of the starting material indicated in Table I (0.01 mol) and phosphoryl chloride or phosphorus tribromide (20 mL) in a sealed tube was heated at 180–200 °C for 5–40 h and then poured into ice water. The precipitate which formed was collected by filtration, and the mother liquor was extracted with ether. The extract was combined with the precipitate, and undissolved matter was removed by filtration. The filtrate was washed with water, dried over magnesium sulfate, evaporated, and recrystallized to afford dihalopyrazine.

Preparation of 2-hydroxy-6-chloro-5-phenylpyrazine is as follows. A mixture of 1-hydroxy-2-keto-5-phenyl-1,2-dihydropyrazine[8] (7.21 g, 0.038 mol) in 30 mL of phosphoryl chloride was refluxed with stirring for 30 min and then poured into ice water. The precipitate which formed was collected by filtration, sublimed at 180–185 °C (0.01 mm), and recrystallized from ethanol to give colorless prisms (4.57 g, 58%): mp 235–236 °C; IR 3050–2550 (br), 1656, 1590, 846 cm^{-1}; NMR δ 12.5 (br s, 1), 8.20 (s, 1), 7.75–7.6 (m, 2), 7.55–7.4 (m, 3).

Anal. Calcd for $C_{10}H_7N_2OCl$: C, 58.13; H, 3.41; N, 13.56; Cl, 17.16. Found: C, 57.92; H, 3.51; N, 13.40; Cl, 17.00.

***N*-(2,2-Dichloroethenyl)-1-imino-1-phenylacetonitrile (3)** was prepared according to the procedure of Minovici and Bente:[2] mp 102 °C from ethanol (lit.[2] mp 102 °C); IR 2210, 1596, 1572, 1448, 1302, 1279, 952, 855 cm^{-1}; NMR δ 7.78 (s, 1), 8.2–8.0 (m, 2), 7.7–7.3 (m, 3); mass spectrum *m/e* 224 (M^+, 64), 228 (8), 226 (42), 200 (6), 198 (9), 191 (36), 189 (100), 183 (9), 182 (7), 164 (7), 162 (20), 154 (7), 153 (31), 129 (10), 115 (19), 114 (11), 113 (14), 112 (14), 111 (10), 104 (21), 103 (20), 102 (10), 99 (10), 97 (13), 95 (14), 88 (14), 85 (28), 83 (16), 81 (18), 77 (24).

Anal. Calcd for $C_{10}H_6N_2Cl_2$: C, 53.36; H, 2.69; N, 12.45; Cl, 31.51. Found: C, 53.44; H, 2.66; N, 12.54; Cl, 31.49.

***N*-(2,2-Dibromoethenyl)-1-imino-1-phenylacetonitrile (4)** was similarly prepared: mp 120 °C from ethanol (lit.[2] mp 120 °C); IR 2205, 1592, 1566, 1442, 1294, 1272, 879, 852 cm^{-1}; NMR δ 8.11 (s, 1), 8.3–8.1 (m, 2), 7.7–7.3 (m, 3); mass spectrum *m/e* 312 (M^+, 44), 314 (88), 316 (44), 290 (2), 288 (4), 286 (2), 235 (38), 233 (38), 208 (8), 206 (9), 187 (5), 185 (10), 183 (5), 155 (13), 154 (100), 152 (35), 127 (20), 115 (14), 114 (12), 104 (31), 103 (21), 102 (24), 88 (16), 77 (24).

Anal. Calcd for $C_{10}H_6N_2Br_2$: C, 38.25; H, 1.93; N, 8.92; Br, 50.90. Found: C, 38.33; H, 2.05; N, 8.84; Br, 50.85.

Acknowledgment. The authors wish to thank Dr. T. Nakagawa for his helpful suggestions.

Registry No.—**3**, 64201-59-8; **4**, 64201-60-1; α-amino-α-phenylacetonitrile, 16750-42-8; chloral, 75-87-6; bromal, 115-17-3; phosphorus tribromide, 7789-60-8; 1-hydroxy-2-keto-5-phenyl-1,2,-dihydropyrazine, 64163-13-9; 2-hydroxy-6-chloro-5-phenylpyrazine, 64163-14-0; phosphoryl chloride, 10025-87-3; 2,3-dihydroxy-5-phenylpyrazine, 32493-63-3; 2-bromo-3-phenyl-5-hydroxypyrazine, 64163-15-1; 2-chloro-3-phenyl-5-hydroxypyrazine, 64163-16-2; 2,5-dichloro-3-phenylpyrazine, 64163-09-3.

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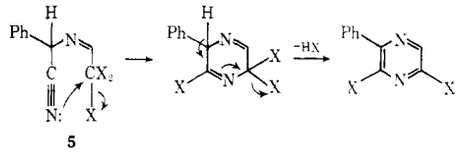

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Studies on Pyrazines. 3.[1] A Facile Synthetic Method for 2,3-Diaminopyrazines

Nobuhiro Sato* and Jiro Adachi

Department of Chemistry, Yokohama City University, Mutsuura-cho, Kanazawa-ku, Yokohama 236, Japan

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Methods for the preparation of 2,3-diaminopyrazines **1** have hitherto involved amination of 2,3-dihalopyrazines or 2-amino-3-halopyrazines, whose synthesis requires several steps.[2-5] We have found a more direct synthetic method for

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