

QUINOLONE ANALOGUES 5.¹⁻⁴ SYNTHESIS OF 1-METHYL-PYRIDAZINO[3,4-*b*]QUINOXALIN-4(1*H*)-ONES

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Abstract - The reaction of the quinoxaline *N*-oxide (**8a**) with diethyl ethoxymethylenemalonate gave the 1,4-dihydropyridazino[3,4-*b*]quinoxaline-4,4-dicarboxylate (**10c**), whose reaction with a base afforded the 1,5-dihydropyridazino[3,4-*b*]quinoxaline-4-carboxylate (**6a**). The oxidation of compound (**6a**) with nitrous acid provided the 1,4-dihydro-4-hydroxypyridazino[3,4-*b*]quinoxaline-4-carboxylate (**7**), whose reaction with potassium hydroxide gave 7-chloro-1-methylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-one (**5a**). On the other hand, the reaction of the quinoxaline *N*-oxide (**8b**) with acetylacetaldehyde dimethyl acetal afforded 4-acetyl-1,5-dihydro-1-methylpyridazino[3,4-*b*]quinoxaline (**6b**), whose oxidation with selenium dioxide provided 1-methylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-one (**5b**).

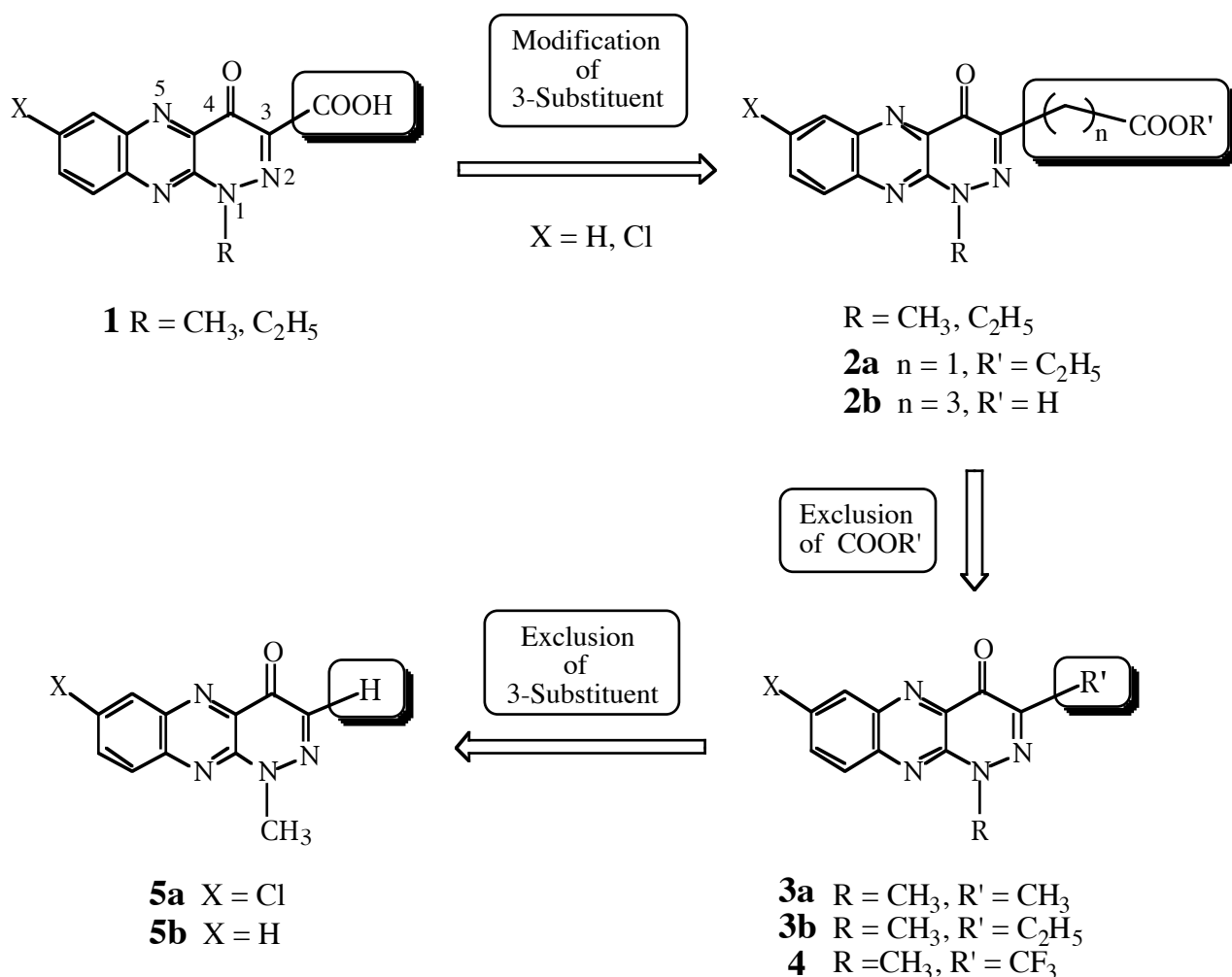
INTRODUCTION

In a previous paper,¹ we reported the synthesis of the 1-alkyl-1,4-dihydro-4-oxopyridazino[3,4-*b*]quinoxaline-3-carboxylic acids (**1**) as candidates of antibacterial quinolone analogues (Scheme 1), and compounds (**1**) were found to have weak antibacterial activities from our screening data. Then, we modified the 3-substituent of compounds (**1**) and synthesized the (1-alkyl-1,4-dihydro-4-oxopyridazino[3,4-*b*]quinoxalin-3-yl)acetates (**2a**) and 4-(1-alkyl-1,4-dihydro-4-oxopyridazino[3,4-*b*]quinoxalin-3-yl)butanoic acids (**2b**) (Scheme 1) in order to improve the antibacterial activities.²

However, this modification was not successful in the improvement of antibacterial activities, and hence we further converted the structure of compounds (**2a,b**) and synthesized the 1,3-dialkylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-ones (**3a,b**) (Scheme 1), which had not carboxyl or carboxylate function in the 3-substituent.³ As the result, compounds (**3a,b**) were shown to possess better antibacterial activities than

those of compounds (**1** and **2a,b**).³ In addition, compounds (**3a,b**) were clarified to have antifungal activities.^{5,6} The 3-trifluoromethyl homologues 1-methyl-3-trifluoromethylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-ones (**4**)⁴ (Scheme 1) also exhibited the antibacterial and antifungal activities⁶ in similar extent to those of the 1,3-dimethylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-ones (**3a**).⁶ In the present investigation, we have transformed the structure of compounds (**3a,b** and **4**) and synthesized the 1-methylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-ones (**5a,b**) (Scheme 1), which were the 3-H homologues. Since compounds (**3a,b** and **4**) without the carboxyl group at the 3-position showed antifungal activities, compounds (**5a,b**) without the carboxyl group at the 3-position were also expected to exhibit some antifungal activities.⁷⁻⁹

Scheme 1



METHODS FOR THE SYNTHESIS OF COMPOUNDS (**5a,b**)

In order to synthesize the 3-H homologues (**5a,b**), the decarboxylation of the 3-carboxylic acid homologues (**1**) would be convenient, but this attempt was not successful. Accordingly, we undertook methods shown in Scheme 2. Compound (**5a**) was synthesized *via* oxidation of compound (**6a**) with nitrous acid and then treatment of compound (**7**) with a base (route A), while compound (**5b**) was produced *via* oxidation of compound (**6b**) with selenium dioxide (route B). Compounds (**1**¹ and **4**⁴) and compounds (**2a,b**² and **3a,b**³) were also synthesized by the methods of the routes A and B, respectively.

SYNTHESIS OF COMPOUND (5a)

In a previous paper,¹⁰ we reported that the reaction of the quinoxaline *N*-oxide (8a) with ethyl ethoxymethylenecyanoacetate or ethoxymethylenemalononitrile gave the quinoxaline *N*-oxide (9a or 9b), respectively (Chart 1). Moreover, compound (9a) was cyclized into the 1,5-dihydropyridazino[3,4-*b*]quinoxaline-4-carbonitrile (6c)^{4,10-14} under a basic condition, while the quinoxaline *N*-oxide (9b) was not cyclized under the same condition. However, we found in the present investigation that the quinoxaline *N*-oxides (9a,b) were easily cyclized into the 1,4-dihydropyridazino[3,4-*b*]quinoxalines (10a,b), respectively, under reflux in acetic acid (Scheme 3). This cyclization method enabled us to synthesize the quinolone analogue (5a) as shown in Scheme 4.

Scheme 2

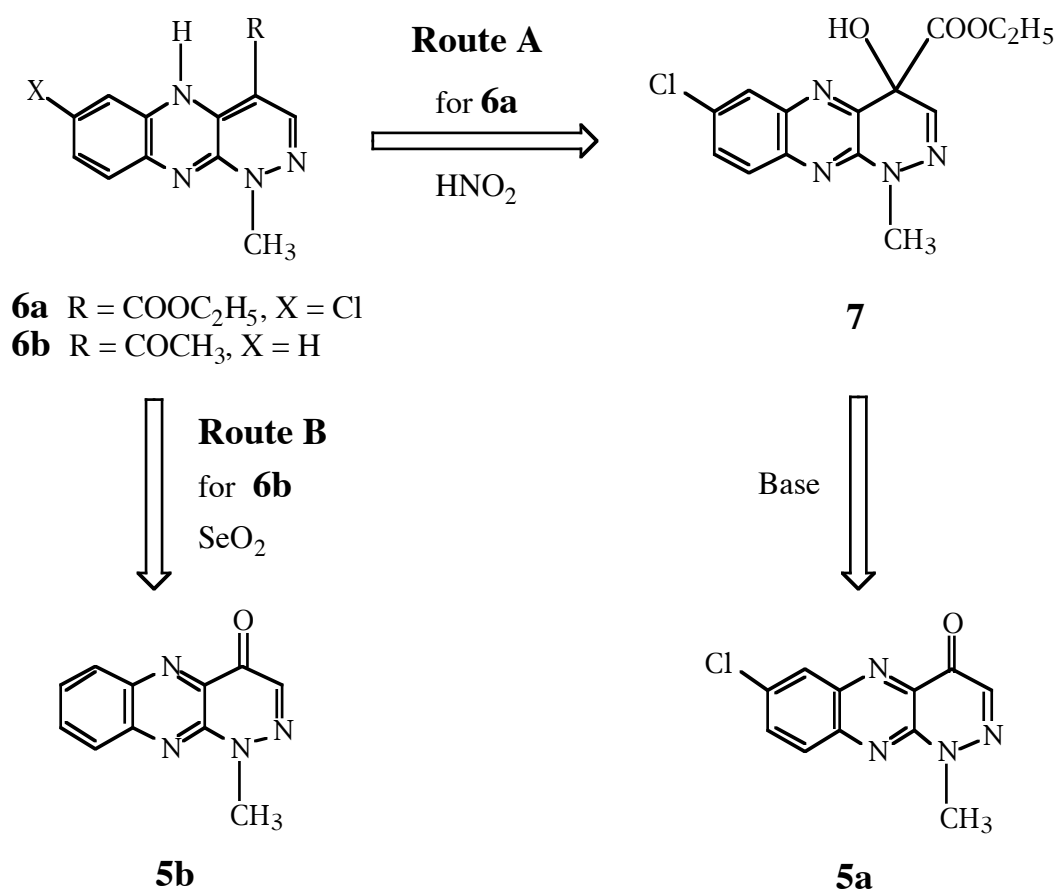
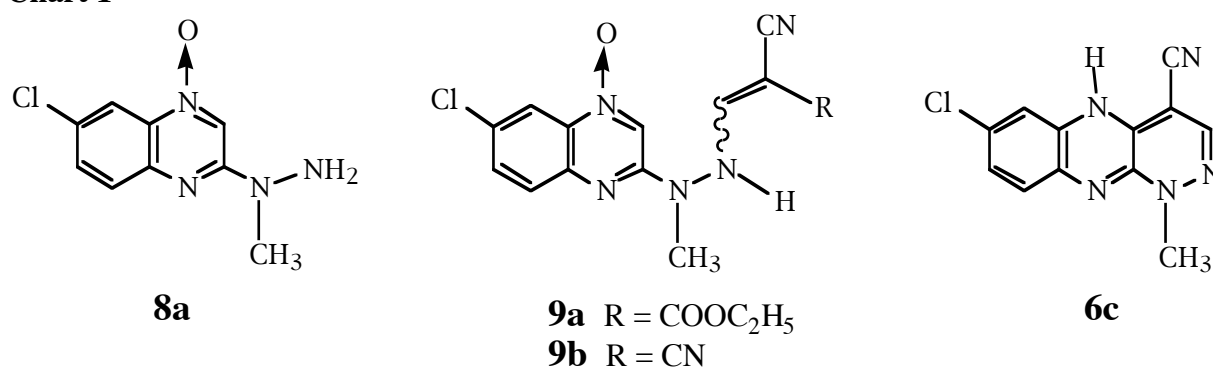
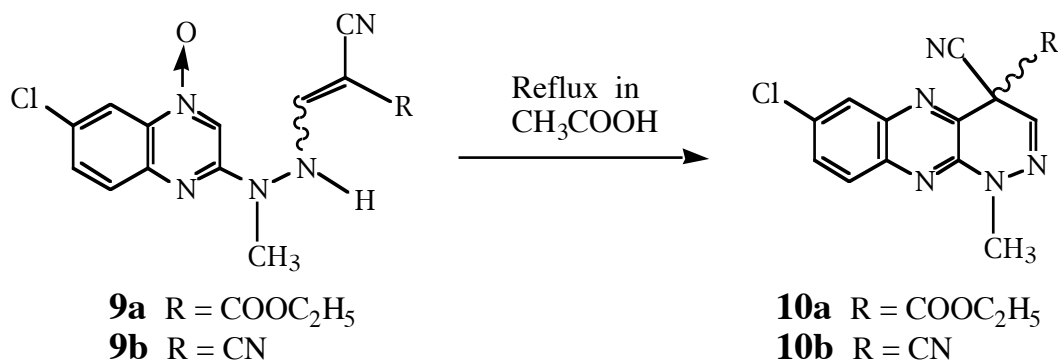


Chart 1

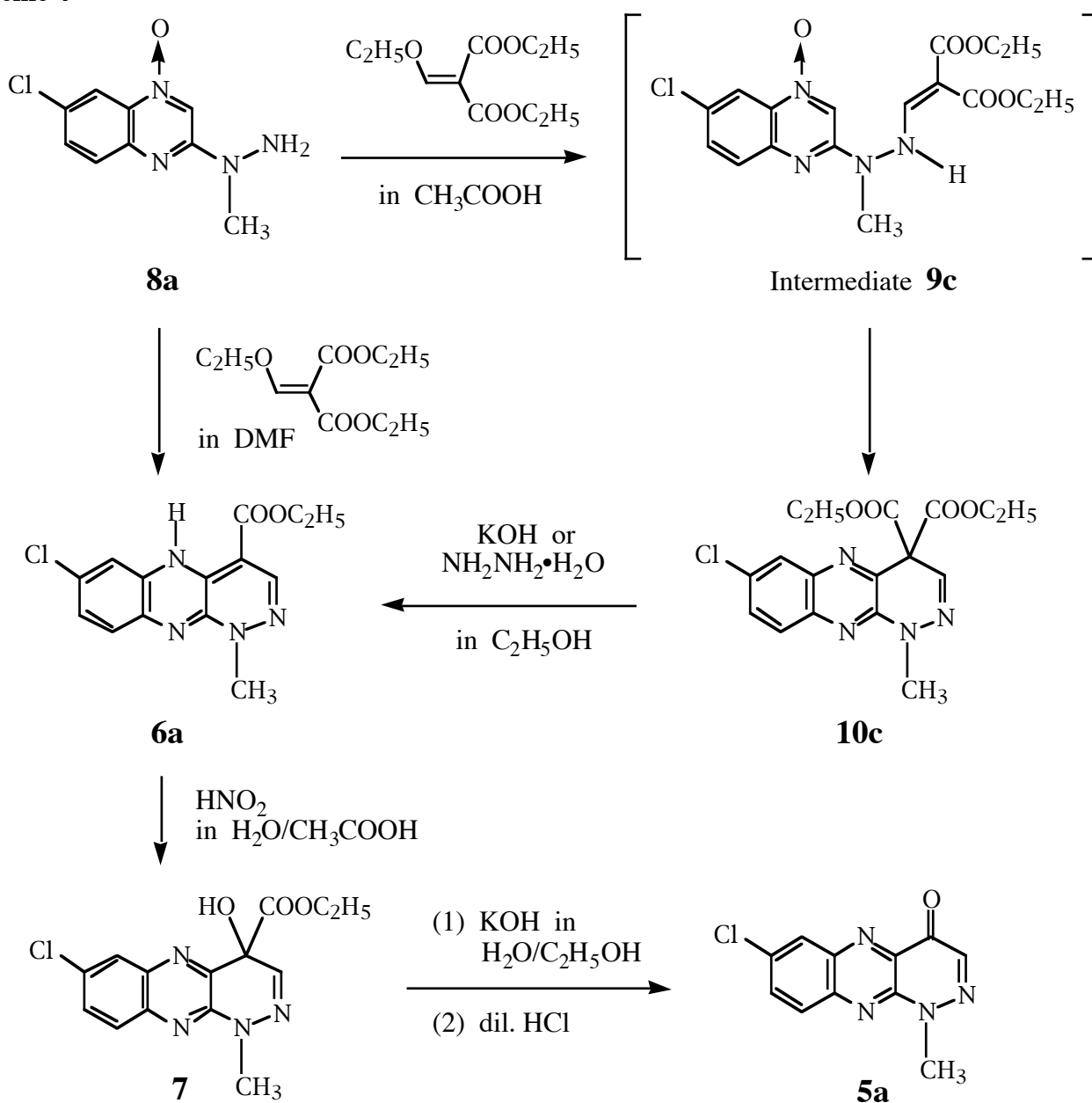


The reaction of the quinoxaline *N*-oxide (**8a**) with diethyl ethoxymethylenemalonate in acetic acid gave

Scheme 3



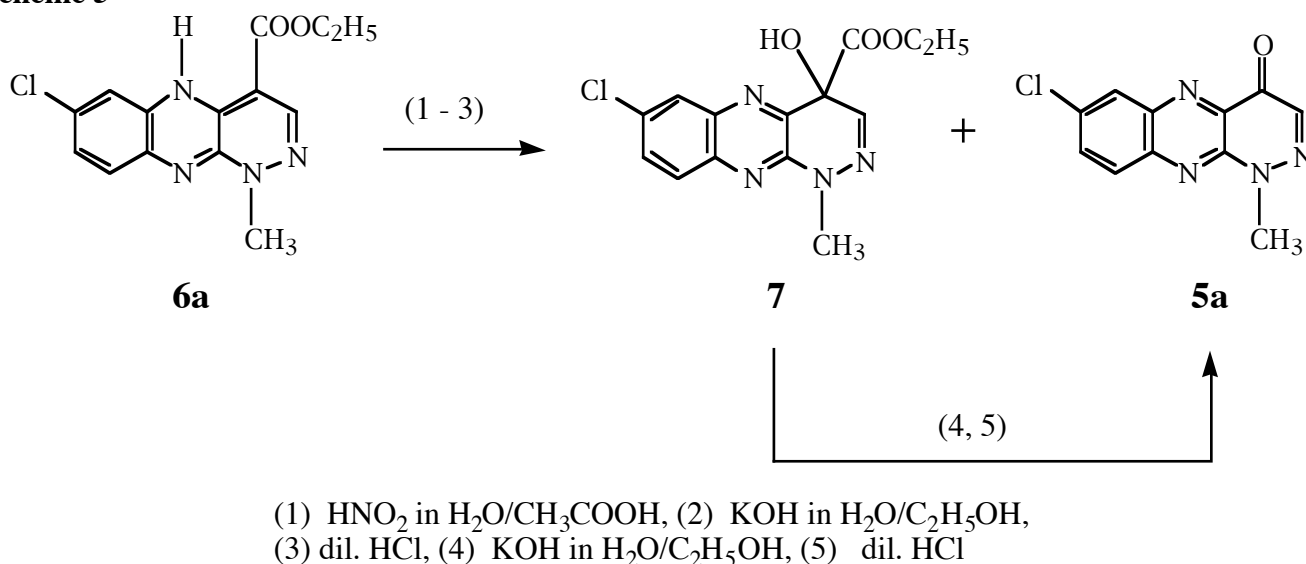
Scheme 4



the 1,4-dihydropyridazino[3,4-*b*]quinoxaline-4,4-dicarboxylate (**10c**) presumably *via* an intermediate (**9c**) (Scheme 4), whose reaction with potassium hydroxide or hydrazine hydrate resulted in hydrolysis and decarboxylation to afford the 1,5-dihydropyridazino[3,4-*b*]quinoxaline-4-carboxylate (**6a**).^{4,10-14} Compound (**6a**) was also obtained directly by the reaction of the quinoxaline *N*-oxide (**8a**) with diethyl ethoxymethylenemalonate in *N,N*-dimethylformamide. The yield of compound (**6a**) was better in the direct synthesis (**8a**→**6a**, 87%) than in the synthesis *via* compound (**10c**) (**8a**→**10c**→**6a**, 71%). The reaction of compound (**6a**) with nitrous acid effected oxidation^{1,2,4} to provide the 1,4-dihydro-4-hydroxypyridazino[3,4-*b*]quinoxaline-4-carboxylate (**7**), whose reaction with potassium hydroxide resulted in elimination of formate^{1,2} to give the quinolone analogue (**5a**). In the Scheme 4, compound (**7**) was obtained in low yield (44%) after recrystallization,¹⁵ which led to a low yield of compound (**5a**). Accordingly, we devised the procedure to improve the yield of compound (**5a**) from compound (**6a**) as shown in Scheme 5.

The oxidation of compound (**6a**) with nitrous acid, treatment with potassium hydroxide, and then neutralization with hydrochloric acid were carried out in the one-pot procedure to afford compound (**7**) (59%) and compound (**5a**) (35%). Further reaction of compound (**7**) with potassium hydroxide provided compound (**5a**) (73%). After all, compound (**5a**) was obtained in 77% yield from compound (**6a**) by the procedure in Scheme 5.

Scheme 5



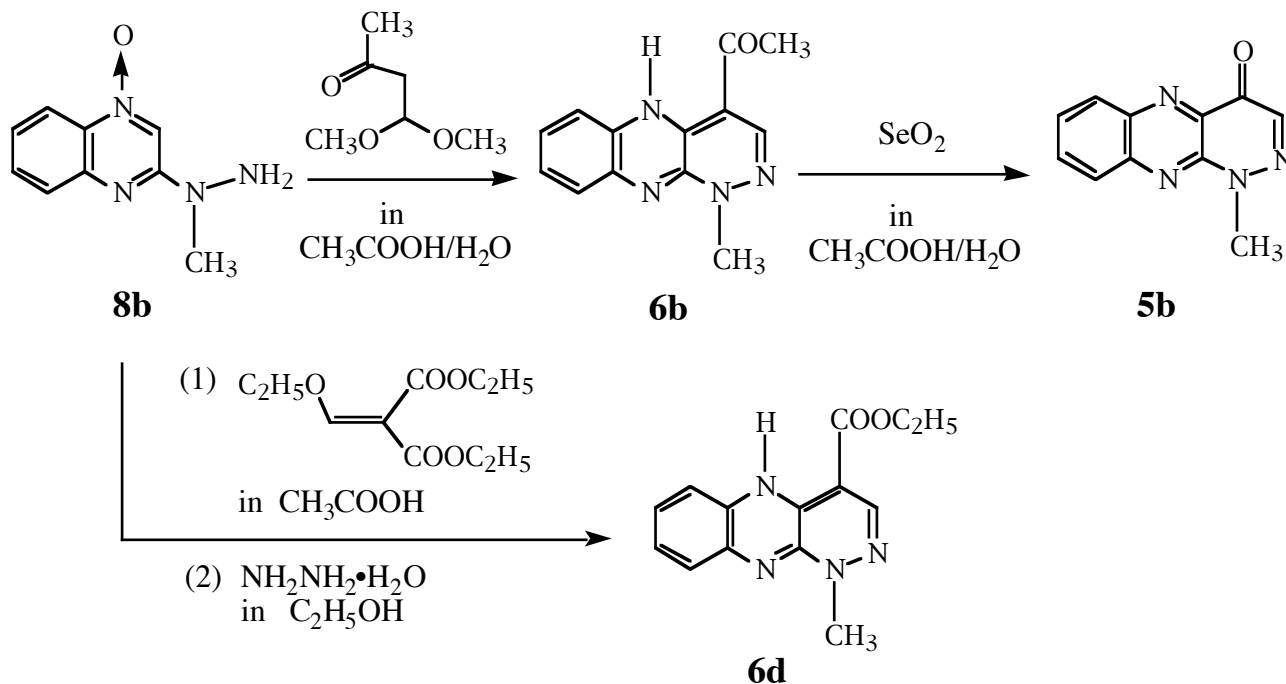
SYNTHESIS OF COMPOUND (**5b**)

The route A method shown in Scheme 2 was not suitable for the synthesis of compound (**5b**). Consequently, we adopted the route B method exhibited in Scheme 2, as described below.

The reaction of compound (**8b**) with diethyl ethoxymethylenemalonate and subsequent reaction with hydrazine hydrate provided the 1,5-dihydropyridazino[3,4-*b*]quinoxaline-4-carboxylate (**6d**) (Scheme 6). The oxidation of compound (**6d**) with nitrous acid did not bring about favorable result for the synthesis of compound (**5b**).

The reaction of the quinoxaline *N*-oxide (**8b**) with acetylacetaldehyde dimethyl acetal gave 4-acetyl-1,5-dihydro-1-methylpyridazino[3,4-*b*]quinoxaline (**6b**),^{4,10-14} whose oxidation with selenium dioxide afforded 1-methylpyridazino[3,4-*b*]quinoxalin-4(1*H*)-one (**5b**) (Scheme 6). Compounds (**6b** and **5b**) were obtained in low yields, and hence some alternate routes should be devised in order to improve the yields of compounds (**6b** and **5b**).

Scheme 6



SCREENING DATA

Compounds (**5a,b**) showed antifungal activities *in vitro* against *Trichophyton mentagrophytes* (*T. m.*) and *Trichophyton rubrum* (*T. r.*). The minimum inhibitory concentrations of compound (**5a**) were 1 and 0.5 ppm against *T. m.* and *T. r.*, and those of compound (**5b**) were 1 ppm against *T. m.* and *T. r.*, respectively.⁶

EXPERIMENTAL

All melting points were determined on a Yazawa micro melting point BY-2 apparatus and are uncorrected. The IR spectra (potassium bromide) were recorded with a JASCO FT/IR-200 spectrophotometer. The NMR spectra were measured with a Varian XL-400 spectrometer at 400 MHz. The chemical shifts are given in the δ scale. The MS spectra were determined with a JEOL JMS-01S spectrometer. Elemental analyses were performed on a Perkin-Elmer 240B instrument.

Ethyl 7-Chloro-4-cyano-1,4-dihydro-1-methylpyridazino[3,4-*b*]quinoxaline-4-carboxyl-ate (**10a**)

A solution of compound (**9a**) (2 g) in acetic acid (50 mL) was refluxed for 2 h. Evaporation of the solvent *in vacuo* afforded yellow crystals of compound (**10a**) (1.48 g, 78%). Recrystallization from

N,N-dimethylformamide/ethanol/water gave yellow needles, mp 162-163 °C; IR: ν cm⁻¹ 2210, 2185, 1750; MS: *m/z* 329 (M⁺), 331 (M⁺ + 2); NMR (deuteriodimethyl sulfoxide): 8.11 (d, *J* = 2.0 Hz, 1H, 6-H), 7.90 (d, *J* = 9.0 Hz, 1H, 9-H), 7.82 (dd, *J* = 2.0, 9.0 Hz, 1H, 8-H), 7.32 (s, 1H, 3-H), 4.26 (dq, *J* = 7.0, 10.0 Hz, 1H, methylene H), 4.22 (dq, *J* = 7.0, 10.0 Hz, 1H, methylene H), 3.61 (s, 3H, N-CH₃), 1.14 (dd, *J* = 7.0, 7.0 Hz, 3H, CH₃). *Anal.* Calcd for C₁₅H₁₂N₃O₂Cl: C, 54.64; H, 3.67; N, 21.24. Found: C, 54.48; H, 3.71; N, 21.52.

7-Chloro-1,4-dihydro-1-methylpyridazino[3,4-*b*]quinoxaline-4,4-dicarbonitrile (10b)

A solution of compound (**9b**) (2.5 g) in acetic acid (50 mL) was refluxed for 2 h to precipitate brick red needles of compound (**10b**), which were collected by filtration and then washed with ethanol/*n*-hexane to give an analytically pure sample (1.09 g, 46%), mp 294-295 °C; IR: ν cm⁻¹ 3090, 2200, 2190, 2170, 1590; MS: *m/z* 282 (M⁺), 284 (M⁺ + 2); NMR (deuteriodimethyl sulfoxide): 10.38 (s, 1H, 3-H), 8.28 (d, *J* = 2.0 Hz, 1H, 6-H), 7.70 (d, *J* = 9.0 Hz, 1H, 9-H), 7.54 (dd, *J* = 2.0, 9.0 Hz, 1H, 8-H), 4.45 (s, 3H, N-CH₃). *Anal.* Calcd for C₁₃H₇N₆Cl: C, 55.23; H, 2.50; N, 29.73. Found: C, 55.18; H, 2.58; N, 29.43.

Diethyl 7-Chloro-1,4-dihydro-1-methylpyridazino[3,4-*b*]quinoxaline-4,4-dicarboxylate (10c)

A solution of compound (**8a**) (10 g, 44.5 mmol) and diethyl ethoxymethylenemalonate (12.5 g, 57.9 mmol) in acetic acid (200 mL) was refluxed for 2 h. Evaporation of the solvent *in vacuo* gave yellow crystals of compound (**10c**), which were triturated with ethanol/water and collected by filtration (13.66 g, 81%). Recrystallization from ethanol gave yellow needles, mp 105-106 °C; IR: ν cm⁻¹ 2980, 2930, 2900, 1760, 1730, 1605; MS: *m/z* 376 (M⁺), 378 (M⁺ + 2); NMR (deuteriodimethyl sulfoxide): 8.03 (d, *J* = 2.5 Hz, 1H, 6-H), 7.90 (d, *J* = 9.0 Hz, 1H, 9-H), 7.78 (dd, *J* = 2.5, 9.0 Hz, 1H, 8-H), 7.32 (s, 1H, 3-H), 4.24 (q, *J* = 7.0 Hz, 4H, CH₂), 3.59 (s, 3H, N-CH₃), 1.19 (t, *J* = 7.0 Hz, 6H, CH₃). *Anal.* Calcd for C₁₇H₁₇N₄O₄Cl: C, 54.19; H, 4.55; N, 14.87. Found: C, 54.06; H, 4.63; N, 14.93.

Ethyl 7-Chloro-1,5-dihydro-1-methylpyridazino[3,4-*b*]quinoxaline-4-carboxylate (6a)

Method 1. A solution of compound (**10c**) (10 g, 26.6 mmol) and 100% hydrazine hydrate (3.32 g, 66.4 mmol) in ethanol (300 mL) was refluxed for 1 h to precipitate orange needles of compound (**6a**), which were collected by filtration to give an analytically pure sample (7.02 g, 87%).

Method 2. A solution of compound (**10c**) (10 g, 26.6 mmol) and potassium hydroxide (1 g, 17.9 mmol) in ethanol (300 mL)/water (30 mL) was refluxed for 2 h. After the solution was cooled to rt, 1*N* hydrochloric acid (18 mL) and acetic acid (5 mL) were added to the solution. Evaporation of the solvent *in vacuo* gave orange crystals of compound (**6a**), which were triturated with water and collected by filtration (6.95 g, 86%). Recrystallization from *N,N*-dimethylformamide/ethanol/water afforded orange needles.

Method 3. A solution of compound (**8a**) (3 g, 13.4 mmol) and diethyl ethoxymethylenemalonate (4.34 g, 20.1 mmol) in *N,N*-dimethylformamide (50 mL) was refluxed for 1 h. The solution was allowed to stand overnight at rt to precipitate orange needles of compound (**6a**), which were collected by filtration

and then washed with ethanol to provide an analytically pure sample (1.70 g, 42%).

Compound (**6a**) had mp 215-216 °C; IR: ν cm⁻¹ 1655, 1615; MS: m/z 304 (M⁺), 306 (M⁺ + 2); NMR (deuteriodimethyl sulfoxide): 7.13 (s, 1H, 3-H), 7.07 (s, 1H, 6-H), 6.75 (d, J = 7.0 Hz, 1H, aromatic H), 6.63 (d, J = 7.0 Hz, 1H, aromatic H), 4.17 (q, J = 7.0 Hz, 2H, CH₂), 3.11 (s, 3H, N-CH₃), 1.23 (t, J = 7.0 Hz, 3H, CH₃). *Anal.* Calcd for C₁₃H₁₅N₄O₃Cl: C, 55.18; H, 4.30; N, 11.63. Found: C, 55.05; H, 4.28; N, 11.75.

Ethyl 7-Chloro-1,4-dihydro-4-hydroxy-1-methylpyridazino[3,4-*b*]quinoxaline-4-carboxylate (7)

A solution of sodium nitrite (1.70 g, 24.6 mmol) in water (25 mL) was added to a suspension of compound (**6a**) (5 g, 16.4 mmol) in acetic acid (200 mL)/water (25 mL) with stirring in an ice-water bath. The mixture was heated at 70-80 °C for 30 min and then at 90-110 °C for 30 min. The solvent was evaporated *in vacuo* to give yellow crystals, whose recrystallization from acetic acid/water afforded yellow needles of compound (**7**) (2.26 g, 43%), mp 150-151 °C; IR: ν cm⁻¹ 1750, 1605; MS: m/z 320 (M⁺), 322 (M⁺ + 2); NMR (deuteriodimethyl sulfoxide): 8.01 (d, J = 2.5 Hz, 1H, 6-H), 7.88 (d, J = 9.0 Hz, 1H, 9-H), 7.77 (dd, J = 9.0, 2.5 Hz, 1H, 8-H), 7.18 (s, 1H, OH), 7.10 (s, 1H, 3-H), 4.14 (q, J = 7.0 Hz, 2H, CH₂), 3.67 (s, 3H, N-CH₃), 1.08 (t, J = 7.0 Hz, 3H, CH₃). *Anal.* Calcd for C₁₄H₁₃N₄O₃Cl: C, 52.43; H, 4.09; N, 17.47. Found: C, 52.14; H, 4.14; N, 17.41.

7-Chloro-1-methylpyridazino[3,4-*b*]quinoxalin-4(1H)-one (5a)

Method 1. A solution of compound (**7**) (2 g, 6.24 mmol) and potassium hydroxide (349 mg, 6.24 mmol) in ethanol (50 mL)/water (1 mL) was refluxed for 1 h to precipitate crystals. After cooling to rt, 5*N* hydrochloric acid (1.3 mL) was added to the reaction mixture with stirring to give yellow crystals, which were collected by filtration. Recrystallization from *N,N*-dimethylformamide/ethanol afforded yellow needles of compound (**5a**) (0.85 g, 74%).

Method 2. A solution of sodium nitrite (1.70 g, 24.6 mmol) in water (25 mL) was added to a solution of compound (**6a**) (5 g, 16.4 mmol) in acetic acid (200 mL)/water (25 mL) with stirring in an ice-water bath. Then, the mixture was heated at 90-100 °C for 30 min with stirring. Evaporation of the solvent *in vacuo* gave an oily substance, which was dissolved in a solution of potassium hydroxide (1.15 g, 20.5 mmol) in ethanol (130 mL)/water (1 mL). The solution was refluxed for 2 h to precipitate brown crystals of compound (**5a**). After 5*N* hydrochloric acid (4.1 mL) was added to the reaction mixture, the yellow crystals of compound (**5a**) were collected by filtration (1.40 g, 35%). Evaporation of the filtrate *in vacuo* provided yellow crystals of compound (**7**), which were triturated with water and then collected by filtration (3.1 g, 59%). Subsequently, a solution of compound (**7**) (3.1 g, 9.67 mmol) and potassium hydroxide (1.10 g, 19.7 mmol) in ethanol (130 mL)/water (1 mL) was refluxed for 2 h to precipitate yellow crystals of compound (**5a**), which were collected by filtration (1.72 g, 73%), total yield, 3.12 g (77%).

Compound (**5a**) had mp 309-310 °C; IR: ν cm⁻¹ 3065, 1650, 1610, 1540, 1525; MS: m/z 246 (M⁺), 248 (M⁺ + 2); NMR (deuteriodimethyl sulfoxide): 8.40 (dd, J = 2.5, 0.5 Hz, 1H, 6-H), 8.16 (dd, J = 9.0, 0.5

Hz, 1H, 9-H), 8.06 (dd, $J = 9.0, 2.5$ Hz, 1H, 8-H), 7.94 (s, 1H, 3-H), 4.12 (s, 3H, N-CH₃). *Anal.* Calcd for C₁₁H₇N₄OCl: C, 53.56; H, 2.86; N, 22.71. Found: C, 53.41; H, 3.03; N, 22.59.

4-Acetyl-1,5-dihydro-1-methylpyridazino[3,4-*b*]quinoxaline (6b)

A solution of acetylacetaldehyde dimethyl acetal (5.21 g, 39.5 mmol) in acetic acid (80 mL)/water (20 mL) was heated at 90-100 °C for 30 min. Compound (8b) (5 g, 26.3 mmol) was then added to the solution, and the whole mixture was refluxed for 2 h with stirring. Evaporation of the solvent *in vacuo* afforded crystals, which were dissolved in chloroform and then submitted to column chromatography on silica gel, eluting with chloroform. The first fraction was collected and evaporated *in vacuo* to give red crystals of compound (6b) (1.18 g, 19%), IR: ν cm⁻¹ 1620¹¹, 1610, 1590; MS: m/z 240 (M⁺).¹⁴ This sample was used for the synthesis of compound (5b) without further purification.

1-Methylpyridazino[3,4-*b*]quinoxalin-4(1H)-one (5b)

A solution of compound (6b) (1 g, 4.17 mmol) and selenium dioxide (1.14 g, 10.4 mmol) in acetic acid (40 mL)/water (10 mL) was refluxed for 1 h. After precipitate was filtered off, mother liquor was evaporated *in vacuo* to give crystals, which were dissolved in chloroform/*n*-hexane (10 : 1) and then submitted to column chromatography on silica gel, eluting with chloroform/*n*-hexane (10 : 1). The first fraction was collected and evaporated *in vacuo* to give yellow crystals of compound (5b) (350 mg, 40%). Recrystallization from ethanol/water provided yellow needles, mp 249-250 °C; IR: ν cm⁻¹ 3050, 1650; MS: m/z 212 (M⁺); NMR (deuteriodimethyl sulfoxide): 8.26 (ddd, $J = 8.5, 1.5, 0.8$ Hz, 1H, aromatic H), 8.12 (ddd, $J = 8.5, 1.5, 0.8$ Hz, 1H, aromatic H), 8.06 (ddd, $J = 8.5, 7.5, 1.5$ Hz, 1H, aromatic H), 7.93 (s, 1H, 3-H), 7.92 (ddd, $J = 8.5, 7.5, 1.5$ Hz, 1H, aromatic H), 4.13 (s, 3H, N-CH₃). *Anal.* Calcd for C₁₁H₈N₄O: C, 62.26; H, 3.80; N, 26.40. Found: C, 62.45; H, 4.00; N, 26.33.

Ethyl 1,5-Dihydro-1-methylpyridazino[3,4-*b*]quinoxaline-4-carboxylate (6d)

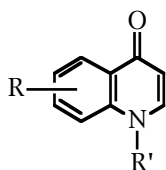
A solution of compound (8b) (10 g, 52.6 mmol) and diethyl ethoxymethylenemalonate (17.04 g, 78.9 mmol) in acetic acid (200 mL) was refluxed for 2 h. Evaporation of the solvent *in vacuo* gave an oily substance, which was dissolved in a solution of 100% hydrazine hydrate (5 g, 0.1 mol) in ethanol (200 mL). The solution was refluxed for 1 h to precipitate yellow needles of compound (6d), which were collected by filtration and washed with ethanol to provide an analytically pure sample (4.78 g). Evaporation of the filtrate *in vacuo* afforded yellow needles of compound (6d), total yield, 5.31 g (37%). Compound (6d) had mp 127-128 °C; IR: ν cm⁻¹ 1670, 1655, 1618; MS: m/z 270 (M⁺); NMR (deuteriodimethyl sulfoxide): 10.24 (s, 1H, NH), 6.93 (dd, $J = 8.0, 1.5$ Hz, 1H, aromatic H), 6.77 (dd, $J = 7.5, 1.5$ Hz, 1H, aromatic H), 6.70 (dd, $J = 8.0, 1.5$ Hz, 1H, aromatic H), 6.70 (dd, $J = 7.5, 1.5$ Hz, 1H, aromatic H), 7.04 (s, 1H, 3-H), 4.16 (q, $J = 7.0$ Hz, 2H, CH₂), 3.12 (s, 3H, N-CH₃), 1.23 (t, $J = 7.0$ Hz, 3H, CH₃). *Anal.* Calcd for C₁₄H₁₄N₄O₂: C, 62.09; H, 5.29; N, 21.01. Found: C, 62.21; H, 5.22; N, 20.73.

ACKNOWLEDGEMENT

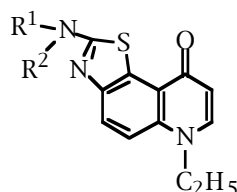
We wish to thank Nissan Chemical Industries, Ltd. and SSP Company, Ltd. for the antimicrobial screening tests.

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5. For example, the minimum inhibitory concentrations of compounds (**3a,b**) were between 1.0 and 2.0 ppm against *Bacillus subtilis* (bacteria) and *Trichophyton mentagrophytes* (fungi).
6. The detailed screening data will be reported elsewhere.
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9. No or insignificant antimicrobial activities have been reported for the 3-H quinolone homologues (**11**⁷ and **12**⁸) shown below.



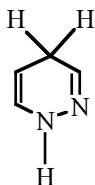
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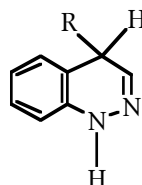
12 R¹ = CH₃, C₂H₅, R² = CH₃, H

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14. This type of compounds were clarified by us to exist as the 1,5-dihydropyridazino[3,4-*b*]-quinoxaline form, but not the 1,4-dihydropyridazino[3,4-*b*]quinoxaline form, in solution and solid state,¹¹ while dihydropyridazine¹² and dihydrocinnolines¹³ were reported to predominate as the 1,4-dihydro form.



Dihydropyridazine¹²



Dihydrocinnolines¹³

15. The recovery was not so good.