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Diazepinoquinoxalines **3**, **4** and imidazolobenzopteridines **5**, **6a-d**, **7a-d**, **8**, **9** were synthesized from 3-allylamino-6,7-dimethyl-2-quinoxalinecarboxamide (**1**) and 2-allylamino-6,7-dimethyl-3,4-dihydrobenzo[*g*]pteridin-4-one (**2**) by the intramolecular cyclization using phenylselenenyl chloride.

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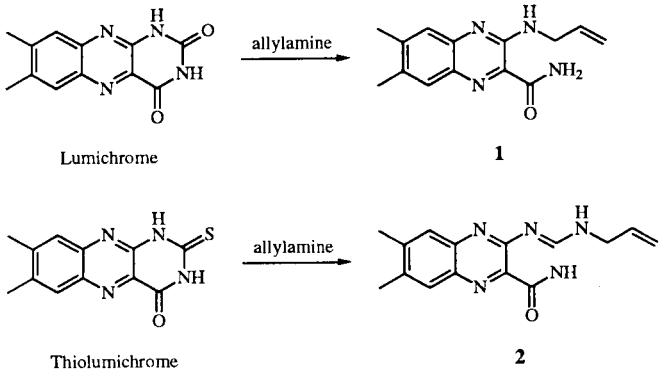
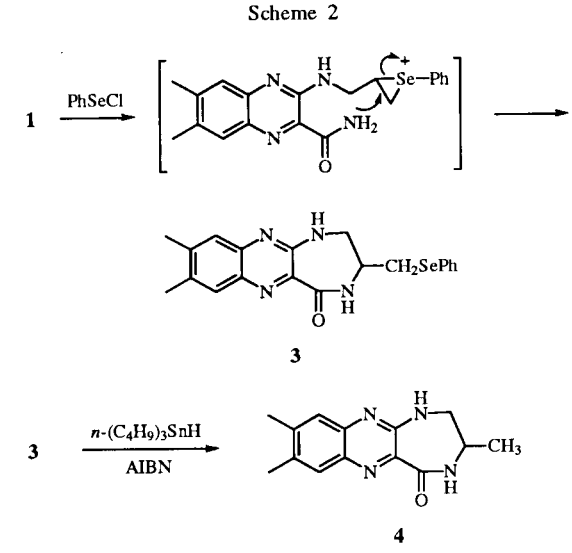
In the course of the study of the reactivity of pyrimidines or fused pyrimidines [1], we previously found that the reaction of lumichrome or thiolumichrome with allylamine gave 3-allylamino-6,7-dimethyl-2-quinoxalinecarboxamide (**1**) or 2-allylamino-6,7-dimethyl-3,4-dihydrobenzo[*g*]pteridin-4-one (**2**) [2]. These compounds containing allyl and amino functions in their side chains seemed to be suitable candidates for further chemical modifications and lead to usefull pharmacological active compounds. This paper reports the synthesis of diazepinoquinoxalines **3**, **4** and imidazolobenzopteridines **5**, **6a-d**, **7a-d**, **8**, **9** by the intramolecular cyclization of **1** or **2** using phenylselenenyl chloride [3].

Scheme 1



We expected that the synthesis of 8,9-dimethyl-3-phenylselenomethyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepino-[6,7-*b*]quinoxalin-5-one (**3**) by the intramolecular cyclization of **1** would proceed as depicted in Scheme 2. The intermediate would prefer to exocyclization in accordance with Baldwin rule [4]. Thus the reaction of **1** with phenylselenenyl chloride in tetrahydrofuran in the presence of silver trifluoromethanesulfonate [5] was carried out to give **3** in a moderate yield. The ^{1}H-nmr spectrum of **3** showed diazepine ring methylene at δ 4.01 and 4.31 ppm as double doublet (J = 7, 15.5 Hz, J = 9.5, 15.5 Hz) and methine at δ 4.97 ppm as multiplet. The mass spectrum was consistent with the assigned structure [m/z: 412 (M^+)]. Initial attempts to remove phenylselenenyl group from **3** with Raney nickel catalyst by the method of Servin [6] or with nickel boride by the method of Back [7] did not give the product, 3,8,9-trimethyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepino[6,7-*b*]quinoxalin-5-one (**4**), but ring opened product, 3-propylamino-6,7-dimethyl-2-quinoxalinecarboxamide [2]. Treatment of **3** with tributyltin hydride [8] in the presence of 2,2'-azobis(isobutylonitrile) (AIBN) in toluene gave **4** successfully.

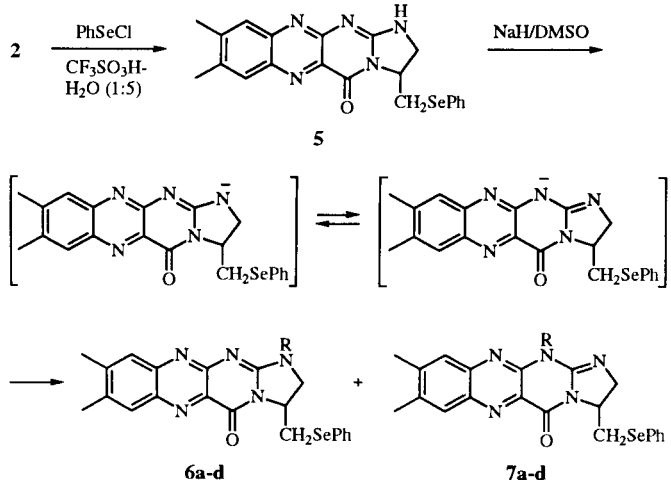
Scheme 2



As for the synthesis of imidazolobenzopteridines, intramolecular cyclization of **2** was carried out by means of phenylselenenyl chloride in acetonitrile in the presence of trifluoromethanesulfonic acid-water (1:5) according to the method of Toshimitsu *et al.* [9]. 8,9-Dimethyl-3-phenylselenomethyl-2,3-dihydro-1*H*-imidazolo[2,3-*b*]-benzo[*g*]pteridin-5-one (**5**) was obtained in 82% yield and its ^{1}H-nmr and mass spectra were consistent with the assigned structure. Alkylation of **5** with an alkyl halide in the presence of sodium hydride in dimethyl sulfoxide gave 1-alkyl-8,9-dimethyl-3-phenylselenomethyl-2,3-dihydro-1*H*-imidazolo[2,3-*b*]benzo[*g*]pteridin-5-ones **6a-d** accompanied by their isomers, 12-alkyl-8,9-dimethyl-3-phenylselenomethyl-2,3-dihydro-1*H*-imidazolo[2,3-*b*]-benzo[*g*]pteridin-5-ones **7a-d** whose formation would be explained by the isomerization of deprotonated intermediate (Scheme 3). In the ^{1}H-nmr spectrum signals of

N-alkyl groups of **7a-d** were observed at lower field than those of **6a-d** due to the low electron density at N(12) position.

Scheme 3

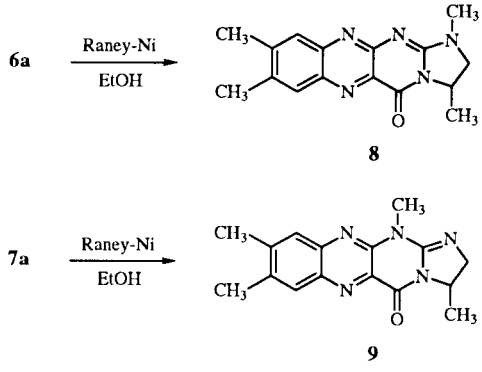


6a-d **7a-d**

a: R = CH_3, b: R = *n*-C_3H_7, c: R = *n*-C_4H_9, d: R = *n*-C_6H_{13}

Deselenation of **6a** or **7a** with Raney nickel catalyst (W-2) in refluxing ethanol according to the method of Servin [6] successfully proceeded to give 1,3,8,9-tetramethyl-2,3-dihydro-1*H*-imidazolo[2,3-*b*]benzo[*g*]pteridin-5-one (**8**) or 3,8,9,12-tetramethyl-2,3-dihydro-1*H*-imidazolo[2,3-*b*]benzo[*g*]pteridin-5-one (**9**) (Scheme 4).

Scheme 4



EXPERIMENTAL

All melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. The infrared spectra were measured with a JASCO IR-810 spectro photometer. Mass spectra were measured with a JEOL JMS-DX 300 spectrometer. Proton nuclear magnetic resonance spectra were recorded with a JEOL JNM-MH-100, JNM-FX-100 or JNM-GSX-400 spectrometer using tetramethylsilane as an internal standard. Abbreviations are as follows: s, singlet; d, doublet; q, quartet; br, broad; m, multiplet.

8,9-Dimethyl-3-phenylselenomethyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepino[6,7-*b*]quinoxalin-5-one (**3**).

A mixture of **1** (100 mg), silver triflate (120 mg) and phenylselenyl chloride (91 mg) in 20 ml of dry tetrahydrofuran was stirred for 8 hours at room temperature. The solvent was distilled off and the residue was column chromatographed on silica gel eluting with a mixture of *n*-hexane-ethyl acetate (1:1). The eluate was collected and the solvent was distilled off. The residue was crystallized from acetonitrile to give yellow crystals, mp 254-255°, yield 108 mg (67%); ^{1}H-nmr (deuteriochloroform): δ 2.39 and 2.42 (each 3H, each s, C8-Me, C9-Me), 3.11 and 3.43 (each 1H, each dd, J = 13 Hz, 9 Hz, and J = 13 Hz, 4 Hz, -CH_2Se-), 4.01 and 4.31 (each 1H, each dd, J = 15.5 Hz, 7 Hz and J = 15.5 Hz, 9.5 Hz, C2-CH_2-), 4.97 (1H, m, C3-H), 6.94 (1H, broad, CONH-), 7.23-7.73 (7H, m, PhSe- and aromatic protons); ir (potassium bromide): ν max 3340, 3150 cm^{-1} (NH), 1680 cm^{-1} (C = O); ms: m/z 412 (M$^+$).

Anal. Calcd. for $C_{20}H_{20}N_4OSe$: C, 58.40; H, 4.90; N, 13.62. Found: C, 58.67; H, 5.00; N, 13.79.

3,8,9-Trimethyl-2,3,4,5-tetrahydro-1*H*-1,4-diazepino[6,7-*b*]-quinoxalin-5-one (**4**).

A mixture of **3** (100 mg), tributyltin hydride (105 mg) and AIBN (42 mg) in toluene (20 ml) was refluxed for 12 hours under a nitrogen atmosphere. The solvent was distilled and the residue was column chromatographed on silica gel eluting with a mixture of chloroform-acetone (20:1). The eluate was collected and the solvent was distilled off. The residue was crystallized from acetonitrile to give yellow crystalline powder, mp 230-232°, yield 16 mg (25%); ^{1}H-nmr (deuteriochloroform): δ 1.46 (3H, d, J = 6 Hz, C3-CH_3), 2.31 and 2.35 (each 3H, each s, C8 and C9-CH_3), 3.67 and 4.23 (each 1H, each dd, J = 9.5, 15 Hz and J = 8, 15 Hz, C2-CH_2-), 4.88 (1H, ddd, J = 8, 9.5, 15 Hz, C3-H), 7.32 and 7.77 (each 1H, each s, C7, 10-H); ir (potassium bromide): ν max 3420, 3280 cm^{-1} (NH), 1680 cm^{-1} (C=O); ms: m/z 256 (M$^+$).

Anal. Calcd. for $C_{14}H_{16}N_4O$: C, 65.61; H, 6.29; N, 21.86. Found: C, 65.59; H, 6.31; N, 21.92.

8,9-Dimethyl-3-phenylselenomethyl-2,3-dihydro-1*H*-imidazolo[2,3-*b*]benzo[*g*]pteridin-5-one (**5**).

A mixture of **2** (200 mg), trifluorosulfonic acid-water (1:5) (205 mg), phenylselenyl chloride (165 mg) in acetonitrile (50 mg) was stirred for 8 hours at room temperature. The reaction mixture was neutralized with saturated potassium carbonate. Solvent was distilled and the residue was column chromatographed on silica gel eluting with a mixture of chloroform-acetone (20:1) to give crystals, which were recrystallized from methanol, mp 167-169°, yield 255 mg (82%); ^{1}H-nmr (deuteriochloroform): δ 2.38 and 2.43 (each 3H, each s, C8-CH_3 and C9-CH_3), 3.34 and 4.20 (each 1H, each dd, J = 2.5, 14 Hz and J = 4, 14 Hz, C3-CH_2-SePh), 4.25 and 4.55 (each 1H, each dd, J = 4.5, 10 Hz, and J = 9.5, 15.5 Hz, C2-CH_2-), 5.62 (1H, m, C3-H), 6.75-7.29 (5H, m, phenylselenyl), 7.82 and 7.91 (each 1H, each s, C7-H and C10-H); ir (potassium bromide): ν max 3300 cm^{-1} (NH), 1650 cm^{-1} (C=O); ms: m/z 437 (M$^+$), 266 (M$^+$-CH_2SePh).

1-Alkyl-8,9-dimethyl-3-phenylselenomethyl-2,3-dihydro-1*H*-imidazolo[2,3-*b*]benzo[*g*]pteridin-5-ones **6a-d** and 12-Alkyl-

8,9-dimethyl-3-phenylselenomethyl-2,3-dihydro-1*H*-imidazolo[2,3-*b*]benzo[*g*]pteridin-5-ones **7a-d**.

To a solution of **5** (100 mg) in dry DMSO (50 ml) sodium hydride (8 mg) and alkyl halide (1.5 molar equivalents) were added. The mixture was stirred for 3 hours at room temperature. The reaction mixture was dried over magnesium sulfate and the solvent was distilled off. The residue was column chromatographed on silica gel by eluting with chloroform-acetone (10:1). From the first eluate **7** was obtained and the second eluate gave **6**.

Compound **6a** had mp 281-282° (from benzene), yield 60%; ^{1}H-nmr (deuteriochloroform): δ 2.47 and 2.49 (each 3H, each s, C8-CH_3 and C9-CH_3), 3.16 (3H, s, N-CH_3), 3.51 and 3.77 (each 1H, each dd, J = 3, 14 Hz and J = 6.5, 14 Hz, C3-CH_2SePh), 3.69 and 4.03 (each 1H, each dd, J = 4, 10 Hz and J = 10, 10 Hz, C2-CH_2-), 5.14 (1H, m, C3-H), 6.93-7.38 (5H, m, PhSe-), 7.53 and 7.98 (each 1H, each s, C7 and C10-H); ir (potassium bromide): ν max 1670 cm^{-1} (C=O); ms m/z: 451 (M$^+$).

Anal. Calcd. for $C_{22}H_{21}N_5OSe$: C, 58.67; H, 4.70; N, 15.54. Found: C, 58.80; H, 4.75; N, 15.21.

Compound **6b** had mp 161-163° (from benzene), yield 41%; ^{1}H-nmr (deuteriochloroform): δ 1.02 (3H, t, J = 7 Hz, -$CH_2CH_2CH_3$), 1.72 (2H, sextet, J = 7 Hz, -$CH_2CH_2CH_3$), 2.47 and 2.48 (each 3H, each s, C8 and C9-CH_3), 3.46 and 3.82 (each 1H, each dd, J = 3, 14.4 and 6.5, 10 Hz, C3-CH_2Se-), 3.74 and 4.02 (each 1H, each dd, J = 4, 10 Hz and 10, 10 Hz, C2-CH_2-), 5.15 (1H, m, C3-H), 6.88-7.35 (5H, m, SePh), 7.50 and 7.96 (each 1H, each s, C7 and C10-H); ir (potassium bromide): ν max 1670 cm^{-1} (C=O).

Anal. Calcd. for $C_{24}H_{25}N_5OSe$: C, 60.25; H, 5.27; N, 14.64. Found: 60.24; H, 5.14; N, 14.35.

Compound **6c** had mp 106-108° (from benzene), yield 37%; ^{1}H-nmr (deuteriochloroform): δ 0.98 (3H, t, J = 7 Hz, -$(CH_2)_3CH_3$), 1.43 (2H, m, -$(CH_2)_2CH_2(CH_3)$, 1.66 (2H, m, -$CH_2CH_2CH_2CH_3$), 2.46 and 2.47 (each 3H, each s, C8 and C9-CH_3), 3.45 and 3.70 (2H, dd, J = 7.5, 14 Hz, -$NCH_2(CH_2)_2CH_3$), 3.73 and 4.03 (each 1H, each dd, J = 4, 10 Hz and 10, 10 Hz, C2-CH_2-), 3.46 and 3.82 (each 1H, each dd, J = 3, 14 Hz and 6.5, 14 Hz, C3-CH_2Se), 5.15 (1H, m, C3-CH-), 6.88-7.35 (5H, m, PhSe-), 7.49 and 7.96 (each 1H, each s, C7 and C9-H); ir (potassium bromide): ν max 1670 cm^{-1} (C=O).

Anal. Calcd. for $C_{25}H_{27}N_5OSe$: C, 60.97; H, 5.53; N, 14.22. Found: C, 61.21; H, 5.45; N, 14.22.

Compound **6d** had mp 158-159° (from benzene), yield 40%; ^{1}H-nmr (deuteriochloroform): δ 0.91 (3H, t, J = 7 Hz, -$(CH_2)_5CH_3$), 1.36 (6H, m, -$(CH_2)_2(CH_2)_3CH_3$), 1.67 (2H, quintet, J = 7 Hz, N-$CH_2CH_2(CH_2)_2CH_3$, 2.46 and 2.47 (each 3H, each s, C8 and C9-CH_3), 3.45 and 3.47 (each 1H, AB quartet, J = 7.5, 14 Hz, N-CH_2-), 3.46 and 3.82 (each 1H, each dd, J = 3, 14 Hz, 6.5, 14 Hz, C3-CH_2Se), 3.72 and 4.03 (each 1H, each dd, J = 4, 10 Hz and 10, 10 Hz, C2-CH_2-), 5.14 (1H, m, C3-H), 6.87-7.34 (5H, m, PhSe-), 7.48 and 7.95 (each 1H, each S, C7-H, C10-H); ir (potassium bromide): ν max 1670 cm^{-1} (C=O).

Anal. Calcd. for $C_{27}H_{31}N_5OSe$: C, 62.30; H, 6.00; N, 13.45. Found: C, 62.05; H, 6.00; N, 13.45.

Compound **7a** had mp 196-197° (from ethanol), yield 27%; ^{1}H-nmr (deuteriochloroform): δ 2.46 and 2.50 (each 3H, each s, C8 and C9-Me), 3.54 (3H, s, N12-CH_3), 3.37 and 3.82 (each 1H, each dd, J = 3, 13.5 Hz and 6, 13.5 Hz, C3-CH_2Se-), 4.00 and 4.22 (each 1H, each dd, J = 5, 14.5 Hz, 9.5, 14.5 Hz, C2-CH_2-), 5.01 (1H, m, C3-H), 6.91-7.41 (5H, m, -SePh), 7.55 and 7.90 (each 1H, each s, C7 and C10-H); ir (potassium bromide): ν max 1700 cm^{-1} (C=O); ms m/z: 451 (M$^+$).

Anal. Calcd. for $C_{22}H_{21}N_5OSe$: C, 58.67; H, 4.70; N, 15.54. Found: C, 58.54; H, 4.56; N, 15.33.

Compound **7b** had mp 165-157° (from ethanol), yield 26%; ^{1}H-nmr (deuteriochloroform): δ 1.05 (3H, t, J = 7 Hz, -$(CH_2)_2CH_3$), 1.68 (2H, sextet, J = 7 Hz, -$CH_2CH_2CH_3$), 2.45 and 2.49 (each 3H, each s, C8-, C9-CH_3), 3.40 and 3.81 (each 1H, each dd, J = 2.5, 13.5 Hz, C3-CH_2Se-), 3.98 and 4.22 (each 1H, each dd, J = 5, 14.5 and J = 9.5, 14.5 Hz), 5.08 (1H, m, C3-H), 6.91-7.42 (5H, m, PhSe-), 7.55 and 7.89 (each 1H, each s, C7-, C10-H); ir (potassium bromide): ν max 1700 cm^{-1} (C=O).

Anal. Calcd. for $C_{24}H_{25}N_5OSe$: C, 60.25; H, 5.27; N, 14.64. Found: C, 59.70; H, 5.18; N, 14.16.

Compound **7c** had mp 112-114° (from ethanol), yield 27%; ir (potassium bromide): ν max 1700 cm^{-1} (C=O); ms: m/z 403 (M$^+$).

Anal. Calcd. for $C_{25}H_{27}N_5OSe$: C, 60.97; H, 5.53; N, 14.22. Found: C, 60.71; H, 5.28; N, 14.04.

Compound **7d** had mp 145-147° (from ethanol); ^{1}H-nmr (deuteriochloroform): δ 0.89 (3H, t, J = 7 Hz, -CH_2CH_3), 1.31-1.48 (6H, m, -$(CH_2)_3$-CH_3), 1.74-1.84 (2H, m, -CH_2-CH_2N), 2.47 and 2.50 (each 3H, each s, C8- and C9-CH_3), 3.42 and 3.82 (each 1H, each dd, J = 2.5, 13.5 Hz, -CH_2SePh), 3.98 and 4.23 (each 1H, each dd, J = 5, 14.5 Hz and J = 9.5, 14.5 Hz, C2-CH_2-), 5.10 (1H, m, C3-H), 6.91-7.43 (5H, m, PhSe-), 7.55 and 7.89 (each 1H, each s, C7- and C10-H); ir (potassium bromide): ν max 1700 cm^{-1} (C=O); ms: m/z 521 (M$^+$).

Anal. Calcd. for $C_{27}H_{31}N_5OSe$: C, 62.30; H, 6.00; N, 13.45. Found: C, 62.12; H, 5.86; N, 13.17.

1,3,8,9-Tetramethyl-2,3-dihydro-1*H*-imidazolo[2,3-*b*]-benzo[*g*]pteridin-5-one (**8**).

To a solution of **6a** (150 mg) in ethanol (20 ml), Raney nickel catalyst (W-2, prepared from 3 g of alloy) was added. The mixture was stirred for 12 hours under refluxing. The mixture was filtered and the filtrate was evaporated to dryness and the residue was column chromatographed on silica gel eluting with a mixture of chloroform and acetone (20:1). The eluate was collected and the solvent was distilled off. The residue was crystallized from benzene to give yellow crystalline powder, mp> 300°, yield 53 mg (54%); ^{1}H-nmr (deuteriochloroform): δ 1.70 (3H, d, J = 6 Hz, C3-CH_3), 2.47 and 2.48 (each 3H, each s, C8 and C9-CH_3), 3.16 (3H, s, N-CH_3), 3.44 and 4.07 (each 1H, dd, J = 4, 9.5 Hz, and 9.5, 9.5 Hz, C2-CH_2-), 4.97 (1H, m, C3-H), 7.65 and 8.05 (each 1H, each s, C7 and C10-H); ir (potassium bromide): ν max 1670 cm^{-1} (C=O); ms: m/z 295 (M$^+$).

3,8,9,12-Tetramethyl-2,3-dihydro-1*H*-imidazolo[2,3-*b*]-benzo[*g*]pteridin-5-one (**9**).

To a solution of **7a** (50 mg) in ethanol (20 ml) was added Raney nickel catalyst (W-2, prepared from 1 g of alloy). The mixture was stirred for 12 hours under refluxing. The reaction mixture was filtered and the filtrate was evaporated to dryness. The residue was column chromatographed on silica gel eluting with a mixture of benzene and methanol (10:1). The eluate was collected and the solvent was distilled off. The residue was crystallized from ethanol to give yellow needles of mp 234-235°, yield 20 mg (61%); ^{1}H-nmr (deuteriochloroform): δ 1.62 (3H, d, J = 6 Hz, C3-CH_3), 2.45 and 2.48 (each 3H, each s, C8 and C9-CH_3), 3.58 (3H, s, N-CH_3), 3.67 and 4.22 (each 1H, each dd, J = 5, 14 and 9, 14 Hz, C2-CH_2-), 4.89 (1H, m, C3-H), 7.62 and

7.95 (each 1H, each s, C7 and C10-H); ir (potassium bromide): ν max 1705 cm^{-1} (C=O); ms: m/z 295 (M^+).

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