Polycyclic *N*-Heterocyclic Compounds. Part 65[1]: Ring Cleavage Reactions of Fused Furo[2,3-*c*]isoquinolines and Related Compounds with Various Nucleophiles

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Reaction of fused 2,3-dihydrofuro[2,3-*b*]pyridines with various nucleophiles (N and O) gave dihydrofuran ring cleaved products. The scope of this reaction was investigated in detail.

Key words ring cleavage; furo[2,3-*b*]pyridine; heterocycle; nucleophile

We have recently reported that reaction of 5-bromo-1,2,6,7-tetrahydrobenzo[*f*]furo[2,3-*c*]isoquinoline (**1a**) with imidazolate anion gave the dihydrofuran ring cleaved product 4-bromo-2-hydroxy-1-[2-(imidazol-1-yl)ethyl]-5,6-dihydrobenzo[*f*]isoquinoline (**2**) instead of the expected substituted 5-(imidazol-1-yl)-1,2,6,7-tetrahydrobenzo[*f*]furo-[2,3-*c*]isoquinoline (**3**) (Fig. 1).[1] Furthermore, compound **2** turned out to be a promising bronchodilator, with potency comparable to that of 3-isobutyl-1-methylxanthine. Although similar acid-mediated ring cleavage reactions of fused 2,3-dihydrofuro[2,3-*b*]pyridines have been previously reported by us and other researchers,[2—4] there is only one prior report of such a ring cleavage reaction resulting from base treatment (Grignard reagent).[5] We now report further details of this reaction and the extension thereof with a goal to develop to additional pharmaceutical agents.

Reaction of **1a** with excess piperidine at 80 °C gave the 5-substituted product (**4**) as expected in 54% yield (Chart 1). Next, we found that reaction of **1b** with imidazolate anion in dry dioxane at 90 °C produced the furan ring opened compound (**5**) in 39% yield just as reaction of **1a** gave **2** (Chart 2).[1,6] A similar reaction with the pyrrolate anion, prepared by reaction of pyrrole with sodium hydride in dry dioxane, with **1a** and **1b** produced **6a** in 50% yield and **6b** in 42% yield, respectively.

The chemoselectivity (5-subsitution *vs.* dihydrofuran ring cleavage at 2-position) that is dependent on the nature of the *N*-nucleophile can be explained as follows. Analysis of **1a** with B3LYP/6-31G* by Gaussian03W[7] shows that the atomic charge of the hydrogens of 2-C is 0.280011, while that of 5-C is 0.159558. Therefore, it is reasonable that hard nucleophiles such as imidazolate prefer to attack at the more electropositive 2-C position. On the other hand, the $2p_z$ molecular orbital coefficient at 2-C of LUMO is −0.00725, while that at 5-C is −0.05387. Thus, it is reasonable that soft nucleophiles such as piperidine prefer to attack at the 5-C position that possesses the larger orbital coefficient.

To extend the study of this reaction, we explored the behavior of **1a** with aniline, either to introduce this group at the 5-C position or to effect ring opening as above. Thus, to a solution of **1a** in dry dioxane was added a mixture of aniline and sodium hydride in dry dioxane and the mixture was then heated at 80 °C. When an equimolar mixture of aniline, sodium hydride, and **1a** was used, the reaction did not proceed smoothly. Employing an excess of aniline and sodium hydride (2.0 eq) gave no improvement and some starting material still remained. The reaction was quenched and the mixture was subjected to the usual work up. Purification by column chromatography of the residue afforded the furan ring opened vinyl derivative (**7**) that retains the bromine atom in 41% yield (Chart 3). Typical vinyl protons were observed at 5.67—6.83 ppm in the ^{1}H-NMR spectrum. A similar reaction with 4-chloroaniline instead of aniline gave the same product **7** in 38% yield. A plausible reaction mechanism is shown in Chart 4. The slow rate of reaction that was observed was

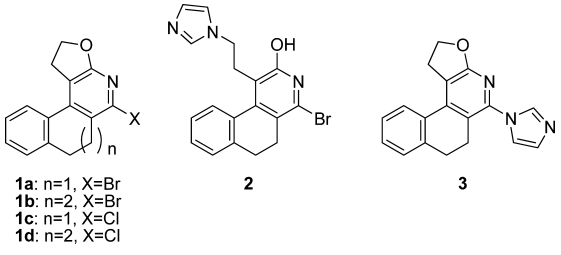

Fig. 1. Substrates (**1**) and the Ring Cleaved Product (**2**)

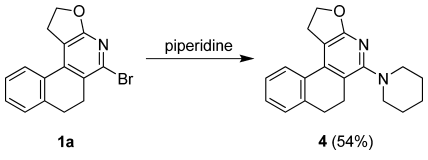

Chart 1. Reaction of **1a** with Piperidine

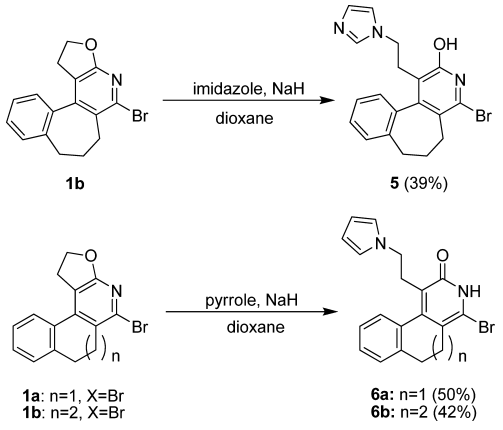

Chart 2. Reaction of **1b** with Imidazolate Anion and Reactions of **1a** and **1b** with Pyrrolate Anion

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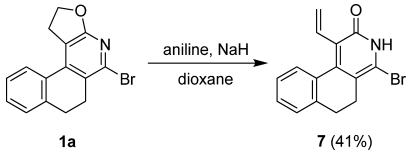

Chart 3. Reaction of **1a** with Anilide Anion

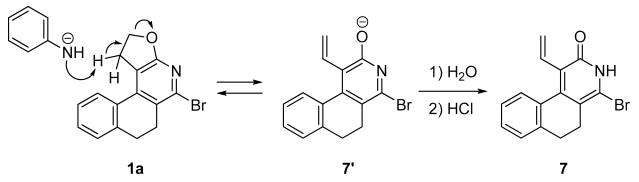

Chart 4. Mechanistic Proposal for Formation of **7**

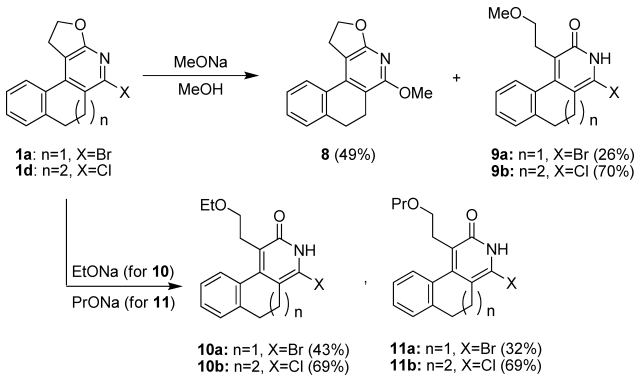

Chart 5. Reactions of **1a** and **1d** with Alcoholate

probably due to a Michael and *retro*-Michael reaction equilibrium of **1a** and **7′**. The strong basicity of the anilide anion (aniline pK_a 30.6) over imidazolate (imidazole pK_a 18.6) and pyrrolate (pyrrole pK_a 23.0)[8] causes the anilide anion to function as a base rather than a nucleophile in this experiment.

Finally, reactions of **1a** and **1d** with alcoholates were explored. Compound **1a** was allowed to react with sodium methoxide under reflux condition and the resulting mixture was separated by column chromatography to give the 5-methoxy derivative (**8**) in 49% yield as well as the furan ring opened product (**9a**) in 26% yield, respectively (Chart 5). Treatment of 5-chloro derivative **1d** with sodium methoxide afforded ring cleaved **9b** only in 70% yield. Similar reactions of **1a** and **1d** with sodium ethoxide gave ring opened **10a** in 43% yield and **10b** in 69% yield, while sodium propoxide gave ring opened **11a** in 32% yield and **11b** in 69% yield.

The biological properties of the new products will be examined in due course with the goal of developing new pharmaceutical agents.

Experimental

All melting points were determined on a Yanagimoto micro-melting point apparatus, and are uncorrected. Elemental analyses were performed on a Yanagimoto MT-5 CHN Corder elemental analyzer. The FAB-mass and ESI-mass spectra were obtained on a VG 70 mass or a Micromass Autospec-OA-Tof spectrometer and *m*-nitrobenzyl alcohol was used as the matrix. The IR spectra were recorded on a Japan Spectroscopic FT/IR-200 spectrophotometer with potassium bromide and frequencies are expressed in cm^{-1}. The ^{1}H-NMR spectra were recorded on a Varian VXR-200 instrument operating at 200 MHz with tetramethylsilane as an internal standard. Chemical shifts are given in ppm (δ) and J values in Hz, and the signals are designated as follows: s, singlet; d, doublet; dd, double doublet; t, triplet; q, quartet; br, broad; sex: sextet; m, multiplet. Column chromatography was performed on silica gel (IR-60-63-210-W, Daiso). TLC was carried out on Kieselgel 60F254 (Merck) or silica gel 70FM (Wako). Compounds **1a**—**d** were prepared according to the literature.[1)]

5-Piperidino-1,2,6,7-tetrahydrobenzo[*f*]furo[2,3-*c*]isoquinoline (4) A solution of **1a** (300 mg, 0.993 mmol) in piperidine (2.0 ml) was heated at 80 °C for 6 d. Ice water (150 ml) was added to the reaction mixture which was then extracted with ethyl acetate (100 ml×3). The combined organic phase was washed with saturated brine, dried over anhydrous Na_2SO_4, and then evaporated *in vacuo*. The residue was chromatographed on silica gel. The eluate of benzene–ethyl acetate (19 : 1) was evaporated and the residue was recrystallized from ethanol–water to give **4** (163 mg, 54%) as colorless prisms, mp 121—122 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.57 (6H, m, H-3′, 4′, 5′), 2.76 (4H, m, H-6, 7), 3.06 (4H, m, H-2′, 6′), 3.48 (2H, t, J=8.4 Hz, H-1), 4.60 (2H, t, J=8.4 Hz, H-2), 7.30 (3H, m, H-8, 9, 10), 7.60 (1H, m, H-11). FAB-MS m/z: 307 (MH$^+$). *Anal.* Calcd for $C_{20}H_{22}N_2O$: C, 78.40; H, 7.24; N 9.14. Found: C, 78.54; H, 7.36; N, 9.14.

4-Bromo-2-hydroxy-1-[2-(imidazol-1-yl)ethyl]-6,7-dihydro-5*H*-benzo[3,4]cyclohepta[1,2-*c*]pyridine (5) To a solution of imidazole (539 mg, 7.92 mmol) in dry dioxane (3.0 ml) was added NaH (190 mg, 7.92 mmol) and the mixture was stirred until generation of hydrogen gas stopped. Compound **1b** (250 mg, 0.791 mmol) was added to the solution which was then heated at 90 °C for 114 h under stirring. Ice water (150 ml) was poured into the mixture which was then extracted with ethyl acetate (100 ml×3). The combined organic layer was washed with saturated brine, dried over anhydrous Na_2SO_4, and then evaporated *in vacuo*. The residue was chromatographed on silica gel. The eluate of ethyl acetate–acetone (7 : 3) was evaporated and the residue was recrystallized from ethanol to give **5** (117 mg, 39%) as colorless prisms, mp 230—231 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.91, 2.52, 2.81 (4H, 1H, 1H, each m, H-5, 6, 7), 3.11 (2H, m, H-1′), 4.22 (2H, m, H-2′), 6.59, 6.93 (each 1H, each br s, imidazole-H-4′, 5′), 6.96 (1H, m, H-11, high field shift due to anisotropic effect of imidazole ring), 7.31 (4H, m, H-8, 9, 10, imidazole-H-2′). IR (KBr) cm^{-1}: 2550 (br, OH). FAB-MS m/z: 384 (MH$^+$), 386 (MH$^+$+2). *Anal.* Calcd for $C_{19}H_{18}BrN_3O$: C, 59.39; H, 4.72; N, 10.94. Found: C, 59.13; H, 4.87; N, 10.72.

4-Bromo-1-[2-(pyrrol-1-yl)ethyl]-5,6-dihydrobenzo[*f*]isoquinolin-2(3*H*)-one (6a) To a solution of pyrrole (1.33 g, 19.8 mmol) in dry dioxane (3.0 ml) was added NaH (477 mg, 19.9 mmol) and the mixture was stirred until generation of hydrogen gas stopped. Compound **1a** (300 mg, 0.993 mmol) was added to the mixture which was then stirred at 80 °C for 47 h. After evaporation of solvent, ice water (100 ml) was poured into the residue and the aqueous was extracted with ethyl acetate (100 ml×3). The combined organic layer was washed with saturated brine, dried over anhydrous Na_2SO_4, and then evaporated *in vacuo*. The residue was chromatographed on silica gel. The eluate of benzene–ethyl acetate (9 : 1) was evaporated and the residue was recrystallized from ethanol to give **6a** (182 mg, 50%) as colorless prisms, mp 220—223 °C. ^{1}H-NMR ($CDCl_3$) δ: 2.72 (4H, br s, H-5, 6), 3.35 (2H, t, J=7.4 Hz, H-1′), 4.40 (2H, t, J=7.4 Hz, H-2′), 6.10 (2H, t, J=2.1 Hz, pyrrole-3′, 4′), 6.66 (2H, t, J=2.1 Hz, pyrrole-2′, 5′), 7.29 (4H, m, H-7, 8, 9, 10), 11.81 (1H, br, D_2O exchangeable NH). IR (KBr) cm^{-1}: 3100—2500 (br, NH), 1625 (CO). FAB-MS m/z: 369 (MH$^+$), 371 (MH$^+$+2). *Anal.* Calcd for $C_{19}H_{17}BrN_2O$: C, 61.80; H, 4.64.; N, 7.59. Found: C, 62.02; H, 4.78; N, 7.46.

4-Bromo-1-[2-(pyrrol-1-yl)ethyl]-6,7-dihydro-5*H*-benzo[3,4]cyclohepta[1,2-*c*]pyridin-2(3*H*)-one (6b) To a solution of pyrrole (1.27g, 18.9 mmol) in dry dioxane (3.0 ml) was added NaH (455 mg, 19.0 mmol) and the mixture was stirred until generation of hydrogen gas stopped. Compound **1b** (300 mg, 0.949 mmol) was added to the mixture which was then stirred at 80 °C for 70 h. Ice water (150 ml) was poured into the reaction mixture which was then extracted with ethyl acetate (100 ml×3). The combined organic layer was washed with saturated brine, dried over anhydrous Na_2SO_4, and then evaporated *in vacuo*. The residue was chromatographed on silica gel. The eluate of benzene–ethyl acetate (17 : 3) was evaporated and the residue was recrystallized from ethanol to give **6b** (153 mg, 42%) as colorless prisms, mp 203—204 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.89, 2.16, 2.53, 2.82 (3H, 1H, 1H, 1H, each m, H-5, 6, 7), 3.05 (2H, m, H-1′), 4.16 (2H, t, J=7.2 Hz, H-2′), 6.03 (2H, t, J=2.1 Hz, pyrrole-3′, 4′), 6.45 (2H, t, J=2.1 Hz, pyrrole-2′, 5′), 6.81 (1H, m, upper field shift with anisotropic effect of pyrrole ring, H-11), 7.29 (3H, m, H-8, 9, 10), 11.51 (1H, br, D_2O exchangeable, NH). IR (KBr) cm^{-1}: 3100—2550 (br, NH), 1630 (CO). FAB-MS m/z: 383 (MH$^+$), 385 (MH$^+$+2). *Anal.* Calcd for $C_{20}H_{19}BrN_2O$: C, 62.67; H, 5.00; N, 7.31. Found: C, 62.74; H, 5.07; N, 7.16.

4-Bromo-1-vinyl-5,6-dihydrobenzo[*f*]isoquinolin-2(3*H*)-one (7) To a solution of **1a** (300 mg, 0.993 mmol) in dry dioxane (10 ml) was added a mixture of aniline (278 mg, 2.99 mmol) and NaH (48 mg, 2.00 mmol) in dry

dioxane (1.0 ml) and the reaction was stirred at 80 °C for 20 min. When ice water (150 ml) was poured into the mixture a solid precipitated which was filtered off. The mother liquid was neutralized with 1.0 M hydrochloric acid and solid precipitated again which was filtered off. The combined solids were recrystallized from ethanol to give **7** (122 mg, 41%) as colorless plates. mp 220—221 °C. ^{1}H-NMR ($CDCl_3$) δ: 2.77 (4H, m, H-5, 6), [5.67 (1H, dd, J=11.6, 2.4 Hz), 6.44 (1H, dd, J=17.7, 2.4 Hz), 6.83 (1H, dd, J=17.7, 11.6 Hz), vinyl protons], 7.30 (3H, m, H-7, 8, 9), 7.78 (1H, m, H-10), 10.92 (1H, br s, D_2O exchangeable, NH). IR (KBr) cm^{-1}: 3100—2500 (br, NH), 1635 (CO). FAB-MS *m/z*: 302 (MH^+), 304 (MH^++2). *Anal.* Calcd for $C_{15}H_{12}BrNO$: C, 59.62; H, 4.00; N, 4.64. Found: C, 59.37; H, 4.07; N, 4.66.

In a similar procedure as described above for aniline, 4-chloroaniline (0.993 mmol scale at 80 °C for 20 min) produced the same compound **7** (38%) identical with **7** formed from aniline.

5-Methoxy-1,2,6,7-tetrahydrobenzo[*f*]furo[2,3-*c*]isoquinoline (8) and 4-Bromo-1-(2-methoxyethyl)-5,6-dihydrobenzo[*f*]isoquinolin-2(3*H*)-one (9a) To a solution of sodium metal (644 mg, 28.0 mmol) in methanol (10 ml) was added compound **1a** (300 mg, 0.993 mmol) and the reaction was refluxed for 27 h with stirring. After addition of ice water (150 ml), the solution was neutralized with 1.0 M hydrochloric acid. The precipitated solid was collected by filtration and chromatographed on silica gel. The eluate of benzene–ethyl acetate (9 : 1) was evaporated and the residue was recrystallized from methanol to give **8** (124 mg, 49%) as colorless needles. A further the eluate of benzene–ethyl acetate (7 : 3) was evaporated and the residue was recrystallized from methanol to give **9a** (87.6 mg, 26%) as colorless needles. **8**: mp 124—125 °C. ^{1}H-NMR ($CDCl_3$) δ: 2.79 (4H, m, H-6, 7), 3.52 (2H, t, J=8.5 Hz, H-1), 3.96 (3H, s, CH_3), 4.64 (2H, t, J=8.5 Hz, H-2), 7.30 (3H, m, H-8, 9, 10), 7.65 (1H, m, H-11). ESI-MS *m/z*: 254 (MH^+). *Anal.* Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.58; H, 6.10; N, 5.43. **9a**: mp 166—167 °C. ^{1}H-NMR ($CDCl_3$) δ: 2.76 (4H, s, H-5, 6), 3.17 (2H, t, J=6.7 Hz, H-1′), 3.43 (3H, s, CH_3), 3.93 (2H, t, J=6.7 Hz, H-2′), 7.33 (3H, m, H-7, 8, 9), 7.80 (1H, m, H-10), 10.85 (1H, br, D_2O exchangeable, NH). IR (KBr) cm^{-1}: 3100—2500 (br, NH), 1630 (CO). ESI-MS *m/z*: 334 (MH^+), 336 (MH^++2). *Anal.* Calcd for $C_{16}H_{16}BrNO_2$: C, 57.50; H, 4.83; N, 4.19. Found: C, 57.78; H, 4.99; N, 4.22.

4-Chloro-1-(2-methoxyethyl)-6,7-dihydro-5*H*-benzo[3,4]cyclohepta[1,2-*c*]pyridin-2(3*H*)-one (9b) To a solution of sodium metal (509 mg, 22.1 mmol) in methanol (10 ml) was added compound **1d** (300 mg, 1.10 mmol) and the solution was refluxed for 64 h. After evaporation of solvent, ice water (150 ml) was added and the mixture was neutralized with 1.0 M hydrochloric acid. The precipitated solid was collected by filtration and chromatographed on silica gel. The eluate of benzene–ethyl acetate (7 : 3) was evaporated and the residue was recrystallized from methanol to give **9b** (234 mg, 70%) as colorless prisms, mp 121 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.95, 2.33, 2.60, 2.92 (3H, 1H, 1H, 3H, each m, H-5, 6, 7, 1′), 3.23 (3H, s, CH_3), 3.60 (2H, m, H-2′), 7.30 (4H, m, H-8, 9, 10, 11), 11.31 (1H, br, D_2O exchangeable, NH). IR (KBr) cm^{-1}: 3070—2500 (br, NH), 1635 (CO). ESI-MS *m/z*: 304 (MH^+), 306 (MH^++2). *Anal.* Calcd for $C_{17}H_{18}ClNO_2$: C, 67.21; H, 5.97; N, 4.61. Found: C, 67.43; H, 6.06; N, 4.64.

4-Bromo-1-(2-ethoxyethyl)-5,6-dihydrobenzo[*f*]isoquinolin-2(3*H*)-one (10a) To a solution of sodium metal (644 mg, 28.0 mmol) in dry ethanol (10 ml) was added compound **1a** (300 mg, 0.993 mmol) and the solution was refluxed for 52 h with stirring. Ice water (150 ml) was poured into the reaction mixture which was then extracted with ethyl acetate (100 ml×3). The combined organic layer was washed with saturated brine, dried over Na_2SO_4, and then evaporated *in vacuo*. The residue was recrystallized from ethyl acetate to give **10a** (150 mg, 43%) as colorless prisms, mp 205—206 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.24 (3H, t, J=7.0 Hz, CH_3), 2.76 (4H, br s, H-5, 6), 3.15 (2H, t, J=6.5 Hz, H-1′), 3.82 (2H, q, J=7.0 Hz, $C\underline{H}_2CH_3$), 3.97 (2H, t, J=6.5 Hz, H-2′), 7.31 (3H, m, H-7, 8, 9), 7.76 (1H, m, H-10), 10.33 (1H, br, D_2O exchangeable, NH). IR (KBr) cm^{-1}: 3100—2500 (br, NH), 1625 (CO). FAB-MS *m/z*: 348 (MH^+), 350 (MH^++2). *Anal.* Calcd for $C_{17}H_{18}BrNO_2$: C, 58.63; H, 5.21; N, 4.02. Found: C, 58.75; H, 5.22; N, 3.91.

4-Chloro-1-(2-ethoxyethyl)-6,7-dihydro-5*H*-benzo[3,4]cyclohepta[1,2-*c*]pyridin-2(3*H*)-one (10b) To a solution of sodium metal (509 mg, 22.1 mmol) in dry ethanol (10.0 ml) was added **1d** (300 mg, 1.10 mmol) and the stirred solution was refluxed for 43 h. After evaporation of solvent, ice water (150 ml) was added to the mixture which was then extracted with ethyl acetate (100 ml×3). The combined organic layer was washed with saturated brine, dried over anhydrous Na_2SO_4, and then evaporated *in vacuo*. The residue was chromatographed on silica gel and the eluate of benzene–ethyl acetate (4 : 1) was evaporated and the residue was recrystallized from methanol to give **10b** (243 mg, 69%) as colorless prisms, mp 121—122 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.13 (3H, t, J=7.1 Hz, CH_3), 1.94, 2.35, 2.59, 2.93 (3H, 1H, 1H, 3H, each m, H-5, 6, 7, 1′), 3.39, 3.65 (each 2H, each m, CH_2OCH_2), 7.29 (4H, m, H-8, 9, 10, 11), 11.84 (1H, br, D_2O exchangeable, NH). IR (KBr) cm^{-1}: 3060—2500 (br, NH), 1635 (CO). ESI-MS *m/z*: 318 (MH^+), 320, (MH^++2). *Anal.* Calcd for $C_{18}H_{20}ClNO_2$: C, 68.03; H, 6.34; N, 4.41. Found: C, 68.23; H, 6.47; N, 4.36.

4-Bromo-1-(2-propoxyethyl)-5,6-dihydrobenzo[*f*]isoquinolin-2(3*H*)-one (11a) To a solution of sodium metal (644 mg, 28.0 mmol) in dry 1-propanol (10 ml) was added compound **1a** (300 mg, 0.993 mmol) and the reaction was then stirred at 80 °C for 99 h. Ice water (150 ml) was poured into the mixture which was then neutralized with 1.0 M hydrochloric acid and extracted with ethyl acetate (100 ml×3). The combined organic layer was washed with saturated brine, dried over anhydrous Na_2SO_4, and then evaporated *in vacuo*. The residue was chromatographed on silica gel and the eluate of benzene–ethyl acetate (4 : 1) was evaporated and the residue was recrystallized from methanol to give **11a** (116 mg, 32%) as colorless prisms, mp 115—116 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.94 (3H, t, J=7.0 Hz, CH_3), 1.63 (2H, sex, J=7.0 Hz, $C\underline{H}_2CH_3$), 2.76 (4H, br s, H-5, 6), 3.16 (2H, t, J=6.4 Hz, H-1′), 3.49 (2H, t, J=7.0 Hz, $C\underline{H}_2CH_2CH_3$), 3.97 (2H, t, J=6.4 Hz, H-2′), 7.31 (3H, m, H-7, 8, 9), 7.81 (1H, m, H-10), 10.92 (1H, br s, D_2O exchangeable, NH). IR (KBr) cm^{-1}: 3100—2500 (br, NH), 1625 (CO). ESI-MS *m/z*: 362 (MH^+), 364 (MH^++2). *Anal.* Calcd for $C_{18}H_{20}BrNO_2$: C, 59.68; H, 5.56; N, 3.87. Found: C, 59.90; H, 5.68; N, 3.91.

4-Chloro-1-(2-propoxyethyl)-6,7-dihydro-5*H*-benzo[3,4]cyclohepta[1,2-*c*]pyridin-2(3*H*)-one (11b) To a solution of sodium metal (509 mg, 22.1 mmol) in dry 1-propanol (10.0 ml) was added **1d** (300 mg, 1.10 mmol) and the solution was then stirred at 80 °C for 25 h. After evaporation of solvent, ice water (150 ml) was added to the mixture which was then neutralized with 1.0 M hydrochloric acid and extracted with ethyl acetate (100 ml×3). The combined organic layer was washed with saturated brine, dried over anhydrous Na_2SO_4, and then evaporated *in vacuo*. The residue was chromatographed on silica gel and the eluate of benzene–ethyl acetate (7 : 3) was evaporated and the residue was recrystallized from methanol to give **11b** (254 mg, 69%) as colorless prisms, mp 129—131 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.86 (3H, t, J=7.2 Hz, CH_3), 1.53 (2H, sex, J=7.2 Hz, $C\underline{H}_2CH_3$), 1.94, 2.32, 2.58, 2.91 (3H, 1H, 1H, 3H, each m, H-5, 6, 7, 1′), 3.30, 3.69 (each 2H, each m, CH_2OCH_2), 7.31 (4H, m, H-8, 9, 10, 11), 10.93 (1H, br, D_2O exchangeable, NH). IR (KBr) cm^{-1}: 3060—2500 (br, NH), 1635 (CO). ESI-MS *m/z*: 332 (MH^+), 334, (MH^++2). *Anal.* Calcd for $C_{19}H_{22}ClNO_2$: C, 68.77; H, 6.68; N, 4.22. Found: C, 69.16; H, 6.83; N, 4.24.

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References and Notes

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