Syntheses of Naphthonaphthyridines by Skraup Reaction Using 3-Aminobenzo[*g* or *h*]quinoline

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Naphtho[2,1-*f*][1,7]naphthyridine (5, angular type) and naphtho[2,1-*b*][1,5]naphthyridine (6, linear type) were obtained by the Skraup reaction of 3-aminobenzo[*h*]quinoline (4), but 3-aminobenzo[*g*]quinoline gave only naphtho-[2,3-*f*][1,7]naphthyridine (18, angular type).

Keywords Skraup reaction; cyclization; naphtho[2,1-*f*][1,7]naphthyridine; naphtho[2,1-*b*][1,5]naphthyridine; naphtho-[2,3-*f*][1,7]naphthyridine; 4,6-phenanthroline

Naphthonaphthyridine should have 36 skeletal isomers, with two nitrogen atoms in the four differently annelated ring skeletons. Three of them have been synthesized by reactions *via* benzyne type intermediates.[1] We also synthesized naphtho[2,1-*b*][1,5]naphthyridine[2] using the Skraup reaction of 2-aminobenzo[*f*]quinoline, and that was the first example of a linear-type compound obtained by the Skraup reaction with a heterocyclic system. The Skraup cyclization reaction tends to produce angular-type heterocycles when 2-naphthylamine[3] and 2- or 3-amino-phenanthrene[4] are used as the starting materials. The reactions of these naphthonaphthyridines are very interesting because their reactivities have been hitherto unknown and because some naphthonaphthyridines have a skeleton similar to that of carcinogenic benzacridines.[5] This report concerns synthesis of naphthonaphthyridines by using the Skraup reaction with 3-aminobenzo[*g* or *h*]quinoline.

Results

Condensation of 1-naphthylamine (**1**) with sodium nitromalonaldehyde monohydrate,[6] which was synthesized from mucobromic acid, gave *N*-(2-formyl-2-nitroethyl-idene)-1-naphthylamine (**2**). The product **2** was cyclized to 3-nitrobenzo[*h*]quinoline (**3**) by using zinc chloride in dimethylacetamide (DMA). The nitro compound **3** was reduced to the amino compound (**4**) with Raney nickel. The amino compound **4** was, in turn, cyclized by means of a modified Skraup reaction. Thus, glycerol was allowed to react with **4** in the presence of Sulfo-mix,[7] ferrous sulfate, and boric acid.

Two products were obtained, **5** (6.8% yield, mp 175—177 °C) and **6** (4.5% yield, mp 157—159 °C), as shown in Chart 1.

The structures of **5** and **6** were determined by proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy. Compound **5** has a singlet proton signal at δ 9.75 and the chemical shift is similar to that of 5-H (δ 9.48) of 4,6-phenanthroline.[8] The signal pattern of hydrogens at the 2, 3 and 4 positions of **5** was also similar to that of 4,6-phenanthroline. The ultraviolet (UV) spectrum of **5** showed a closer similarity to that of chrysene than to that of benz[*c*]anthracene, as shown in Fig. 1.

These facts showed that **5** was an angular-type product, naphtho[2,1-*f*][1,7]naphthyridine. Compound **6** also has a singlet proton signal (δ 8.97) which corresponds to the 7-H signal (δ 8.11) of benz[*c*]acridine. The signal (δ 8.97) of **6** is shifted to a lower field due to the magnetic anisotropy effect of nitrogen at the 7 position. Thus, **6** is the linear type product, naphtho[1,2-*b*][1,5]naphthyridine. The UV spectrum of **6** supports linear-type annelation, based on its similarity to the spectrum of benz[*a*]anthracene. Compound **5** was alternatively synthesized in the following manner. First, compound **8** was prepared from 5-aminotetralin (**7**) in the same manner as in the synthesis of **2**. As the cyclization of **8** by zinc chloride in DMA involves a high risk of exothermic explosion, **8** was cyclized to compound **9** by using polyphosphoric acid (PPA). Compound **9** was reduced to the amino compound (**10**) in the same manner as in the

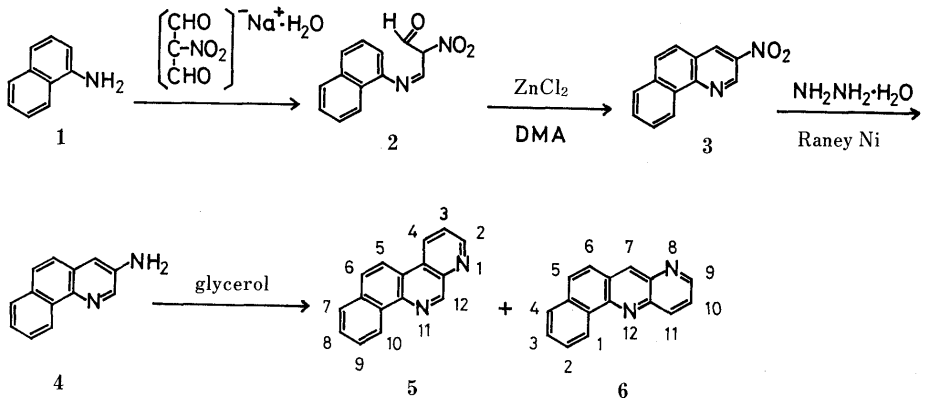

Chart 1

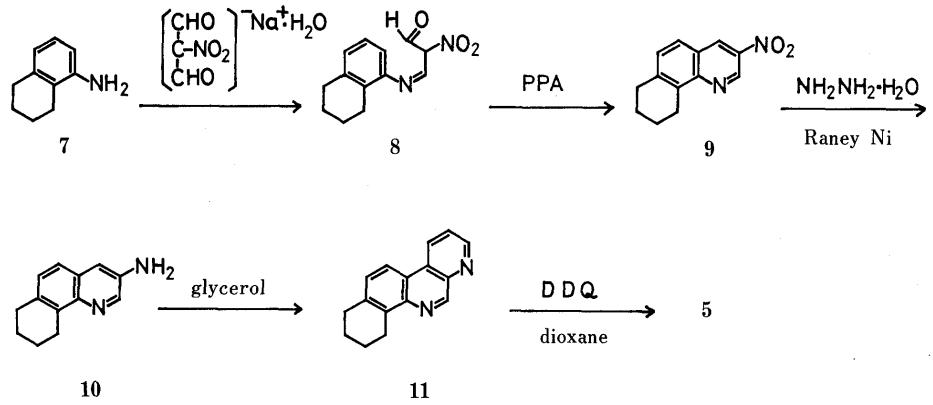

Chart 2

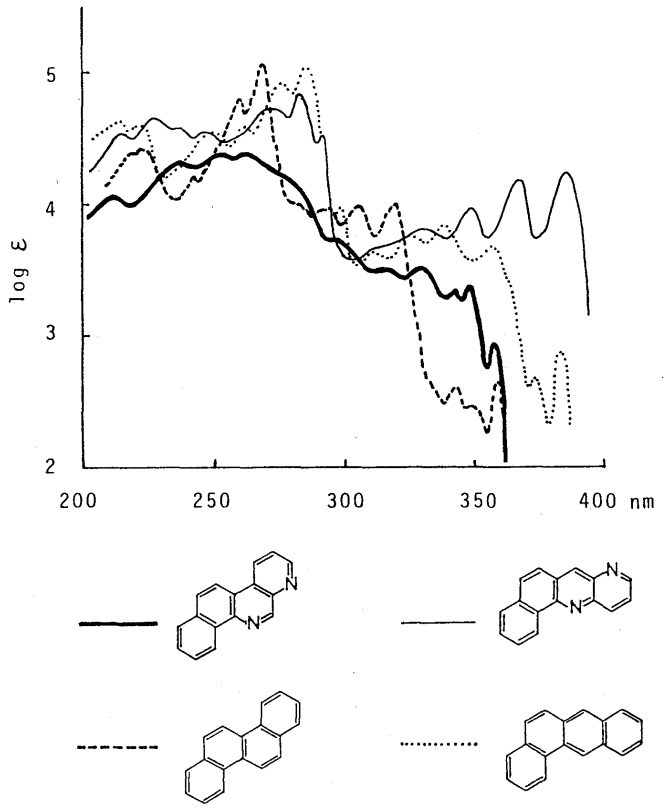

Fig. 1. Ultraviolet Absorption Spectra in Cyclohexane

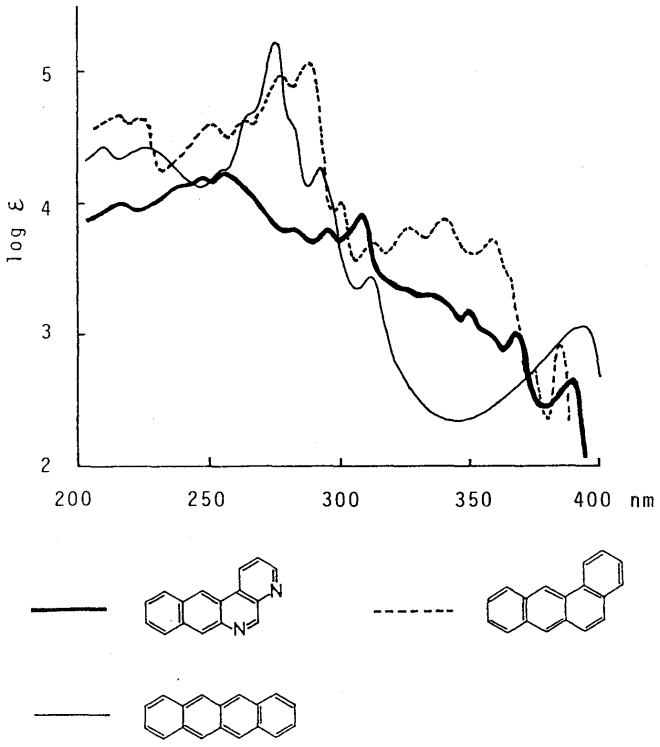

Fig. 2. Ultraviolet Absorption Spectra in Cyclohexane

synthesis of **4**, and the Skraup reaction of **10** gave the angular-type compound (**11**) in 29% yield, as shown in Chart 2.

Compound **11** was presumed to have a 4,6-phenanthroline skeleton based on its ^{1}H-NMR spectrum. Compound **11** was dehydrogenated with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) to **5**, which was identified by the mixed melting point test, and examination of the spectral data.

In order to examine the Skraup reaction of 3-aminobenzo[*g*]quinoline (**17**),[9] compound **17** was synthesized in the following manner. Compound **13** was obtained from 6-aminotetralin (**12**) in the same manner as in the synthesis of **2**. The cyclization of **13** with PPA gave a mixture (*ca.* 1 : 1) of the linear-type compound (**14**) and the angular-type compound (**15**), which were separated by column chromatography. Compound **14** was dehydrogenated to 3-nitrobenzo[*g*]quinoline (**16**) with DDQ, and the nitro group of **16** was reduced to an amino group (**17**)[9] by using hydrazine hydrate and Raney Ni. The Skraup reaction of **17** gave only compound **18** in low yield (4.2%). The structure of **18** was determined to be naphtho[2,3-*f*][1,7]-naphthyridine (angular type) by examination of the ^{1}H-NMR spectrum. The UV spectrum of **18** was compared with those of linear-type (naphthacene) and angular-type hydrocarbons (3,4-benzphenanthrene), but was different from that of either benzacridine or naphthacene as shown in Fig. 2. As further evidence for the structure of **18**, compound **18** was synthesized in another way. The nitro compound (**14**) was reduced to the amino compound (**19**), and an angular-type product (**20**) was obtained by means of the Skraup reaction of **19**. The ^{1}H-NMR chemical shifts of aromatic protons of **20** were similar to those of 4,6-phenanthroline. The compound obtained by dehydrogenation of **20** with palladium–charcoal (Pd–C) was identified as **18** by the mixed melting point test with the

compound previously obtained from **17**, and their spectral data also agreed with each other. Compound **18** was more conveniently synthesized from **20** *via* **19** (Chart 3).

Discussion

The Skraup reaction can be regarded as an electrophilic reaction to aromatic hydrocarbons. It is well known that σ-complex of the α-adduct of a naphthalene intermediate is more stable than the β-adduct of σ-complex as regards benzenoid stability. The Skraup reaction of 2- or 3-aminophenanthrene[4] and 3-aminobenzo[*g*]quinoline affords corresponding angular-type products owing to the influence of benzenoid stability, but 3-aminobenzo[*f* or *h*]quinoline gave the linear-type products. The formation of linear-type products may be ascribed to stronger para-deactivation by the electron-withdrawing influence of the ring nitrogen as compared with benzenoid stabilization in the formation of 1,5-naphthyridine from 3-aminopyridine.[10] These experimental results of the Skraup reaction of aminobenzoquinolines were compared with those for aminophenanthrenes and aminoanthracene as shown in Chart 4.

The reactivity indices obtained by the molecular orbital (PM3) method are in accord with the experimental results, as will be separately reported.

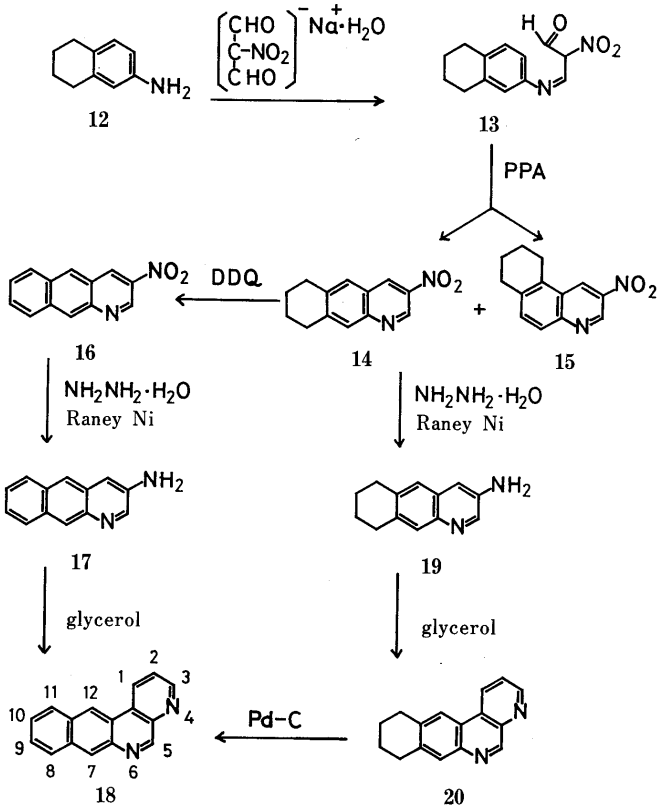

Chart 3

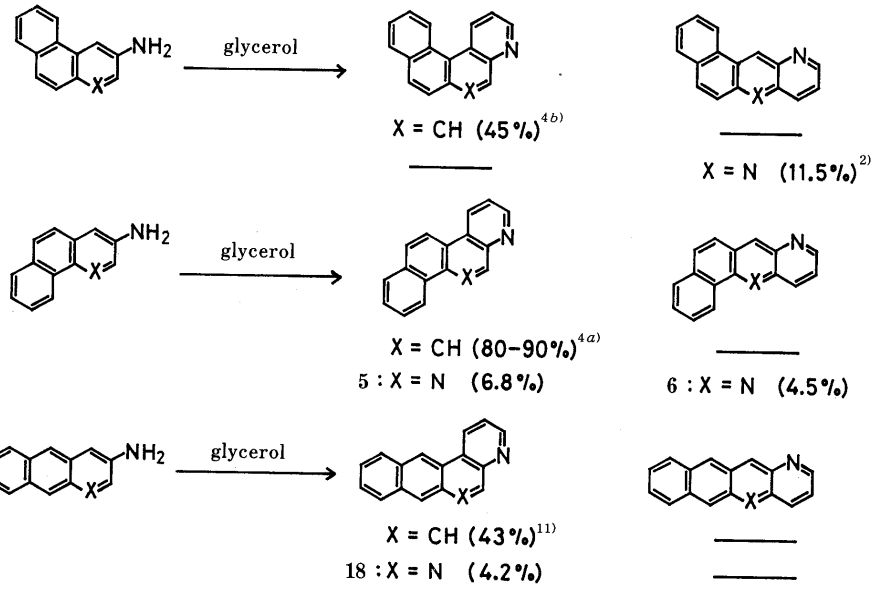

Chart 4

Experimental

^{1}H-NMR spectra were recorded with a JEOL JNM GX-270 spectrometer with tetramethylsilane (TMS) as an internal standard. Chemical shifts are given on the δ scale (ppm). The following abbreviations are used: s = singlet, d = doublet, dd = double doublet, ddd = double double doublet, m = multiplet, and br = broad. Mass spectra (MS) were taken with a Hitachi GC-MS M-80 spectrometer. Infrared (IR) spectra and UV spectra were recorded on a JASCO IRA-I and a Shimadzu UV-240 spectrophotometer.

***N*-(2-Formyl-2-nitroethylidene)-1-naphthylamine (2)** A solution of sodium nitromalonaldehyde monohydrate[6] (11 g, 0.07 mol) in water (105 ml) was added to a solution of 1-naphthylamine (**1**) (10.1 g 0.07 mol) in 2% HCl (628 ml) at 50 °C, and the mixture was stirred for 30 min. The resulting precipitate was collected by filtration and recrystallized from EtOH to give 14.6 g (86%) of **2** as yellow needles, mp 150—153 °C. ^{1}H-NMR ($CDCl_3$) δ: 7.50—8.05 (7H, m, 2—8-H), 9.08 (1H, dd, J = 12.4, 3.7 Hz, $CHNO_2$), 10.67 (1H, d, J = 3.7 Hz, N=CH), 12.97 (1H, br d, J = 12.4 Hz, CHO). MS *m/z*: 242 (M^+). *Anal.* Calcd for $C_{13}H_{10}N_2O_3$: C, 64.46; H, 4.16; N, 11.56. Found: C, 64.77; H, 4.32; N, 11.51.

3-Nitrobenzo[*h*]quinoline (3) A mixture of **2** (24.2 g, 0.1 mol) and $ZnCl_2$ (13.6 g, 0.1 mol) in DMA (18 ml) was heated at 180 °C with stirring for 1 h. After cooling to room temperature, the reaction mixture was poured into H_2O (200 ml). The resulting precipitate was collected by filtration and recrystallized from benzene to give 14.7 g (66%) of **3** as yellow needles, mp 165—168 °C. ^{1}H-NMR ($CDCl_3$) δ: 7.28 (2H, m, 8, 9-H), 7.83 (1H, d, J = 8.4 Hz, 6-H), 7.97 (1H, m, 7-H), 7.98 (1H, d, J = 8.4 Hz, 5-H), 9.01 (1H, d, J = 2.7 Hz, 4-H), 9.33 (1H, m, 10-H), 9.33 (1H, d, J = 2.7 Hz, 2-H). MS *m/z*: 224 (M^+). *Anal.* Calcd for $C_{13}H_8N_2O_2$: C, 69.64; H, 3.60; N, 12.49. Found: C, 69.37; H, 3.54; N, 12.36.

3-Aminobenzo[*h*]quinoline (4) A suspension of **3** (4.48 g, 0.02 mol) and Raney Ni (*ca.* 1 g) in EtOH (100 ml) was treated dropwise with $NH_2NH_2 \cdot H_2O$ (6 ml, 0.12 mol) at 40—50 °C during 1 h. The solution was

stirred for 30 min at the same temperature. The catalyst was filtered off, the filtrate was concentrated *in vacuo*, and the residue was recrystallized from CCl_4 to give 2.3 g (59%) of **4** as yellow needles, mp 110—112 °C. ^{1}H-NMR ($CDCl_3$) δ: 3.59 (2H, br s, NH_2), 7.24 (1H, d, J=2.7 Hz, 4-H), 7.47 (1H, d, J=8.4 Hz, 5-H), 7.52—7.70 (2H, m, 8, 9-H), 7.69 (1H, d, J=8.4 Hz, 6-H), 7.82 (1H, m, 7-H), 8.52 (1H, d, J=2.7 Hz, 2-H), 9.10 (1H, m, 10-H). MS *m/z*: 194 (M^+). *Anal.* Calcd for $C_{13}H_{10}N_2$: C, 80.39; H, 5.19; N, 14.42. Found: C, 80.40; H, 5.03; N, 14.48.

Skraup Reaction of 4 A mixture of Sulfo-mix[7] [prepared from 11.9 g of $H_2SO_4 \cdot SO_3$ (20%) and 2.7 g of nitrobenzene], $FeSO_4 \cdot 7H_2O$ (0.35 g), and H_3BO_3 (0.5 g) was chilled to 0—5 °C, and anhydrous glycerol (3.4 g, 0.037 mol) was added to the mixture, followed by the addition of **4** (1.94 g, 0.01 mol) and warm water (5 ml, 50 °C). The mixure was stirred at 140—150 °C for 3 h. The reaction mixture was made alkaline with 28% NH_4OH, and the resulting precipitate was collected by filtration. The precipitate was extracted with hot MeOH. The MeOH extract was concentrated *in vacuo*, and the residue was dissolved in $CHCl_3$. After removal of the $CHCl_3$, the residue was chromatographed on silica gel ($CHCl_3$: CH_2Cl_2 = 3 : 1) to give 0.94 g (6.8%) of **6** as yellow needles, mp 175—177 °C (from benzene), and 0.62 g (4.5%) of **5** as yellow needles, mp 157—159 °C (from benzene).

5: ^{1}H-NMR ($CDCl_3$) δ: 7.70—7.85 (2H, m, 8, 9-H), 7.79 (1H, dd, J=8.4, 4.0 Hz, 3-H), 8.00 (1H, m, 7-H), 8.07 (1H, d, J=9.1 Hz, 6-H), 8.45 (1H, d, J=9.1 Hz, 5-H), 8.97 (1H, ddd, J=8.4, 1.5, 0.5 Hz, 4-H), 9.10 (1H, dd, J=4.0, 1.5 Hz, 2-H), 9.43 (1H, m, 10-H), 9.75 (1H, s, 12-H). MS *m/z*: 230 (M^+). *Anal.* Calcd for $C_{16}H_{10}N_2$: C, 83.46; H, 4.38; N, 12.17. Found: C, 83.63; H, 4.22; N, 12.19.

6: ^{1}H-NMR ($CDCl_3$) δ: 7.77 (1H, dd, J=8.7, 4.0 Hz, 10-H), 7.79 (2H, m, 2, 3-H), 7.80 (1H, d, J=8.4 Hz, 5-H), 7.84 (1H, d, J=8.4 Hz, 6-H), 7.92 (1H, m, 4-H), 8.74 (1H, ddd, J=8.7, 1.5, 0.5 Hz, 11-H), 8.97 (1H, d, J=0.5 Hz, 7-H), 9.10 (1H, dd, J=4.0, 1.5 Hz, 9-H), 9.48 (1H, m, 1-H). MS *m/z*: 230 (M^+). *Anal.* Calcd for $C_{16}H_{10}N_2$: C, 83.46; H, 4.38; N, 12.17. Found: C, 83.31; H, 4.00; N, 12.07.

***N*-(2-Formyl-2-nitroethylidene)-5-aminotetralin (8)** A solution of sodium nitromalonaldehyde monohydrate (15.7 g, 0.1 mol) in water (200 ml) was added to a solution of the HCl salt of **7** (18.4 g, 0.1 mol) in water (1000 ml) at 50 °C, and the mixture was stirred for 30 min. The resulting precipitate was collected by filtration and recrystallized from EtOH to give 17.8 g (72%) of **8** as yellow needles, mp 151—153 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.82 (2H, m, 6-H), 1.92 (2H, m, 7-H), 2.78 (2H, m, 5-H), 2.82 (2H, m, 8-H), 7.05—7.25 (3H, m, 2—4-H), 8.95 (1H, dd, J=12.4, 3.7 Hz, $CHNO_2$), 10.27 (1H, d, J=3.7 Hz, N=CH), 12.37 (1H, br d, J=3.7 Hz, CHO). MS *m/z*: 246 (M^+). *Anal.* Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.49; H, 5.88; N, 11.20.

3-Nitro-7,8,9,10-tetrahydrobenzo[*h*]quinoline (9) A mixture of **8** (89 g, 0.362 mol) and PPA (1000 g) was heated at 160 °C with stirring for 1.5 h. After cooling to room temperature, the reaction mixture was poured into H_2O (1000 ml). The mixture was made alkaline with 30% NaOH, and the resulting precipitate was collected by filtration and recrystallized from Me_2CO to give 65.5 g (79%) of **9** as yellow needles, mp 140—143 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.96 (4H, m, 8, 9-H), 3.00 (2H, m, 7-H), 3.35 (2H, m, 10-H), 7.43 (1H, d, J=8.4 Hz, 6-H), 7.74 (1H, d, J=8.4 Hz, 5-H), 8.93 (1H, d, J=2.4 Hz, 4-H), 9.61 (1H, d, J=2.4 Hz, 2-H). MS *m/z*: 228 (M^+). *Anal.* Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.53; H, 5.51; N, 12.18.

3-Amino-7,8,9,10-tetrahydrobenzo[*h*]quinoline (10) A suspension of **9** (5 g, 0.02 mol) and Raney Ni (*ca.* 3 g) in BuOH (500 ml) was treated dropwise with $NH_2NH_2 \cdot H_2O$ (6 ml, 0.12 mol) at 110 °C during 1 h. The solution was stirred for 30 min at the same temperature. The reaction mixture was treated in the same manner as described for the synthesis of **4**, and the residue was recrystallized from CCl_4 to give 2.52 g (65%) of **10** as pale yellow prisms, mp 128—130 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.91 (4H, m, 8, 9-H), 2.88 (2H, m, 7-H), 3.27 (2H, m, 10-H), 3.83 (2H, br s, NH_2), 7.17 (1H, d, J=8.4 Hz, 6-H), 7.20 (1H, d, J=2.7 Hz, 4-H), 7.37 (1H, d, J=8.4 Hz, 5-H), 8.50 (1H, d, J=2.7 Hz, 2-H). MS *m/z*: 198 (M^+). *Anal.* Calcd for $C_{13}H_{14}N_2$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.48; H, 7.36; N, 13.92.

Skraup Reaction of 10 A mixture of Sulfo-mix (12 ml, 16.6 g), $FeSO_4 \cdot 7H_2O$ (0.35 g), and H_3BO_3 (0.5 g) was chilled to 0—5 °C, and anhydrous glycerol (3.4 g, 0.037 mol) was added to the mixture, followed by the addition of **10** (1.5 g, 0.007 mol) and warm water (5 ml, 50 °C). The reaction mixture was treated in the same manner as for the Skraup reaction of **4**. The residue was recrystallized from cyclohexane to give 0.52 g (29%) of **11** as colorless needles, mp 142—146 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.97 (4H, m, 8, 9-H), 3.02 (2H, m, 7-H), 3.45 (2H, m, 10-H), 7.47 (1H, d, J=8.4 Hz, 6-H), 7.73 (1H, dd, J=8.4, 4.4 Hz, 3-H), 8.28 (1H, d, J=8.4 Hz, 5-H), 8.88 (1H, dd, J=8.4, 1.7 Hz, 4-H), 9.03 (1H, dd, J=4.4, 1.7 Hz, 2-H), 9.56 (1H, s, 12-H). MS *m/z*: 234 (M^+). *Anal.* Calcd for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02; N, 11.96. Found: C, 82.15; H, 5.68; N, 11.93.

Dehydrogenation of 11 with DDQ A solution of DDQ (2.72 g, 0.012 mol) and **11** (0.9 g, 0.004 mol) in dry dioxane (40 ml) was heated at 120 °C for 15 h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo* and taken up in $CHCl_3$ (100 ml). The resulting precipitate was filtered off, and the filtrate was chromatographed on silica gel with $CHCl_3$ to give 0.24 g (27%) of **5** as colorless needles (from cyclohexane), mp 175—177 °C. The product was identical with **5** synthesized by means of the Skraup reaction of **4**, by the mixed melting point test and by comparison of the IR and NMR spectra.

***N*-(2-Formyl-2-nitroethylidene)-6-aminotetralin (13)** A solution of sodium nitromalonaldehyde monohydrate (15.7 g, 0.1 mol) in water (200 ml) was added to a solution of the HCl salt of **12** (18.4 g, 0.1 mol) in water (1000 ml) at 50 °C, and the mixture was stirred for 30 min. The resulting precipitate was collected by filtration, and recrystallized from EtOH to give 22.6 g (92%) of **13** as yellow needles, mp 170—173 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.82 (4H, m, 6, 7-H), 2.78 (4H, m, 5, 8-H), 6.99 (1H, s, 1-H), 7.00 (1H, d, J=8.4 Hz, 3-H), 7.15 (1H, d, J=8.4 Hz, 4-H), 8.92 (1H, dd, J=12.4, 3.7 Hz, $CHNO_2$), 10.23 (1H, d, J=3.7 Hz, N=CH), 12.17 (1H, br d, J=3.7 Hz, CHO). MS *m/z*: 246 (M^+). *Anal.* Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.57; H, 5.94; N, 11.15.

Cyclization of 13 with PPA A mixture of **13** (24.6 g, 0.1 mol) and PPA (250 g) was heated at 160 °C with stirring for 1.5 h. The reaction mixture was treated in the same manner as described for the synthesis of **9**. The precipitate was collected by filtration and purified by column chromatography on silica gel (CH_2Cl_2 : benzene = 10 : 1) to give 8.7 g (38%) of **14** as yellow needles, mp 191—194 °C (from EtOH), and 9.1 g (40%) of **15** as yellow needles, mp 143—145 °C (from EtOH).

14: ^{1}H-NMR ($CDCl_3$) δ: 1.92 (4H, m, 7, 8-H), 3.05 (4H, m, 6, 9-H), 7.68 (1H, s, 5-H), 7.91 (1H, s, 10-H), 8.89 (1H, d, J=2.4 Hz, 4-H), 9.52 (1H, d, J=2.4 Hz, 2-H). MS *m/z*: 228 (M^+). *Anal.* Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.16; H, 5.28; N, 12.05.

15: ^{1}H-NMR ($CDCl_3$) δ: 1.97 (4H, m, 8, 9-H), 2.98 (2H, m, 7-H), 3.18 (2H, m, 10-H), 7.63 (1H, d, J=8.7 Hz, 6-H), 7.97 (1H, d, J=8.7 Hz, 5-H), 9.16 (1H, d, J=2.4 Hz, 1-H), 9.58 (1H, d, J=2.4 Hz, 3-H). MS *m/z*: 228 (M^+). *Anal.* Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.64; H, 5.17; N, 12.23.

3-Nitrobenzo[*g*]quinoline (16) A solution of DDQ (4.5 g, 0.02 mol) and **14** (2.3 g, 0.01 mol) in dry dioxane (50 ml) was heated at 120 °C for 15 h. The reaction mixture was treated in the same manner as in the dehydrogenation of **11**. The filtrate was chromatographed on silica gel with $CHCl_3$ to give 0.5 g (23%) of **16** as yellow needles (from benzene), mp 208—210 °C (lit.[9] mp 206 °C). ^{1}H-NMR ($CDCl_3$) δ: 7.67 (2H, m, 7, 8-H), 8.13 (2H, m, 6, 9-H), 8.66 (1H, s, 5-H), 8.81 (1H, s, 10-H), 9.23 (1H, d, J=2.7 Hz, 4-H), 9.67 (1H, d, J=2.7 Hz, 2-H). MS *m/z*: 224 (M^+). *Anal.* Calcd for $C_{13}H_8N_2O_2$: C, 69.64; H, 3.60; N, 12.49. Found: C, 69.58; H, 3.37; N, 12.22.

3-Aminobenzo[*g*]quinoline (17) A suspension of **16** (2.24 g, 0.01 mol) and Raney Ni (*ca.* 1 g) in BuOH (200 ml) was treated dropwise with $NH_2NH_2 \cdot H_2O$ (3 ml, 0.06 mol) at 100 °C during 1 h. The reaction mixture was treated in the same manner as described for the synthesis of **4**. The residue was recrystallized from AcOEt to give 0.83 g (43%) of **17** as pale yellow green prisms, mp 238—240 °C (lit.[9] mp 240—241 °C). ^{1}H-NMR ($CDCl_3$) δ: 3.99 (2H, br s, NH_2), 7.32 (1H, d, J=2.7 Hz, 4-H), 7.43 (2H, m, 7, 8-H), 7.92 (1H, m, 6-H), 8.01 (1H, m, 9-H), 8.11 (1H, s, 5-H), 8.56 (1H, s, 10-H), 8.63 (1H, d, J=2.7 Hz, 2-H). MS *m/z*: 194 (M^+). *Anal.* Calcd for $C_{13}H_{10}N_2$: C, 80.39; H, 5.19; N, 14.42. Found: C, 80.56; H, 5.24; N, 14.19.

Skraup Reaction of 17 A mixture of Sulfo-mix (36 ml, 50 g), $FeSO_4 \cdot 7H_2O$ (1 g), and H_3BO_3 (1.5 g) was chilled to 0—5 °C, and anhydrous glycerol (10.2 g, 0.11 mol) was added to the mixture, followed by the addition of **10** (1.0 g, 0.0052 mol) and warm water (15 ml, 50 °C). The reaction mixture was treated in the same manner as in the Skraup reaction of **4**. The residue was purified on pre-coated thin-layer chromatography (TLC) plates (Kieselgel $60F_{254}$ 20 × 20 cm, layer thickness 0.5 mm, Merck) developed with $CHCl_3$ to give 0.05 g (4.2%) of naphtho[2,3-*f*][1,7]naphthyridine (**18**) as colorless needles (from AcOEt), mp 202—204 °C. ^{1}H-NMR ($CDCl_3$) δ: 7.63 (2H, m, 9, 10-H), 7.78 (1H, dd, J=8.4, 4.4 Hz, 2-H), 8.14 (2H, m, 8, 11-H), 8.73 (1H, s, 12-H), 8.99 (1H, s, 7-H), 9.02 (1H, dd, J=8.4, 1.3 Hz, 1-H), 9.05 (1H, dd, J=4.4, 1.3 Hz, 3-H), 9.46 (1H, s, 5-H). MS *m/z*: 230 (M^+). *Anal.* Calcd for

$C_{16}H_{10}N_2$: C, 83.46; H, 4.38; N, 12.17. Found: C, 83.29; H, 4.27; N, 11.89.

3-Amino-6,7,8,9-tetrahydrobenzo[*g*]quinoline (19) A suspension of **14** (2.28 g, 0.01 mol) and Raney Ni (*ca.* 1 g) in BuOH (130 ml) was treated dropwise with $NH_2NH_2 \cdot H_2O$ (12 ml, 0.24 mol) at 120 °C during 1 h. The solution was stirred for 30 min at the same temperature. The reaction mixture was treated in the same manner as described for the synthesis of **4**, and the residue was recrystallized from ligroin–AcOEt (10 : 1) to give 1.35 g (68%) of **19** as yellow needles, mp 131—133 °C. ^{1}H-NMR ($CDCl_3$) δ: 1.84 (4H, m, 7, 8-H), 2.92 (4H, m, 6, 9-H), 3.84 (2H, br s, NH_2), 7.11 (1H, d, J=2.7 Hz, 4-H), 7.26 (1H, s, 5-H), 7.65 (1H, s, 10-H), 8.40 (1H, d, J=2.7 Hz, 2-H). MS *m/z*: 198 (M^+). *Anal.* Calcd for $C_{13}H_{14}N_2$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.77; H, 7.03; N, 14.35.

Skraup Reaction of 19 A mixture of Sulfo-mix (36 ml, 50 g), $FeSO_4 \cdot 7H_2O$ (1 g) and H_3BO_3 (1.5 g) was chilled to 0—5 °C, and anhydrous glycerol (10.2 g, 0.11 mol) was added to the mixture, followed by the addition of **19** (4 g, 0.02 mol) and warm water (15 ml, 50 °C). The reaction mixture was treated in the same manner as in the Skraup reaction of **4**. The residue was chromatographed on silica gel ($CHCl_3 : CH_3CN$ = 10 : 1) to give 1.05 g (22%) of 8,9,10,11-tetrahydronaphtho[2,3-*f*][1,7]-naphthyridine (**20**) as colorless needles, mp 161—163 °C (from benzene). ^{1}H-NMR ($CDCl_3$) δ: 1.93 (4H, m, 9, 10-H), 3.05 (4H, m, 8, 11-H), 7.70 (1H, dd, J=8.4, 4.4 Hz, 2-H), 7.93 (1H, s, 7-H), 8.18 (1H, s, 12-H), 8.83 (1H, dd, J=8.4, 1.7 Hz, 1-H), 9.00 (1H, dd, J=4.4, 1.7 Hz, 3-H), 9.43 (1H, s, 5-H). MS *m/z*: 234 (M^+). *Anal.* Calcd for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02; N, 11.96. Found: C, 82.30; H, 6.15; N, 11.74.

Dehydrogenation of 20 with Pd–C A mixture of **20** (0.117 g, 0.5 mmol), 25% Pd–C (0.15 g), and *p*-cymene (10 ml) was heated under reflux (180 °C) for 15 h in an N_2 atmosphere. After removal of the catalyst by filtration, the filtrate was extracted with 10% HCl and basified with NH_4OH. The resulting precipitate was collected by filtration and purified by column chromatography on silica gel with $CHCl_3$ to give 23 mg (20%) of **18** as colorless needles (from AcOEt), mp 202—204 °C. The product was identical with **18** synthesized by means of the Skraup reaction of **17**, by the mixed melting point test and by comparison of the IR and NMR spectra.

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