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Cycloadditions in Syntheses. VIII.[1] Synthesis of 1,2-Dihydrocyclobuta[*c*]-pyridine and -quinoline and Their 3-Substituted Derivatives

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1,2-Dihydrocyclobuta[*c*]quinolin-3(4*H*)-one was synthesized from 4-methoxyquinolin-2(1*H*)-one according to our two-step procedure involving photoaddition of the latter to ethylene and subsequent elimination of methanol from the adduct. Chlorination of this compound with phosphoryl chloride afforded 3-chloro-1,2-dihydrocyclobuta[*c*]quinoline. This 3-chloro derivative then afforded either the parent base (1,2-dihydrocyclobuta[*c*]-quinoline) by reductive dechlorination, or a variety of 3-substituted derivatives by reaction with nucleophiles.

In a similar manner, the corresponding 1,2-dihydrocyclobuta[*c*]pyridine and its 3-substituted derivatives were synthesized from 1,2-dihydrocyclobuta[*c*]pyridin-3(4*H*)-one obtained from 4-methoxy- or -acetoxy-pyridin-2(1*H*)-one and ethylene.

Suitable reaction conditions for nucleophilic substitution reactions of the 3-chloro function were determined for each 1,2-dihydrocyclobuta[*c*]-quinoline or -pyridine derivative.

Keywords——aza analog of benzocyclobutene; aza-analog of naphthocyclobutene; 3-chloro-1,2-dihydrocyclobuta[*c*]pyridine; 3-chloro-1,2-dihydrocyclobuta[*c*]quinoline; nucleophilic substitution of 2-chloropyridines under phase-transfer conditions; general synthetic method for 1,2-dihydrocyclobuta[*c*]-pyridines and -quinolines

We have found recently that intermolecular 2+2 cycloadditions of heterocyclic enone compounds having an alkoxy function at the β-position, namely 4-methoxy-2-pyridone[2] and -quinolone[3] with olefins can be effected photochemically and the resultant adducts can be transformed to 1,2-dihydrocyclobuta[*c*]-pyridin- and -quinolin-3(4*H*)-ones by treatment with base.

In part V of this series,[4] we reported briefly the synthesis of 1,2-dihydrocyclobuta[*c*]-quinoline, a new aza-analog of naphthocyclobutene, from 1,2-dihydrocyclobuta[*c*]quinolin-3(4*H*)-one obtained from 4-methoxy-2-quinolone and ethylene by the above two-step procedure, *via* the 3-chloro derivative as a key intermediate.

In this paper, we describe the experimental details as well as the successful conversion of the 3-chloro derivative to a variety of 3-hetero-functionalized 1,2-dihydrocyclobuta[*c*]-quinolines. We also report the synthesis of 1,2-dihydrocyclobuta[*c*]pyridine and its 3-substituted derivatives from 1,2-dihydrocyclobuta[*c*]pyridin-3(4*H*)-one by the same route.

Different reactivity towards nucleophiles between the 3-chloro functions of these cyclobutane-fused quinolines and pyridines has led us to find suitable conditions for the nucleophilic substitution reactions of each compound.

Synthesis of 1,2-Dihydrocyclobuta[*c*]quinoline and Its 3-Substituted Derivatives

1,2-Dihydrocyclobuta[*c*]quinolin-3(4*H*)-one (III), obtained in 87.4% overall yield from 4-methoxy-2-quinolone (I) *via* our two-step procedure (Chart 1), was converted to the 3-chloro derivative (IV) in quantitative yield by refluxing the former compound in phosphoryl chloride. Though reductive dehalogenation of 2- and 4-halogenated pyridines and quinolines is generally achieved by catalytic hydrogenation over palladium on charcoal (1 atm, room temp.),[5] attempted hydrogenation of IV to 1,2-dihydrocyclobuta[*c*]quinoline (V) by this method failed

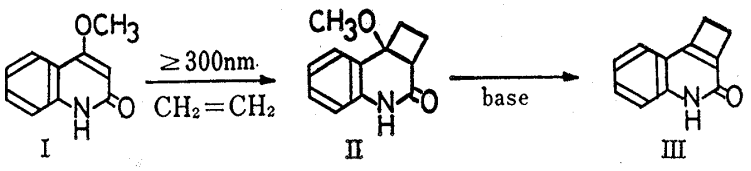

Chart 1

and gave 1,2,2a,3,4,8b-hexahydrocyclobuta[*c*]quinoline (VI) as the major product. Since the fused four-membered ring is known to enhance the susceptibility of the aromatic ring to catalytic hydrogenation,[6] an alternative method for this reductive dechlorination step was examined. As a result, the reduction of IV with zinc in aq. sulfuric acid under reflux was found to give the desired 1,2-dihydrocyclobuta[*c*]quinoline (V) in 25.0% yield. In this case, III was obtained in 52.5% yield. Since the same quinolone was obtained from IV in almost quantitative yield under identical conditions without zinc, it is clear that III is formed by the hydrolysis of IV even in the presence of zinc.

The chloro derivative (IV) was then treated with a variety of nucleophiles to give in all cases the desired 3-substituted derivatives. Thus, refluxing of IV in methanol containing sodium methoxide afforded the 3-methoxy compound (VII). Similarly, the 3-thiomethoxy derivative (VIII) was formed by refluxing of IV in a mixture of aqueous sodium thiomethoxide and dioxane. The 3-amino derivatives (IXa, b) were formed by heating IV with amines at around 100°C. All of the above reactions proceeded almost quantitatively without any by-product formation.

The structures of 1,2-dihydrocyclobuta[*c*]quinoline[7] (V) and its 3-substituted derivatives were established by the presence of the parent ions in high resolution mass spectra and were consistent with the nuclear magnetic resonance (NMR) and ultraviolet absorption (UV) spectra.

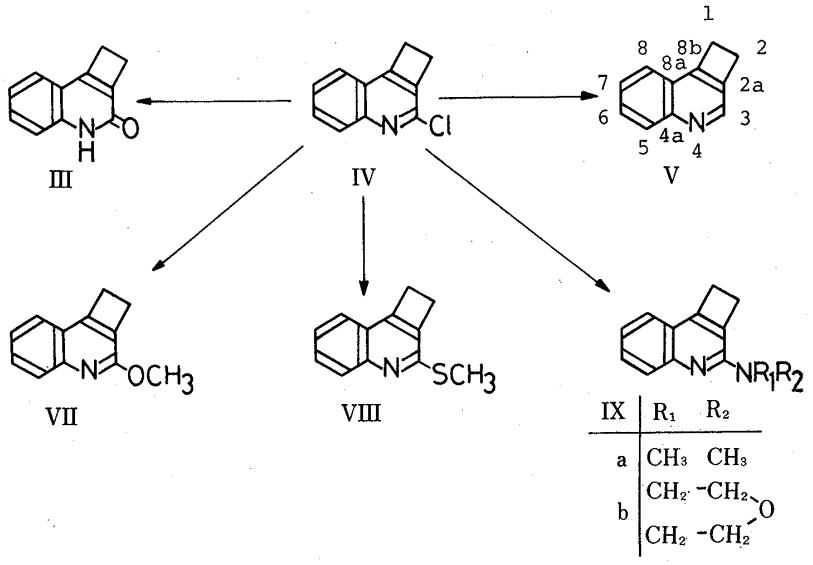

Chart 2

Synthesis of 1,2-Dihydrocyclobuta[*c*]pyridines and Their 3-Substituted Derivatives

1,2-Dihydrocyclobuta[*c*]pyridin-3(4*H*)-one (XII), obtained from 4-methoxy-2-pyridone (X) *via* our two-step procedure, was refluxed in phosphoryl chloride. However, the starting material was recovered unchanged. Refluxing in phosphoryl chloride in the presence of phosphorus pentachloride also failed to give any chlorinated product. Instead of examining higher reaction temperatures with these reagents,[8] we then investigated the use of dimethylformamide-phosphoryl chloride adduct as a suitable reagent for this chlorination.[9] Thus, treatment of XII in refluxing benzene containing phosphoryl chloride ($POCl_3$) and dimethylform-

amide (DMF) was found to give the desired 3-chloro-1,2-dihydrocyclobuta[*c*]pyridine (XIII) in 85.9% yield. The structure of XIII was deduced from the presence of the parent ion in the high resolution mass spectrum and from spectral data.

While the chloride (XIII) afforded the parent 1,2-dihydrocyclobuta[*c*]pyridine[10] (XIV) in 55.3% yield upon reduction with zinc in aqueous sulfuric acid, reactions of XIII with heteronucleophiles under the same conditions as employed in the quinoline series failed. For example, refluxing of XIII either in methanol containing sodium methoxide or in dioxane containing aqueous sodium thiomethoxide resulted in almost complete recovery of the starting material, though in the latter case, a trace of the 3-thiomethoxy derivative was detected in the reaction mixture by UV spectroscopy. The observed lower reactivity of the 3-chloro function in XIII than of that in IV towards nucleophiles parallels the trend in halogenated azines without a cyclobutane ring.[11]

In order to attain the desired nucleophilic substitution reactions of the chloride (XIII), we then examined the use of phase-transfer catalysis.[12,13] Thus, boiling of XIII in toluene containing an alcohol, potassium hydroxide, and 18-crown-6 was found to give the corresponding 3-alkoxy-1,2-dihydrocyclobuta[*c*]pyridines (XVa, b). Under the same conditions, thioethanol also reacted with XIII to give the corresponding 3-thioethoxy derivative (XVI). These experiments clearly indicate that phase-transfer mediated nucleophilic substitution is suitable for these thermally unstable halogenated cyclobutane-fused pyridine derivatives.

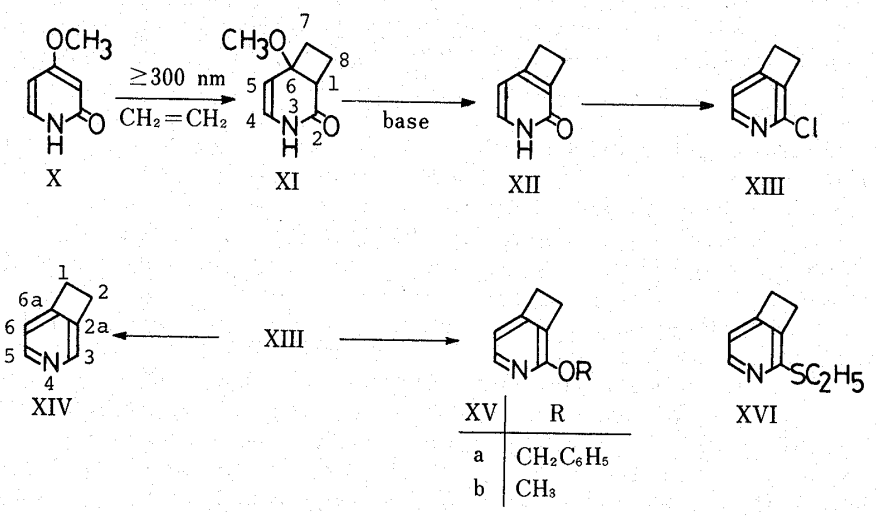

Chart 3

Chlorination as well as the subsequent reductive dechlorination reactions proceeded similarly from 5-methyl-1,2-dihydrocyclobuta[*c*]pyridin-3(4*H*)-one (XIX) as a starting material.

Conclusion

In this paper, syntheses of 1,2-dihydrocyclobuta[*c*]-quinoline, -pyridine, and their 3-substituted derivatives are reported. Since these syntheses used the 3-chloro derivatives (IV, XIII, *etc.*) as key starting materials and these compounds can be easily prepared in high overall yields from 4-oxygenated 2-oxoazines, the present work seems to provide a general synthetic method for the above compounds. As already reported, 1,2-dihydrocyclobuta[*c*]-quinolin-3(4*H*)-ones reacted with olefins in a 4+2 manner, like benzocyclobutenes,[8] and thus compounds prepared in this way may also serve as synthons for the synthesis of 5,6,7,8-tetrahydroisoquinolines and 7,8,9,10-tetrahydrophenanthridines. Studies along this line are in progress in our laboratory.

Experimental

All melting points are uncorrected. Infrared absorption spectra (IR) were recorded on a Shimadzu

IR-420 spectrometer, UV spectra with a Hitachi 320 spectrometer, and NMR spectra on a JEOL JNM-C60 spectrometer (with tetramethylsilane as an internal standard). High resolution mass spectra (high MS) were taken with a Hitachi M-80 spectrometer.

Photolyses were carried out in a Pyrex immersion apparatus equipped with a Toshiba 400P high-pressure mercury lamp (this corresponds to irradiation at $\geq$300 nm) and cooled internally with running water. All irradiations were carried out under argon or nitrogen with stirring.

Photochemical Cycloaddition of 4-Methoxyquinolin-2(1*H*)-one (I) to Ethylene——A solution of I (969.2 mg) in 400 ml of methanol–acetone (2: 3 v/v) was irradiated at $\geq$300 nm with bubbling of ethylene for 10 h. After removal of the solvent by evaporation, the residue was chromatographed on silica gel. Elution with 1% MeOH–CH_2Cl_2 afforded 837.2 mg (89.7% based on the consumed starting material, I) of the 2+2 adduct: 8b-methoxy-1,2,2a,8b-tetrahydrocyclobuta[*c*]quinolin-3(4*H*)-one (II). Further elution with the same solvent gave 164.4 mg of the unreacted starting material. II: mp 172.5—173°C (hexane–acetone), colorless prisms. λ_{max}^{MeOH} nm: 209, 251, 284, 294 sh. ν_{max}^{KBr} cm^{-1}: 3400, 1675. δ ($CDCl_3$): 1.5—2.8 (m, 4H, CH_2–CH_2), 2.94 (s, 3H, CH_3), 3.26 (t, 1H, J=9.5 Hz, C_{2a}–H), 6.7—7.45 (m, 4H, aromatic H), 9.61 (br s, 1H, NH, exchangeable). *Anal.* Calcd for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.45; N, 6.89. Found: C, 70.87; H, 6.51; N, 6.67.

1,2-Dihydrocyclobuta[*c*]quinolin-3(4*H*)-one (III)——A solution of the adduct (II: 398.9 mg) in 15 ml of MeOH containing 410 mg of KOH was refluxed for 1 h. After removal of the solvent and addition of water, the product was extracted with 5% MeOH–CH_2Cl_2. The organic layer was washed with water and dried over Na_2SO_4. Removal of the solvent by evaporation afforded 336.4 mg (97.4%) of III. III: mp 223.5—224.5°C (MeOH), colorless prisms. λ_{max}^{MeOH} nm: 226, 244, 270, 279, 320, 333. ν_{max}^{KBr} cm^{-1}: 3400, 1665. δ (pyridine-d_5): 2.98 (s, 4H, CH_2–CH_2), 7.0—7.65 (m, 4H, aromatic H), 12.43 (br s, 1H, NH, exchangeable). *Anal.* Calcd for $C_{11}H_9NO$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.12; H, 5.34; N, 8.23.

3-Chloro-1,2-dihydrocyclobuta[*c*]quinoline (IV)——A solution of III (537.6 mg) in 20 ml of $POCl_3$ was refluxed for 30 min. The reaction mixture was concentrated *in vacuo* to provide a residue, which was made basic with aq. Na_2CO_3 and extracted with CH_2Cl_2. The dichloromethane solution was washed with water and dried over Na_2SO_4. Removal of the solvent afforded IV in a yield of 579.7 mg (97.3%). IV: mp 115.5—116.5°C (hexane), colorless prisms. λ_{max}^{MeOH} nm (log ε): 210 (4.60), 229.5 (4.67), 234 (4.68), 277.5 (3.67), 306 (3.57), 319 (3.66). δ ($CDCl_3$): 3.35 (s, 4H, CH_2–CH_2), 7.35—8.1 (m, 4H, aromatic H). MS *m/z*: 191 (M^+ for ^{37}Cl), 189 (M^+ for ^{35}Cl), 154.

3-Methoxy-1,2-dihydrocyclobuta[*c*]quinoline (VII)——3-Chloro-1,2-dihydrocyclobuta[*c*]quinoline (IV: 35.9 mg) was added to sodium methoxide–methanol solution obtained by the addition of 70 mg of sodium to 7 ml of ab. MeOH, and the reaction mixture was refluxed overnight. After removal of the solvent by evaporation, the residue was diluted with water and extracted with CH_2Cl_2. The organic layer was washed with water, dried over Na_2SO_4 and concentrated to provide VII in almost quantitative yield (35.1 mg). VII: mp 49.5—50°C (hexane), colorless prisms. λ_{max}^{MeOH} nm (log ε): 226 (4.64), 259 (3.63), 269 (3.61), 304.5 (3.54), 318 (3.68). δ ($CDCl_3$): 3.23 (s, 4H, CH_2–CH_2), 4.01 (s, 3H, CH_3), 7.0—7.9 (m, 4H, aromatic H). High resolution MS *m/z*: M^+ Calcd for $C_{12}H_{11}NO$: 185.0840. Found: 185.0825.

3-Thiomethoxy-1,2-dihydrocyclobuta[*c*]quinoline (VIII)——The chloride (IV: 22.0 mg) was dissolved in a mixture of 2 ml of 15% aq. NaSMe and 1 ml of dioxane. The mixture was refluxed for 2.5 h. The residue obtained after removal of the solvent was diluted with water and extracted with CH_2Cl_2. The organic layer was washed with water, dried over Na_2SO_4 and concentrated to provide VIII in almost quantitative yield (23.4 mg). VIII: mp 68—68.5°C (hexane), colorless needles. λ_{max}^{MeOH} nm: 214, 254, 322, 334.5. δ ($CDCl_3$): 2.67 (s, 3H, CH_3), 3.28 (s, 4H, CH_2–CH_2), 7.1—8.0 (m, 4H, aromatic H). High resolution MS *m/z*: M^+ Calcd for $C_{12}H_{11}NS$: 201.0611). Found: 201.0581.

1,2-Dihydrocyclobuta[*c*]quinoline (V)——Zinc dust (12 mg) was added to a solution of IV (62.1 mg) in 3 ml of 2 N aq. H_2SO_4 and the mixture was refluxed for 4 h. The reaction mixture was basified by the addition of aq. 2 N NaOH, and the whole was extracted with 5% MeOH–CH_2Cl_2. The organic layer was washed with saturated $NaHCO_3$, and dried over Na_2SO_4. The residue obtained after removal of the solvent was recrystallized from methanol to give 10.9 mg of the 2-quinolone (III). The residue obtained from the mother liquor was chromatographed on alumina. Elution with hexane–CH_2Cl_2 (1: 1 v/v) gave 12.3 mg (19.8%) of the unreacted starting material (IV) followed by 10.2 mg (25.0% based on the consumed IV) of V. Elution with 5% MeOH–CH_2Cl_2 gave 13.0 mg of the 2-quinolone (III). The combined yield of III was 23.9 mg (52.3% based on the consumed IV). V: mp 46—47°C (MeOH–H_2O), colorless prisms; picrate, mp 208—211°C, dec. λ_{max}^{MeOH} nm (log ε): 222 (4.73), 277.5 (3.63), 306.5 (3.43), 319.5 (3.49). δ ($CDCl_3$): 3.83 (s, 4H, CH_2–CH_2), 7.2—7.85 (m, 3H, C_6, C_7, C_8–H), 7.85—8.15 (m, 1H, C_5–H), 8.53 (s, 1H, C_3–H). MS *m/z*: 155 (M^+).

1,2,2a,3,4,8b-Hexahydrocyclobuta[*c*]quinoline (VI)——A solution of 208.9 mg of the chloride (IV) in 25 ml of MeOH containing 200 mg of CH_3COONa was hydrogenated over 50 mg of 10% palladium on charcoal at room temp. under atmospheric pressure for 4 h. The catalyst was removed by filtration and the filtrate was evaporated to dryness *in vacuo*. After addition of satulated aq. $NaHCO_3$ solution, the product was extracted with CH_2Cl_2. The CH_2Cl_2 layer was dried over Na_2SO_4 and concentrated to yield an oil. Chromatography of this oil on alumina with hexane afforded VI as a colorless oil in 103.7 mg yield (59.2%). λ_{max}^{MeOH} nm: 209, 243, 295; $\lambda_{max}^{10\%\ HCl\text{-}MeOH}$ nm: 208.5, 252, 259. The spectra were similar to those of aniline. δ ($CDCl_3$): 1.4—3.1 (m, 6H), 3.1—3.7 (m, 2H, C_3–H), 6.35—7.1 (m, 4H, aromatic H). MS *m/z*: 159 (M^+).

Acetylation of VI (79.6 mg) with acetic anhydride (room temp., overnight) afforded the mono-acetate in a yield of 89.3 mg (88.7%) after chromatography on silica gel with hexane–CH_2Cl_2 (2: 1 v/v). The acetate of VI: colorless oil. λ_{max}^{MeOH} nm: 210, 241. δ ($CDCl_3$): 2.26 (s, 3H, CH_3), 1.5—2.65 (m, 4H), 2.7—3.8 (m, 3H), 4.1—4.55 (m, 1H), 6.95—7.25 (m, 4H, aromatic H). MS *m/z*: 201 (M^+), 173, 130.

3-Dimethylamino-1,2-dihydrocyclobuta[*c*]quinoline (IXa)——The chloride (IV: 32.8 mg) in 5.0 ml of 40% aq. dimethylamine was heated for 6 h in a sealed tube in a boiling water bath. The residue obtained after removal of the solvent was basified by the addition of saturated $NaHCO_3$ solution and extracted with 2% MeOH–CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. Column chromatography of the residue on silica gel with CH_2Cl_2 gave IXa in 32.0 mg. IXa: mp 120—121°C (hexane), colorless prisms. λ_{max}^{MeOH} nm: 207, 250, 268.5, 277.5, 338, 352. δ ($CDCl_3$): 3.16 (s, 6H, CH_3), 3.1—3.5 (m, 4H, CH_2CH_2), 7.0—7.75 (m, 4H, aromatic H). High resolution MS *m/z*: M^+ Calcd for $C_{13}H_{14}N_2$: 198.1155. Found: 198.1152.

3-Morpholino-1,2-dihydrocyclobuta[*c*]quinoline (IXb)——A solution of the chloride (IV: 32.8 mg) in 2.0 ml of morpholine was heated on a boiling water bath for 6 h. The same isolation procedure as in the case of IXa afforded IXb in 38.1 mg yield (91.7%) IXb: mp 141—142.5°C (hexane), colorless prisms. λ_{max}^{MeOH} nm: 211, 250, 338. δ ($CDCl_3$): 3.34 (s, 4H, C_1, C_2–H), 3.74 (broad s, 8H, N–CH_2–CH_2–O), 7.0—7.75 (m, 4H, aromatic H). High resolution MS *m/z*: M^+ Calcd for $C_{15}H_{16}N_2O$: 240.1261. Found: 240.1234.

Photochemical Addition of 4-Methoxypyridin-2(1*H*)-one (X) to Ethylene——A solution of X (276.8 mg) in 300 ml of acetone was irradiated at $\geq$300 nm under bubbling of ethylene for 8 h. At this point, no starting material (X) was detected in the reaction mixture by TLC. The residue obtained after removal of the solvent was chromatographed over silica gel. Elution with CH_2Cl_2 gave 161.6 mg (47.7%) of 6-methoxy-3-azabicyclo[4.2.0]-oct-4-en-2-one (XI) followed by 99.6 mg (29.4%) of 5-methoxy-2-azabicyclo[4.2.0]oct-4-en-3-one. XI: mp 129—130°C (CH_3COOEt) colorless prisms. λ_{max}^{MeOH} nm (log ε): 252 (3.71). ν_{max}^{KBr} cm^{-1}: 3200, 1685, 1640. δ ($CDCl_3$): 1.6—2.5 (m, 4H, CH_2–CH_2), 3.10 (t, 1H, J=9.0 Hz, C_1–H), 3.13 (s, 3H, CH_3), 4.89 (d, 1H, J=8.1 Hz, C_5–H), 6.33 (dd, J=8.1 and 5.2 Hz, C_4–H), 7.50 (br s, 1H, NH, exchangeable). MS *m/z*: 153 (M^+). 5-Methoxy-2-azabicyclo[4.2.0]oct-4-en-3-one: mp 131—132°C (CH_3COOEt), colorless prisms. λ_{max}^{MeOH} nm (log ε): 217 (4.15), 251 (3.61). ν_{max}^{KBr} cm^{-1}: 3200, 1660, 1605. δ ($CDCl_3$): 1.6—2.5 (m, 4H, CH_2–CH_2), 3.25 (m, 1H, C_6–H), 3.66 (s, 3H, CH_3), 4.00 (m, 1H, C_1–H), 5.04 (s, 1H, C_4–H). MS *m/z*: 153 (M^+).

1,2-Dihydrocyclobuta[*c*]pyridin-3(4*H*)-one (XII)——The adduct (XI: 816.0 mg) was added to sodium methoxide–methanol solution (prepared by the addition of 890 mg of sodium in 70 ml of ab. methanol). The mixture was refluxed for 7 h. After removal of the solvent and acidification of the residue by the addition of aq. acetic acid, the product was extracted with 8% MeOH–CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated to give a residue, which was recrystallized from ethyl acetate–MeOH to give XII. By column chromatography (silica gel, 3% MeOH–CH_2Cl_2) of the mother fraction, a further amount of XII was obtained. The combined yield of XII was 613.6 mg (95.1%). XII: mp 209—210°C (CH_3COOEt). λ_{max}^{MeOH} nm: 231, 289. ν_{max}^{KBr} cm^{-1}: 3450, 1650, 1595. δ ($CDCl_3$): 3.09 (m, 4H, CH_2–CH_2), 6.21 (d, 1H, J=6.3 Hz, C_6–H), 7.34 (d, 1H, J=6.3 Hz, C_5–H), 12.4 (broad s, 1H, NH, exchangeable).

3-Chloro-1,2-dihydrocyclobuta[*c*]pyridine (XIII)——A solution of 228.6 mg of the pyridone (XII) in 6 ml of benzene was treated with 1.4 ml of $POCl_3$ and 0.5 ml of DMF. The mixture was refluxed for 5 h. Excess reagents were evaporated off, ice-water was added, and the solution was basified by adding aq. 20% KOH. The product was taken up in ether and the ether layer was dried over Na_2SO_4. The residue obtained after removal of the solvent was chromatographed on silica gel with ether to give 194.8 mg (73.9%) of XIII. XIII: mp 48—49°C (hexane), colorless prisms. λ_{max}^{MeOH} nm (log ε): 208.5 (3.84), 254 sh (3.37), 260 (3.47), 267 sh (3.37). ν_{max}^{KBr} cm^{-1}: 1580, 1570, 1410. δ ($CDCl_3$): 3.27 (m, 4H, CH_2–CH_2), 6.89 (d, 1H, J=4.8 Hz, C_6–H), 8.28 (d, 1H, J=4.8 Hz, C_5–H). High resolution MS *m/z*: M^+ Calcd for C_7H_6ClN: 141.0158 (for ^{37}Cl) and 139.0188 (for ^{35}Cl). Found: 141.0153 (for ^{37}Cl) and 139.0170 (for ^{35}C).

1,2-Dihydrocyclobuta[*c*]pyridine (XIV)——Zinc dust (24 mg) was added to a solution of 50.9 mg of XIII in 3 ml of 2 N aq. H_2SO_4. The mixture was refluxed for 3 h. After being basified with saturated aq. $NaHCO_3$, the product was extracted with ether and the ether layer was dried over Na_2SO_4. Removal of the solvent gave 21.1 mg (55.1%) of XIV, which showed a single spot on TLC. XIV: colorless oil; picrate, mp 157—158°C (MeOH). λ_{max}^{MeOH} nm: 226 sh, 251 sh, 257, 262 sh. δ ($CDCl_3$): 3.24 (m, 4H, CH_2–CH_2), 6.96 (dd, 1H, J=5.0 and 1.5 Hz, C_6–H), 8.18 (d, 1H, J=1.5 Hz, C_3–H), 8.39 (d, 1H, J=5.0 Hz, C_5–H). The melting point of the picrate and spectral data are in good accordance with those reported.[10]

A General Procedure for Solid–Liquid Phase-transfer Catalyzed Alkoxide or Thioalkoxide Displacement Reactions of 3-Chloro-1,2-dihydrocyclobuta[*c*]pyridine (XIII)——3-Benzyloxy-1,2-dihydrocyclobuta[*c*]pyridine (XVa): A mixture of XIII (63.6 mg, 0.456 mM), benzyl alcohol (0.1 ml, 0.963 mM), powdered KOH (80 mg, 1.428 mM), and toluene (15 ml) was refluxed under stirring for 4.5 h. The residue obtained after removal of the solvent *in vacuo* was diluted with water and the mixture was extracted with CH_2Cl_2. The organic layer was separated and dried over Na_2SO_4. The residue obtained after removal of the solvent was chromatographed on silica gel. Elution with hexane–CH_2Cl_2 (1: 1 v/v) gave 85.5 mg (88.9%) of XVa. XVa: a colorless oil; picrate, mp 153—155°C (MeOH). λ_{max}^{MeOH} nm: 215, 266; the spectrum is quite similar to that[14] of 2-methoxypyridine. δ ($CDCl_3$): 3.16 (broad s, 4H, CH_2–CH_2), 5.32 (s, 2H, –CH_2–O), 6.60 (d, 1H, J=4.8 Hz, C_6–H), 7.13—7.40 (m, 5H, –C_6H_5), 7.97 (d, 1H, J=4.8 Hz, C_5–H). High resolution MS *m/z*: M^+ Calcd for $C_{14}H_{13}NO$: 211.0997. Found: 211.1010.

Under the same conditions except for the use of 5—10 mol equivalents of methanol or thioethanol with respect to XIII, the corresponding 3-methoxy and 3-thioethoxy derivatives (XVb and XVI) were obtained in yields of 39.0[15] and 79.2%, respectively. XVb: a colorless oil; picrate, mp 146—148°C (MeOH). λ_{max}^{MeOH} nm: 216, 265. δ ($CDCl_3$): 3.13 (br s, 4H, CH_2–CH_2), 3.87 (s, 3H, CH_3), 6.57 (d, 1H, J=5.2 Hz, C_6–H), 7.91 (d, 1H, J=5.2 Hz, C_5–H). MS m/z: 135 (M^+). XVI: a colorless oil; picrate, mp 128—130°C (MeOH). λ_{max}^{MeOH} nm: 205, 250, 286; the spectrum is quite similar to that[16] of 2-thiomethoxypyridine. δ ($CDCl_3$): 1.35 (t, 3H, J=7.2 Hz, CH_3), 3.13 (q, 2H, J=7.2 Hz, CH_2–S), 3.15 (br s, 4H, CH_2–CH_2), 6.64 (d, 1H, J=4.8Hz, C_6–H), 8.18 (d, 1H, J=4.8 Hz, C_5–H). MS m/z: 165 (M^+).

Hydrolysis of 3-Benzyloxy-1,2-dihydrocyclobuta[*c*]pyridine (XVa) to 1,2-Dihydrocyclobuta[*c*]pyridin-3(4*H*)-one (XII)——A solution of XVa (26.2 mg) in a mixture of 10 ml of methanol and 5 ml conc. HCl was refluxed for 6 h. The reaction mixture was evaporated to dryness *in vacuo*, and the residue was basified by the addition of saturated aq. $NaHCO_3$. The product was extracted with 5% MeOH–CH_2Cl_2 and the organic layer was separated and dried over Na_2SO_4. Removal of the solvent gave 13.0 mg (86.5%) of XII, mp 209—210°C (CH_3COOEt). Mixed melting point determination with the sample (XII) obtained from XI confirmed its structure.

5-Methyl-1,2-dihydrocyclobuta[*c*]pyridin-3(4*H*)-one (XIX)——A solution of 311.0 mg of 4-acetoxy-6-methylpyridin-2(1*H*)-one [XVII, mp 205—206°C (benzene), prepared from 6-methyl-2,4-dihydroxypyridine[17] by acetylation with acetic anhydride] in 290 ml of acetone was irradiated at $\geq$300 nm for 8 h under bubbling of ethylene. The residue obtained after removal of the solvent was chromatographed over silica gel. Elution with 1% MeOH–CH_2Cl_2 afforded 300.0 mg (79.0%) of the 2+2 adduct (XVIII). Elution with 2% MeOH–CH_2Cl_2 afforded 25.3 mg (11.8%) of 5-methyl-1,2-dihydrocyclobuta[*c*]pyridin-3(4*H*)-one (XIX). XVIII: mp 133—134°C (ether), colorless prisms. λ_{max}^{MeOH} nm: 251. ν_{max}^{KBr} cm^{-1}: 3200, 1745, 1670. δ ($CDCl_3$): 1.87 (d, 3H, J=1.6 Hz, C_5–CH_3), 1.95 (s, 3H, $COCH_3$), 1.65—2.55 (m, 4H, CH_2–CH_2), 3.20 (br t, 1H, J=9.0 Hz, C_{2a}–H), 4.74 (m, 1H, C_6–H), 7.88 (br s, 1H, NH, exchangeable).

The 2+2 adduct (XVIII: 61.3 mg) obtained as described above was dissolved in 6 ml of methanol. After addition of 0.3 ml of 10% aq. NaOH, the mixture was kept standing at room temperature for 30 min. After removal of the solvent and addition of a small amount of water, the product was extracted with CH_2Cl_2 and the CH_2Cl_2 layer was dried over Na_2SO_4. Removal of the solvent afforded 41.2 mg (97.1%) of XIX. Since this compound was also obtained concomitantly with XVIII in the above photo-addition reaction, the combined yield of XIX from XVII becomes 88.9%. XIX, mp 202—203°C (CH_3COOEt), colorless prisms. λ_{max}^{MeOH} nm: 232, 295. ν_{max}^{KBr} cm^{-1}: 3450, 1645, 1615. δ ($CDCl_3$): 2.32 (s, 3H, CH_3), 2.98 (broad s, 4H, CH_2–CH_2), 5.86 (s, 1H, C_6–H), 12.38 (br s, 1H, NH, exchangeable).

3-Chloro-5-methyl-1,2-dihydrocyclobuta[*c*]pyridine (XX)——A solution of 194.6 mg of the 3-pyridone (XIX) in 5.2 ml of benzene was treated with 1.2 ml of $POCl_3$ and 0.4 ml of DMF. The mixture was refluxed for 5 h. Excess reagents were evaporated off, and the residue was basified by the addition of aq. 20% KOH. The product was taken up in ether and the ether layer was dried over Na_2SO_4. The residue obtained after removal of the ether was chromatographed on silica gel with CH_2Cl_2 to give 188.6 mg (85.2%) of XX. The chloride did not give the picrate on treatment with picric acid in ether. XX: a colorless oil. λ_{max}^{MeOH} nm: 212, 265, 271 sh. δ ($CDCl_3$): 2.47 (s, 3H, CH_3), 3.16 (br s, 4H, CH_2–CH_2), 6.74 (s, 1H, C_6–H). MS m/z: 155 (M^+: ^{37}Cl), 153 (M^+: ^{35}Cl).

5-Methyl-1,2-dihydrocyclobuta[*c*]pyridine (XXI)——Zinc dust (16 mg) was added to a solution of 35.7 mg of the chloride (XX) in 2 ml of 2 N aq. H_2SO_4. The mixture was then refluxed for 2.5 h. After being basified with 20% aq. K_2CO_3, the product was extracted with ether and the ether layer was dried over $MgSO_4$. Removal of the solvent gave 21.2 mg of a colorless oil, whose NMR showed that it was composed of XX and XXI in *ca.* 2: 3 ratio. Separation of the mixture by preparative TLC (silica gel plate, CH_2Cl_2) gave 10.4 mg (37.6%) of XXI and 8.9 mg (24.9%) of XX. XXI: a colorless oil; picrate, mp 157—159°C (MeOH). λ_{max}^{MeOH} nm: 208 sh, 263. δ ($CDCl_3$): 2.48 (s, 3H, CH_3), 3.17 (br s, 4H, CH_2–CH_2), 6.81 (s, 1H, C_6–H), 8.01 (s, 1H, C_3–H). MS m/z: 119 (M^+).

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