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Cyclic Guanidines. XII.[1] Synthesis and Characterization of Tricyclic Guanidinium Salts and Related Compounds

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The synthesis and characterization of tricyclic guanidinium salts and their reduced polycyclic trisaminomethane derivatives are described. N-ω-Chloroalkyl bicyclic guanidines (3) readily gave tricyclic guanidinium salt (4) in a neutral medium. Treatment of the compounds **4** with anion exchange resin caused facile ring cleavage to yield various macrocyclic compounds **6**—**9**. The compounds **6**—**9** reverted to the parent tricyclic guanidinium salts in acidic and basic media as a result of transannular interactions. The guanidinium salts **4** were reduced with sodium borohydride to polycyclic trisaminomethane derivatives (**11**). The structures of **6**—**9** and **11** are proposed on the basis of the spectral data.

Keywords——tricyclic guanidinium salt; ring opening; macrocyclic urea; polycyclic trisaminomethane; transannular interaction

A previous paper of this series reported that N-alkyl derivatives of 5-phenyl-1,2,3,5-tetrahydroimidazo-[1,2-*a*]- and -[2,1-*b*]-quinazolines have potent hypoglycemic activity.[3] It thus seemed of interest to prepare the corresponding tricyclic guanidinium salts and to evaluate their biological activity. We found that N-ω-chloroalkyl bicyclic guanidines ring-closed in a neutral medium to give tricyclic guanidinium salts which could be reduced stereospecifically to give polycyclic trisaminomethane derivatives. This report deals with these findings.

2-Chloro-3-(ω-chloroalkyl)-4-phenyl-3,4-dihydroquinazolines[3] (**1**) were allowed to react with aminoalcohols, such as 2-aminoethanol and 3-aminopropanol, to give 1-(ω-hydroxyalkyl)-5-phenyl-1,2,3,5-tetrahydroimidazo[2,1-*b*]quinazolines (**2a**, **b**) and 1-(ω-hydroxyalkyl)-6-phenyl-1,2,3,4-tetrahydro-6H-pyrimido[2,1-*b*]quinazolines (**2c**, **d**). Treatment of **2a**, **b** with thionyl chloride at room temperature gave the 1-ω-chloroalkyl derivatives (**3a**, **b**) as the crystalline hydrochlorides, which were neutralized to give the free bases as crystals. The free bases were heated in ethanol to afford the desired tricyclic guanidinium chlorides (**4a**, **b**). On the other hand, **3c**, **d** could not be isolated as crystals on treatment as described in the cases of **2a**, **b**. The oily, crude hydrochlorides of **3c**, **d** were neutralized to form water-soluble tricyclic guanidinium salts which could not be isolated. Treatment of the hydrochlorides with anion exchange resin in order to remove hydrochloric acid gave the ring-opened compounds **8** and **9**, respectively. When **4a**, **b** were treated with the resin or sodium hydroxide solution, they gave similar ring-opened derivatives (**6** and **7**).

The structures of **6**—**9** were estimated on the basis of the spectral data shown in Table I. The ultraviolet (UV) spectra of **6**—**9** were measured in chloroform because the spectra in protic solvents did not correspond to the expected structures, as described below. In the cases of **6** and **7**, they showed absorption maxima near 260 and 300 nm, whereas **8** showed only endo absorption. These observations suggests there is a differences of molecular structure between **6** or **7** and **8**. The absorption maxima of **9** were near 270 and 295 nm, being analogous to those of 1- or 3-substituted 2-quinazoline.[3] The infrared (IR) spectra of **6** exhibited strong ab-

1) Part XI: F. Ishikawa, A. Kosasayama, and K. Higashi, *Chem. Pharm. Bull.*, **28**, 2024 (1980).
2) Location: *1-16-13 Kitakasai, Edogawa-ku, Tokyo 132, Japan.*
3) A. Kosasayama, K. Higashi, and F. Ishikawa, *Chem. Pharm. Bull.*, **27**, 880 (1979).

sorptions at 3350 and 1670 cm^{-1}. The former absorption band was assinged to N–H stretching in secondary amine and the latter was attributed to a carbonyl group. In addition, no N–H stretching band was observed in the tricyclic guanidinium salt (**4a**). Similar absorption bands were also observed among **7—9**. The nuclear magnetic resonance (NMR) spectra of **6—9**

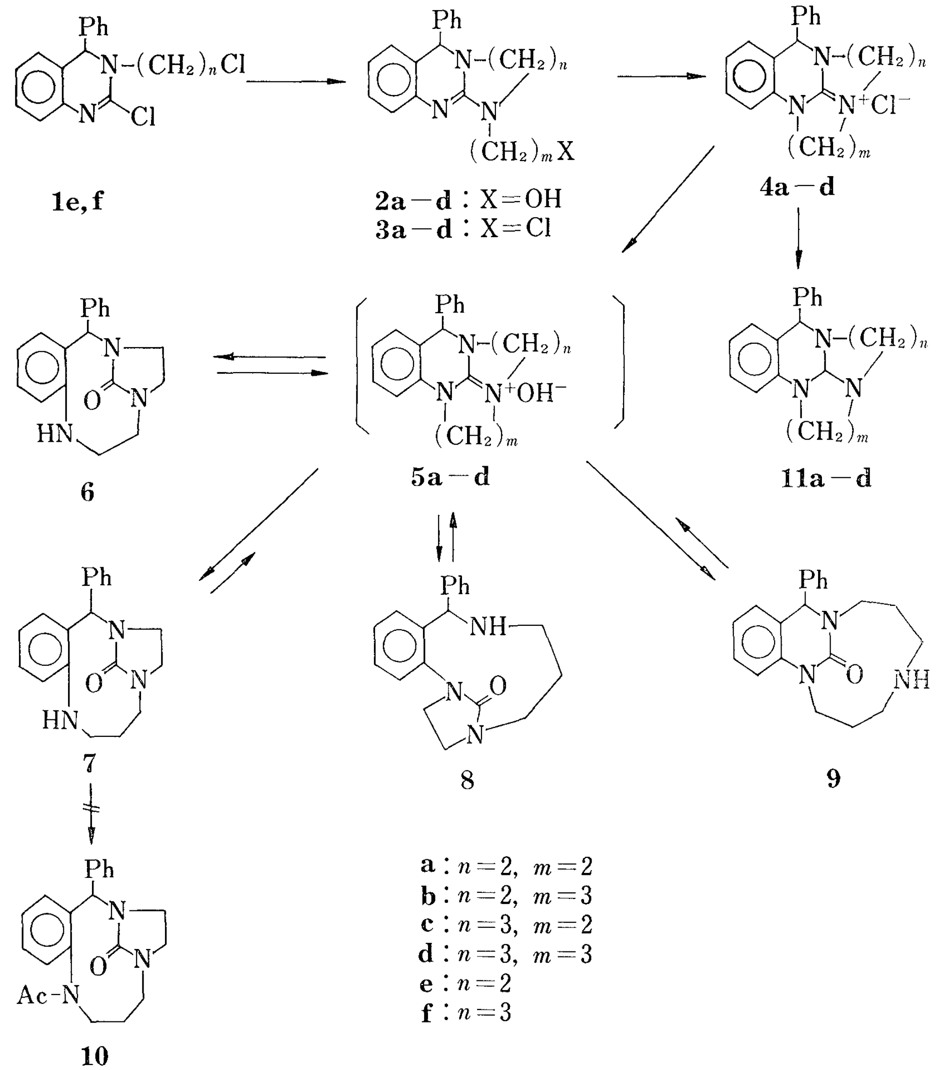


Chart 1

TABLE I. Spectral Data for Ring-opened Compound (**6—9**)

Compd.	UV λ_{max} nm (log ε)				IR ν_{max}^{KBr} cm^{-1}	NMR ($CDCl_3$) δ	
	pH 1	pH 13	EtOH	$CHCl_3$		Methine	Methylene
6	258(3.92)	258(3.92)	258(3.91)	261(3.89) 296(3.37)	3350 1670 1595 1225	6.53 (s)	2.3—3.8 (m, 8H)
7	259(3.89)	259(3.89)	261(3.92) 265(3.91) 308(3.40)	264(3.89)[a] 268(3.90) 311(3.49)	3430 1670 1595 1235	6.56 (s)	1.0—4.4 (m, 10H)
8	256(3.99)	259(3.99)	256(3.99)	[b]	3300 1685 1260	5.00 (s)	0.9—4.4 (m, 10H)
9	259(3.86)	259(3.95)	267(3.95)	271(3.91) 295(3.37)[a]	3310 1640 1595 1270 1250	5.67 (s)	0.9—5.3 (m, 12H)

a) Shoulder.
b) Endo absorption, ε_{250} 3.86.

showed characteristic chemical shifts of the methine protons on the carbon atom adjacent to the phenyl group. These signals of **6** and **7** were observed at δ 6.53 and 6.56, respectively, in the same region as that (δ 6.43) of 1-benzhydryl-2-imidazolidinone (**12**) prepared by alkaline hydrolysis of 1-benzhydryl-2-methylthio-2-imidazolne.[4] That of **8** appeared at higher field (δ 5.00), comparable to the values of δ 4.8—5.1 in 2-(N-substituted amino)benzhydrylamine derivatives.[3] The corresponding signal of **9** appeared at δ 5.67, close to the δ 5.4—5.5 signal of 1- or 3-substituted-4-phenyl-2-quinazoline derivatives.[3]

It has been reported that treatment of 1,10-dimethyl-1,2,3,5-tetrahydroimidazo[2,1-*b*]-quinazolinium iodide with sodium hydroxide gave a ring-opened compound, 1-methyl-3-(2-methylaminobenzyl)-2-imidazolidinone.[5] A similar reaction may occur on treatment of **4** with basic resin. The site of fission may depend upon the ring size or basicity of the ring.

The ring closures of **6**—**9** to the tricyclic guanidinium salts (**4**) were observed in solution by UV and NMR spectroscopy. Compounds **6** and **8** showed almost the same absorption curves in acidic, basic and ethanolic solutions, and these were identical with the UV spectra of **4a** and **4c**, respectively. Hence, they reverted to the parent tricyclic guanidinium salts in protic solvents. The absorption curves of **7** was also the same in both acidic and basic media. However, the curve in ethanol differed from those in the aqueous solvents because of the presence of an equilibrium between the ring-opened and -closed forms (**7** and **5b**). Similar results were obtained for **9**. In addition, the UV absorption curves of **6**—**9** in chloroform changed to those of the tricyclic guanidinium salts (**4a**—**d**), respectively, on addition of methanolic hydrogen chloride. It was observed that the NMR spectra of **6**—**9** in deuterochloroform changed to those of the ring-closed compounds on addition of deuterium chloride solution. This phenomenon is a kind of transannular ring closure which has not previously been reported.

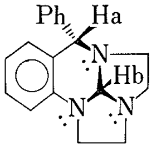
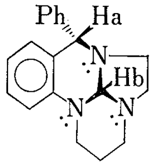
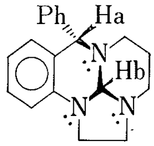
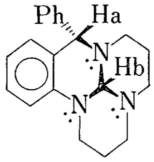
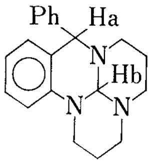
In order to confirm the structure of **7**, acetylation of **7** was attempted but this was unsuccessful. The reaction may not proceed because of the formation of the tricyclic guanidinium salt.

The reaction of 1-(3-chloropropyl)isatonic anhydride with 2-methylthio-2-imidazoline hydroiodide, followed by neutralization, was reported to give a ring-closed compound which was reduced with sodium borohydride to give 2,3,4,4a-tetrahydro-1H-4,5-ethanopyrimido[1,2-*a*]quinazolin-6(5H)-one.[6] Compounds **4a**—**d** were allowed to react with sodium borohydride to give the interesting polycyclic trisaminomethane derivatives (**11**). The reactions of **4a**—**c** each gave single product (**11a**—**c**). On the other hand, the reaction of **4d** with sodium borohydride gave a mixture of **11d** and its isomer **11'd**. The main product at low temperature was **11d** and that above room temperature was **11'd**. The compound **11d** rearranged in part to **11'd** in a solution of chloroform, ethanol, *etc.*, at room temperature to give an equilibrium state with **11'd** predominating. The melting point of **11d** was unclear because rearrangement may occur on heating.

The spectral data for **11** are shown in Table II. The UV spectra of **11** were analogous to that of 2-(N-substituted amino)benzhydrylamine.[3] The IR spectra of **11** showed moderate absorption bands in the 2800—2700 cm^{-1} which might be Bohlmann bands.[7] In the NMR spectra of **11a**, the signals of two methine protons, H_a and H_b, shown in Table II, were observed at δ 5.31 and 5.12, respectively. However, the H_b signals in **11b**—**d** were shifted 1.3—1.7 ppm to higher field as compared to **11a**. Similar results were reported by Atkins.[8] Accord-

4) A. Kosasayama, T. Konno, and F. Ishikawa, *Chem. Pharm. Bull.*, **27**, 841 (1979).
5) T. Jen, B. Dienel, H. Bowman, P. Petta, A. Helt, and B. Loev, *J. Med. Chem.*, **15**, 727 (1972).
6) G.M. Coppola, G.E. Hardymann, and O.R. Rfister, *J. Org. Chem.*, **41**, 825 (1976).
7) F. Bohlmann, *Chem. Ber.*, **91**, 2157 (1958).
8) *a*) T.J. Atkins, ACS/CSJ Chemical Congress, Honolulu, Hawaii, April, 1979, ORGN 106; *b*) *Idem*, U.S. Patent 4085106 (1978) [*C.A.*, **89**, 129553 (1978)].

Table II. Spectral Data for Trisaminomethane Derivatives (**11**)

Compd.	Structure	UV λ_{max} nm (log ε) pH 1	pH 13	EtOH	IR ν_{max}^{KBr} cm^{-1}	NMR ($CDCl_3$) δ H_a	H_b	Methylene
11a		246(3.84) 291(3.18)	251(3.95) 295(3.30)	254(3.97) 300(3.32)	3020 2960 2910 2840 2810 1595 1485 1450 1320	5.31 (s)	5.12 (s)	2.1—3.8 (m, 8H)
11b		242(3.94) 287(3.20)	243(3.92) 288(3.23)	250(3.99) 293(3.28)	3050 3025 2950 2840 2780 1600 1480 1455 1385 1325	4.72 (s)	3.40 (s)	1.7—3.7 (m, 10H)
11c		247(3.99) 293(3.32)	252(3.97) 299(3.32)	255(4.04) 303(3.45)	3025 2940 2880 2850 2810 2780 1600 1490 1360 1335	4.30 (s)	3.78 (s)	1.4—3.7 (m, 10H)
11d		243(3.98) 289(3.30)	248(3.97) 294(3.32)	253(4.03) 298(3.40)	3060 3020 2940 2920 2810 2800 2750 2720 1600 1490 1350 1290	4.42 (s)	3.61 (s)	0.8—3.2 (m, 12H)
11'd		243(3.98) 289(3.30)	248(3.97) 294(3.32)	253(4.03) 298(3.40)	3020 2975 2940 2910 2830 2810 2750 1600 1490 1355 1140	5.21 (s)	4.30 (s)	1.1—3.25 (m, 12H)

ing to his results, the signals of the methine protons in unsubstituted polycyclic trisaminomethane derivatives, 1,4,7-triazatricyclo[5.2.1.$0^{4,10}$]decane, 1,4,7-triazatricyclo[5.3.2.$0^{4,11}$]undecane, 1,4,8-triazatricyclo[6.3.1.$0^{4,12}$]dodecane and 1,5,9-triazatricyclo[7.3.1.$0^{5,13}$]tridecane, appeared at δ 5.03, 4.04, 2.49 and 2.31, respectively.[8b] These successive upfield shifts are due to the lone pair interactions on neighboring nitrogen atoms in the six-membered ring.[8a]

In the sodium borohydride reduction of **4**, hydrogen addition may occur only from the side which does not suffer steric hindrance due to the phenyl group to give an all-*trans* conformation product. Consequently, H_a and H_b exist the same side and the H_b signal is shifted to higher field under the influence of the nitrogen lone pair interactions. The upfield shift of the signal in **11c** and **11d** as compared to **11a** may also due to the interaction of the neighboring basic nitrogens. On the other hand, the H_a and H_b signals in **11'd** were shifted 0.7—0.8 ppm to lower field as compared to that of **11d**. The downfield shifts the H_a and H_b protons may be attributed to conformational conversion somewhere around the three nitrogen atoms. Consequently, the H_b proton of **11'd** must be on the same side as the lone pair on the affected nitrogen and the signal may be shifted to lower field under the influence of the lone pair anisotropy effect.[9] Since **11d** consists of three six-membered rings, it has the greatest flexibility and such conversion may occur easily.

Compounds **4a, b** did not show any hypoglycemic activity in normal fasted rats.

9) M. Uskoković, H. Bruderer, C. von Planta, T. Williams, and A. Brossi, *J. Am. Chem. Soc.*, **86**, 3364 (1964).

Experimental

All melting points are uncorrected. IR spectra were recorded with a Hitachi 285 spectrometer. UV spectra were taken with a Hitachi 323 spectrometer. Mass spectra (MS) were determined on a JEOL OISG-2 spectrometer. NMR spectra were taken with a Hitachi Perkin-Elmer R-20B (60 MHz) spectrometer or a Varian EM-360 (60 MHz) spectrometer with tetramethylsilane as an internal standard (δ value). The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

1-(2-Hydroxyethyl)-5-phenyl-1,2,3,5-tetrahydroimidazo[2,1-*b*]quinazoline (2a)——A solution of 2.68 g (10 mmol) of **1e** and 6.10 g (100 mmol) of 2-aminoethanol in 50 ml of EtOH was refluxed for 5 hr. After cooling, the mixture was made basic with concd. NaOH solution and concentrated *in vacuo*. The residue was mixed with H_2O and extracted with $CHCl_3$. The extract was washed with H_2O, dried, and concentrated *in vacuo* to give 2.20 g (75%) of **2a**; mp 137—138° (Me_2CO); UV $\lambda_{max}^{H_2O\,(pH\,1)}$ nm: 252, $\lambda_{max}^{H_2O\,(pH\,13)}$ nm: 282, λ_{max}^{EtOH} nm: 284; IR ν_{max}^{KBr} cm^{-1}: 1615, 1575, 1565; NMR ($CDCl_3$) δ: 2.85—3.95 (8H, m, CH_2), 5.30 (1H, s, CH). *Anal.* Calcd for $C_{18}H_{19}N_3O$: C, 73.69; H, 6.53; N, 14.33. Found: C, 73.41; H, 6.53; N, 14.21.

Compounds **2b**—**d** were similarly prepared. The results are described below.

2b: Yield 78%; mp 162—163° (Me_2CO); UV $\lambda_{max}^{H_2O\,(pH\,1)}$ nm: 252, $\lambda_{max}^{H_2O\,(pH\,13)}$ nm: 282, λ_{max}^{EtOH} nm: 284; IR ν_{max}^{KBr} cm^{-1}: 1620, 1580, 1565; NMR ($CDCl_3$) δ: 1.4—1.9 (2H, m, CH_2), 2.85—3.7 (8H, m, CH_2), 5.30 (1H, s, CH). *Anal.* Calcd for $C_{19}H_{21}N_3O$: C, 74.24; H, 6.89; N, 13.67. Found: C, 74.23; H, 6.93; N, 13.73.

2c: Yield 75%; mp 147—148° (Me_2CO); UV $\lambda_{max}^{H_2O\,(pH\,1)}$ nm: 258, 221, $\lambda_{max}^{H_2O\,(pH\,13)}$ nm: 290, 224, λ_{max}^{EtOH} nm: 293, 223; IR ν_{max}^{KBr} cm^{-1}: 1520, 1465; NMR ($CDCl_3$) δ: 1.6—2.1 (2H, m, CH_2), 2.85—3.7 (8H, m, CH_2), 5.22 (1H, s, CH). *Anal.* Calcd for $C_{19}H_{21}N_3O$: C, 74.24; H, 6.89; N, 13.67. Found: C, 74.12; H, 6.86; N, 13.51.

2d: Yield 84%; mp 157—159° (Me_2CO); UV $\lambda_{max}^{H_2O\,(pH\,1)}$ nm: 258, 221, $\lambda_{max}^{H_2O\,(pH\,13)}$ nm: 290, 224, λ_{max}^{EtOH} nm: 293, 223; IR ν_{max}^{KBr} cm^{-1}: 1525, 1485; NMR ($CDCl_3$) δ: 1.2—2.2 (4H, m, CH_2), 3.1—4.5 (8H, m, CH_2), 5.21 (1H, s, CH). *Anal.* Calcd for $C_{20}H_{23}N_3O$: C, 74.73; H, 7.21; N, 13.03. Found: C, 74.66; H, 7.19; N, 13.29.

1-(2-Chloroethyl)-5-phenyl-1,2,3,5-tetrahydroimidazo[2,1-*b*]quinazoline (3a)——A mixture of 0.88 g (3 mmol) of **2a** and 10 ml of $SOCl_2$ in 10 ml of $CHCl_3$ was allowed to stand at room temperature for 2 hr, then concentrated *in vacuo*. The residue was treated with Me_2CO to give 1.40 g of the hydrochloride of **3a**, mp 196—197° (iso-PrOH–Me_2CO). The hydrochloride was dissolved in a small volume of MeOH. The solution was neutralized with NaOH solution to pH 8—9 and extracted with $CHCl_3$. The extract was worked up as usual to give 0.89 g (93%) of the free base of **3a**: mp 112—114° (Me_2CO); IR ν_{max}^{KBr} cm^{-1}: 1625, 1580, 1565; NMR ($CDCl_3$) δ: 5.32 (1H, s, CH). *Anal.* Calcd for $C_{18}H_{18}ClN_3$: C, 69.33; H, 5.82; N, 13.48. Found: C, 69.21; H, 5.92; N, 13.25.

The corresponding free base of **3b** was similarly prepared and its properties are listed below.

3b: Yield 94%; mp unclear (Me_2CO); IR ν_{max}^{KBr} cm^{-1}: 1610, 1585, 1560; NMR ($CDCl_3$) δ: 5.37 (1H, s, CH). *Anal.* Calcd for $C_{19}H_{20}ClN_3$: C, 70.03; H, 6.19; N, 12.90. Found: C, 69.67; H, 6.16; N, 12.78.

5-Phenyl-1,2,3,5-tetrahydro-5H-2a,4a,9b-triazapentaleno[1,6-*a*, *b*]naphthalenium Chloride (4a)——A solution of 1.00 g (3.2 mmol) of the free base of **3a** in 15 ml of EtOH was refluxed for 3 hr and concentrated *in vacuo*. The residue was triturated in Me_2CO and the resulting hygroscopic crystals were collected to give 0.95 g (95%) of **4a**; mp 245—247° (iso-PrOH–Me_2CO); UV $\lambda_{max}^{H_2O\,(pH\,1)}$ nm: 258, $\lambda_{max}^{H_2O\,(pH\,13)}$ nm: 257, λ_{max}^{EtOH} nm: 258; IR ν_{max}^{KBr} cm^{-1}: 1700, 1635, 1600, 1485; NMR ($CDCl_3$) δ: 3.7—4.85 (8H, m, CH_2), 6.10 (1H, s, CH). *Anal.* Calcd for $C_{18}H_{18}ClN_3$: C, 69.33; H, 5.82; N, 13.48. Found: C, 69.19; H, 5.82; N, 13.60.

Compound **4d** was similarly prepared and its properties are listed below.

4b: Yield 93%; mp 246—249° (iso-PrOH–Me_2CO); UV $\lambda_{max}^{H_2O\,(pH\,1)}$ nm: 259, $\lambda_{max}^{H_2O\,(pH\,13)}$ nm: 259, λ_{max}^{EtOH} nm: 259; IR ν_{max}^{KBr} cm^{-1}: 1645, 1620, 1490; NMR ($CDCl_3$) δ: 2.3—2.7 (2H, m, CH_2), 3.1—4.2 (8H, m, CH_2), 5.90 (1H, s, CH). *Anal.* Calcd for $C_{18}H_{19}ClN_3 \cdot 1/2H_2O$: C, 68.16; H, 6.32; N, 12.55. Found: C, 68.68; H, 6.19; N, 12.54.

7-Phenyl-2,3,4,5,6,7-hexahydro-1H-4,6-ethano-1,4,6-benzotriazonin-5-one (6)——A solution of 1.00 g (3.2 mmol) of **4a** in 10 ml of H_2O was charged on an ion exchange resin column (Dowex 2×8, hydroxide type, ϕ 2.5×25) and eluted with 50% aqueous MeOH. The effluent (200 ml) was concentrated *in vacuo*. The residue was collected to give 0.60 g (64%) of **6**: mp 205—209° (MeOH–Et_2O). *Anal.* Calcd for $C_{18}H_{19}N_3O$: C, 73.69; H, 6.53; N, 14.33. Found: C, 73.49; H, 6.53; N, 14.04.

8-Phenyl-1,2,3,4,5,6,7,8-octahydro-5,7-ethano-1,5,7-benzotriazecin-6-one (7)——Using the procedure described above, **7** was obtained from **4b** in 72% yield: mp 194—197° (MeOH–$CHCl_3$). *Anal.* Calcd for $C_{19}H_{21}N_3O$: C, 74.24; H, 6.89; N, 13.67. Found: C, 74.19; H, 6.88; N, 13.62.

8-Phenyl-1,2,3,4,5,6,7,8-octahydro-1,3-ethano-1,3,7-benzotriazecin-2-one (8)——A mixture of 0.92 g (3 mmol) of **2c** and 5 ml of $SOCl_2$ in 5 ml of $CHCl_3$ was allowed to stand at room temperature for 2 hr, then concentrated *in vacuo*. The residue was dissolved in a small volume of H_2O. The solution was charged on a column (Dowex 2×8, hydroxide type, ϕ 2.5×25) and eluted with H_2O. The effluent (150 ml) was concentrated *in vacuo*. The residue was triturated in Me_2CO. The crystalline material was collected and recrystallized from $CHCl_3$–Et_2O to give 0.48 g (52%) of **8**: mp 165—175° (unclear). *Anal.* Calcd for $C_{19}H_{21}N_3O$: C, 74.24; H, 6.89; N, 13.67. Found: C, 74.06; H, 6.90; N, 13.58.

4-Phenyl-1,3-(4-azaheptano)-1,2,3,4-tetrahydroquinazolin-2-one (**9**)——Using the procedure described above, **9** was obtained from **2d** in 66% yield: mp 114—116°. *Anal.* Calcd for $C_{20}H_{23}N_3O \cdot 1/2H_2O$: C, 72.70; H, 7.32; N, 12.72. Found: C, 72.84; H, 7.05; N, 12.53.

5-Phenyl-1,2,3,3a,4,5-hexahydro-10H-3,4-ethanoimidazo[1,2-*a*]quinazoline (**11a**)——A solution of 0.11 g (3 mmol) of $NaBH_4$ in 1 ml of H_2O was added to a solution of 0.311 g (1 mmol) of **4a** in 2 ml of H_2O and 4 ml of EtOH at room temperature with stirring. The mixture was stirred for another 1 hr and diluted with a large volume of H_2O. The mixture was then extracted with $CHCl_3$. The extract was worked up as usual to give 0.24 g (87%) of **11a**: mp 141—144° (Et_2O). *Anal.* Calcd for $C_{18}H_{19}N_3$: C, 77.94; H, 6.91; N, 15.15. Found: C, 78.35; H, 6.82; N, 15.39.

6-Phenyl-2,3,4,4a,5,6-hexahydro-1H,11H-4,5-ethanopyrimido[1,2-*a*]quinazoline (**11b**)——Using the procedure described above, **11b** was obtained from **4b** in 93% yield: mp 138—141° (Et_2O). *Anal.* Calcd for $C_{19}H_{20}N_3$: C, 78.31; H, 7.26; N, 14.42. Found: C, 78.02; H, 7.24; N, 14.45.

5-Phenyl-1,2,3,3a,4,5-hexahydro-10H-3,4-propanoimidazo[1,2-*a*]quinazoline (**11c**)——A mixture of 0.307 g (1 mmol) of **2c** and 5 ml of $SOCl_2$ in 5 ml of $CHCl_3$ was allowed to stand at room temperature for 2 hr, then concentrated *in vacuo*. The residue was dissolved in a solution of 2 ml of H_2O and 4 ml of EtOH and the mixture was neutralized with NaOH solution. Next, a solution of 0.11 g (3 mmol) of $NaBH_4$ in 1 ml of H_2O was added at room temperature with stirring. The whole was stirred for 1 hr and worked up as described above to give 0.23 g (79%) of **11c**: mp 136—137° (Et_2O). *Anal.* Calcd for $C_{19}H_{21}N_3$: C, 78.31; H, 7.26; N, 14.42. Found: C, 78.42; H, 7.14; N, 14.31.

6-Phenyl-2,3,4,4a,5,6-hexahydro-1H,11H-4,5-propanopyrimido[1,2-*a*]quinazoline (**11d**)——After treatment of 0.32 g (1 mmol) of **2d** with 2 ml of $SOCl_2$ as described above, the reaction residue was dissolved in 2 ml of H_2O and 4 ml of EtOH and the solution was neutralized with NaOH solution. Next, a solution of 0.11 g (3 mmol) of $NaBH_4$ in 1 ml of H_2O was added at $-5°$ to 0° with stirring. After stirring at the same temperature for 1 hr, ice-cold H_2O was added to the reaction mixture. The whole was extracted with $CHCl_3$. The extract was worked up as usual to give 0.095 g (31%) of **11d**: mp 140—155° (Et_2O). *Anal.* Calcd for $C_{20}H_{25}N_3$: C, 78.64; H, 7.59; N, 13.75. Found: C, 79.00; H, 7.18; N, 13.66.

By a similar procedure, except for the addition of the solution of $NaBH_4$ at room temperature, 0.18 g (59%) of crude isomer **11'd** was obtained and recrystallized from Et_2O give 0.13 g of pure **11'd**: mp 119—121°. *Anal.* Calcd for $C_{20}H_{25}N_3$: C, 78.64; H, 7.59; N, 13.75. Found: C, 78.77; H, 7.48; N, 13.66.

1-Benzhydryl-2-imidazolidinone (**12**)——A mixture of 2.05 g (5 mmol) of 1-benzhydryl-2-methylthio-2-imidazoline hydroiodide[4] and 4.0 g of NaOH in 50% aqueous EtOH solution was refluxed for 12 hr. After removal of EtOH *in vacuo*, the precipitate was collected and recrystallized from EtOH to give 0.98 g (78%) of **12**: mp 201—203°; IR ν_{max}^{KBr} cm^{-1}: 1685, 1485; NMR ($CDCl_3$) δ: 3.2—3.45 (4H, m, CH_2), 6.43 (1H, s, CH). *Anal.* Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.19; H, 6.48; N, 11.06.

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