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Heterocycles. X.[1] Synthesis and Reactions of 1,4,5-Benzotriazocinium Salts[2]

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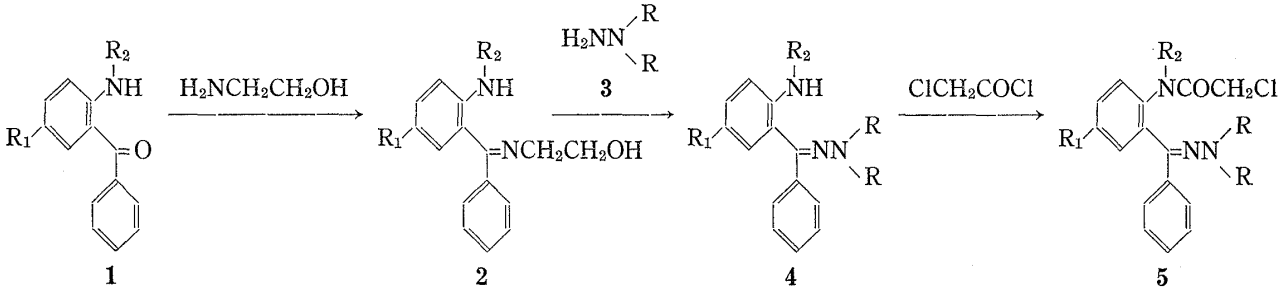
Ring closure reactions of 2-chloroacetamidobenzophenone (N,N-disubstituted)-hydrazones (**5**) afforded 1,4,5-benzotriazocines (**6**), 1,4-benzodiazepines (**9**) and 1,4,5-benzotriazocinium salts (**8**). On treatment with sodium methoxide, **5** and **8** gave 3-(N,N-disubstituted)amino-1,4-benzodiazepin-2-ones (**11**) in good yields through Stevens-type rearrangement.

Keywords——1,4,5-benzotriazocines; 2-aminobenzophenone hydrazones; 1,4-benzodiazepines; 3-(N,N-disubstituted)amino-1,4-benzodiazepin-2-ones; quaternary ammonium salts; Stevens rearrangement

Since the discovery of the interesting pharmacological activity of 1,4-benzodiazepine derivatives[4] as central nervous system (CNS) depressants, considerable research has been carried out on compounds possessing structurally related eight-membered ring systems, such as 1,5-benzodiazocine,[5] 2,5-benzodiazocine[6] and 4,1,5-benzoxadiazocine.[7] In the course of our studies on a series of 1,4-benzodiazepine derivatives, we have also reported[8] the formation of the 6-phenyl-1,4,5-benzotriazocine skeleton by the reaction of 2-chloromethyl-4-phenylquinazoline 3-oxides with hydrazine. This report deals with another facile synthesis of the 1,4,5-benzotriazocine ring system and describes a novel route to 3-(N,N-disubstituted)-amino-1,4-benzodiazepines through a Stevens-type rearrangement of 1,4,5-benzotriazocinium salts.

As an approach to the 1,4,5-benzotriazocines, intramolecular quaternization of 2-chloroacetamidobenzophenone (N,N-disubstituted)hydrazones (**5**) was investigated. The starting hydrazones (**4**) were prepared in good yields using an exchange reaction between the Schiff bases (**2**) and hydrazines (**3**).[9] Direct condensation of 2-aminobenzophenones (**1**) with **3** also gave **4**, but the yield was quite low. Chloroacetylation of **4** afforded **5** in good yields (Chart 1, Table I).[10]

1) Part IX: K. Meguro and Y. Kuwada, *Heterocycles*, **2**, 335 (1974).
2) A part of this paper was presented at the 91st Annual Meeting of the Pharmaceutical Society of Japan, Fukuoka, April, 1971.
3) Location: *Jusohonmachi, Yodogawa-ku, Osaka 532, Japan.*
4) L.H. Sternbach, *Angew. Chem. Int. Ed. Eng.*, **10**, 34 (1971).
5) *a*) M.E. Derieg, R.M. Schweininger, and R.I. Fryer, *J. Org. Chem.*, **34**, 179 (1969); *b*) M. Denzer and H. Ott, *ibid.*, **34**, 183 (1969); *c*) M. Steinmann and J.G. Topliss, *J. Pharm. Sci.*, **58**, 830 (1969); *d*) H. Liepmann, W. Milkowski, and H. Zeugner, *Eur. J. Med. Chem. Chimica Therapeutica*, **11**, 501 (1976).
6) *a*) T.S. Sulkowski, M.A. Wille, A. Mascitti, and J.L. Diebold, *J. Org. Chem.*, **32**, 2180 (1967); *b*) D.H. Kim, A.A. Santilli, T.S. Sulkowski, and S.J. Childress, *ibid.*, **32**, 3720 (1967); *c*) M. Winn and H.E. Zaugg, *ibid.*, **34**, 249 (1969).
7) *a*) A. Stempel, I. Douvan, E. Reeder, and L.H. Sternbach, *J. Org. Chem.*, **32**, 2417 (1967); *b*) P.N. Giraldi, A. Fojanesi, G.P. Tosolini, E. Dradi, and W. Logemann, *J. Heterocycl. Chem.*, **7**, 1429 (1970).
8) *a*) K. Meguro and Y. Kuwada, *Tetrahedron Lett.*, **1970**, 4039; *b*) *Idem*, *Chem. Pharm. Bull.* (Tokyo), **21**, 2375 (1973).
9) A similar exchange reaction has already been reported; *a*) K. Meguro, H. Tawada, and Y. Kuwada, *Yakugaku Zasshi*, **93**, 1253 (1973); *b*) K. Meguro and Y. Kuwada, *ibid.*, **93**, 1263 (1973).
10) S. Kwon and K. Isagawa reported the separation of geometrical isomers of certain 2-aminobenzophenone hydrazones (*Nippon Kagaku Kaishi*, **1974**, 524), but the geometry of **4** and **5** was not investigated in this work.



1, 2

	R_1	R_2
a :	Cl	H
b :	Cl	CH_3
c :	CH_3	H
d :	NO_2	H
e :	H	H

3

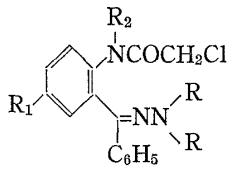
a :	$N(CH_3)_2$
b :	
c :	
d :	

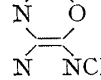
4, 5

	R_1	R_2	
a :	Cl	H	$N(CH_3)_2$
b :	Cl	CH_3	$N(CH_3)_2$
c :	CH_3	H	$N(CH_3)_2$
d :	NO_2	H	$N(CH_3)_2$
e :	H	H	$N(CH_3)_2$
f :	Cl	H	
g :	Cl	H	
h :	Cl	H	

Chart 1

TABLE I. 2-Chloroacetamidobenzophenone Hydrazones (**5**)



Compd.	R_1	R_2		mp (°C)	Yield (%)	Formula	Analysis (%) Calcd. (Found) C	H	N
a	Cl	H	$N(CH_3)_2$	115—116[a]	75[b]	$C_{17}H_{17}Cl_2N_3O$	58.29 (58.25	4.89 4.80	12.00 12.08)
b	Cl	CH_3	$N(CH_3)_2$	120—121[c]	78[d]	$C_{18}H_{19}Cl_2N_3O$	59.35 (59.52	5.26 5.31	11.54 11.44)
c	CH_3	H	$N(CH_3)_2$	105—106[e]	61[f]	$C_{18}H_{20}ClN_3O$	65.54 (65.76	6.11 6.15	12.74 12.67)
d	NO_2	H	$N(CH_3)_2$	151—152[e]	79[d]	$C_{17}H_{17}ClN_4O_3$	56.59 (56.40	4.75 4.72	15.53 15.60)
e	H	H	$N(CH_3)_2$	103—105[e]	73[b]	$C_{17}H_{18}ClN_3O$	64.66 (64.78	5.74 5.72	13.31 13.41)
f	Cl	H		144—145[e]	82[b]	$C_{20}H_{21}Cl_2N_3O$	61.54 (61.66	5.42 5.14	10.77 10.63)
g	Cl	H		155—156[e]	88[b]	$C_{19}H_{19}Cl_2N_3O_4$	58.17 (58.08	4.88 4.80	10.71 10.66)
h	Cl	H		Oil[g]	88[d]	$C_{20}H_{22}Cl_2N_4O$	59.26 —	5.47 —	13.82 —

a) Recrystallized from *n*-hexane.
b) Based on the corresponding 2-amino-*α*-phenylbenzylideneaminoethanol.
c) Not recrystallized.
d) Based on the corresponding 2-aminobenzophenone hydrazone.
e) Recrystallized from methanol.
f) Based on the corresponding 2-aminobenzophenone.
g) Used in the subsequent reactions without purification.

On thermal cyclization of compounds **5a**—**d**, two types of reactions occured, depending on the reaction conditions. When **5a** was heated at 140° in dimethylformamide (DMF) in the presence of sodium iodide, 8-chloro-3,4-dihydro-4-methyl-6-phenyl-1,4,5-benzotriazocin-2(1*H*)-one (**6a**) was obtained in 48% yield. Similarly, **5b** and **5c** gave **6b** and **6c**, respectively. The structures were supported by the results of elemental analyses and by infrared (IR) and nuclear magnetic resonance (NMR) spectral data. Furthermore, **6a** afforded the 1,2,3,4-tetrahydro-1,4,5-benzotriazocine (**7**) on reduction with lithium aluminum hydride. Methylation of **6a** gave **6b**. On the other hand, when fused at 190°, **5a** decomposed with the evolution of an unidentified gas to form a dark brown tar from which the 1,3-dihydro-2*H*-1,4-benzodiazepin-2-one[11] (**9a**) was isolated in 18% yield. A trace of the triazocine (**6a**) was also detected by thin layer chromatography (TLC). Similarly, **9b**[11] (9%) and **9d**[12] (18%) were obtained from **5b** and **5d**, respectively.

Formation of the triazocine (**6**) and the diazepine (**9**) can be rationalized by assuming the intermediates **8** and **10**, respectively. Isolation of the quaternary salt (**8** or **10**) was therefore attempted. When **5a** was stirred with sodium iodide in acetone at room temperature for 24 hr, the quaternary salt (**8a**) was obtained in 66% yield. Compound **8a** gave a positive silver nitrate test and showed an amide carbonyl absorption at 1695 cm^{-1} in the IR spectrum. The NMR spectrum of **8a** in hexadeuterodimethylsulfoxide (DMSO-d_6) exhibited two singlets due to $\overset{+}{N}Me_2$ at 3.47 and 3.81 ppm, and a characteristic AB pattern at 4.28 and 4.58 ppm (each 1H, d, J=13 Hz) attributable to the methylene protons at C-3. On heating in DMF at 140°, **8a** afforded only the triazocine (**6a**) in high yield (85%) and formation of the diazepine was not observed. However, when **8a** was heated at 170° without any solvent, a trace of **9a** together with **6a** (49%) was detected by TLC. Formation of **9a** from **8a** may be explained in terms of intermediate formation of **10** *via* thermolytic cleavage of the triazocine ring regenerating **5a** or ring contraction of **8a** (Chart 3).

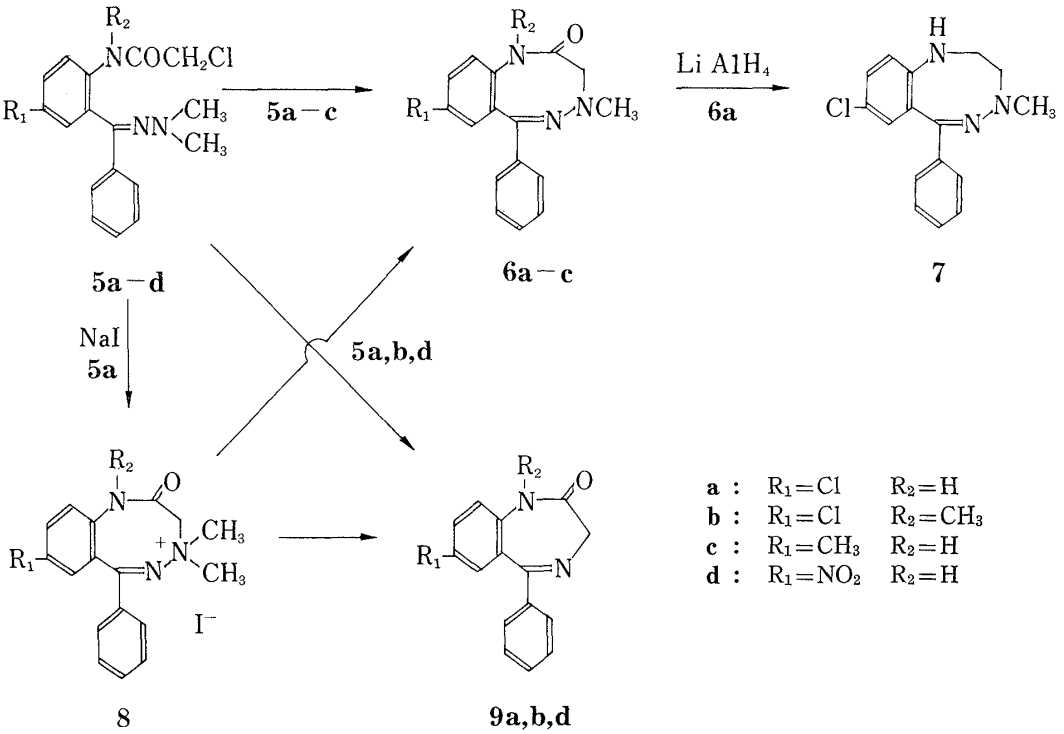


Chart 2

11) L.H. Sternbach and E. Reeder, *J. Org. Chem.*, **26**, 4936 (1961).
12) L.H. Sternbach, R.I. Fryer, O. Keller, W. Metlesics, G. Sach, and N. Steigner, *J. Med. Chem.*, **6**, 261 (1961).

The 1,4,5-benzotriazocinium salts (**8**) (Table II) were similarly obtained from the corresponding compounds **5**. In the case of **5d** and **5h**, however, the corresponding triazocinium salts could not be isolated. Compound **5d**, which was converted to the diazepine (**9d**) as mentioned above, did not give any quaternary salt even when the reaction was continued for 3 days at room temperature. Compound **5h** gave a complex mixture of quaternary salts. Cyclization of **5b** to **8b** proceeded very smoothly in the absence of sodium iodide.

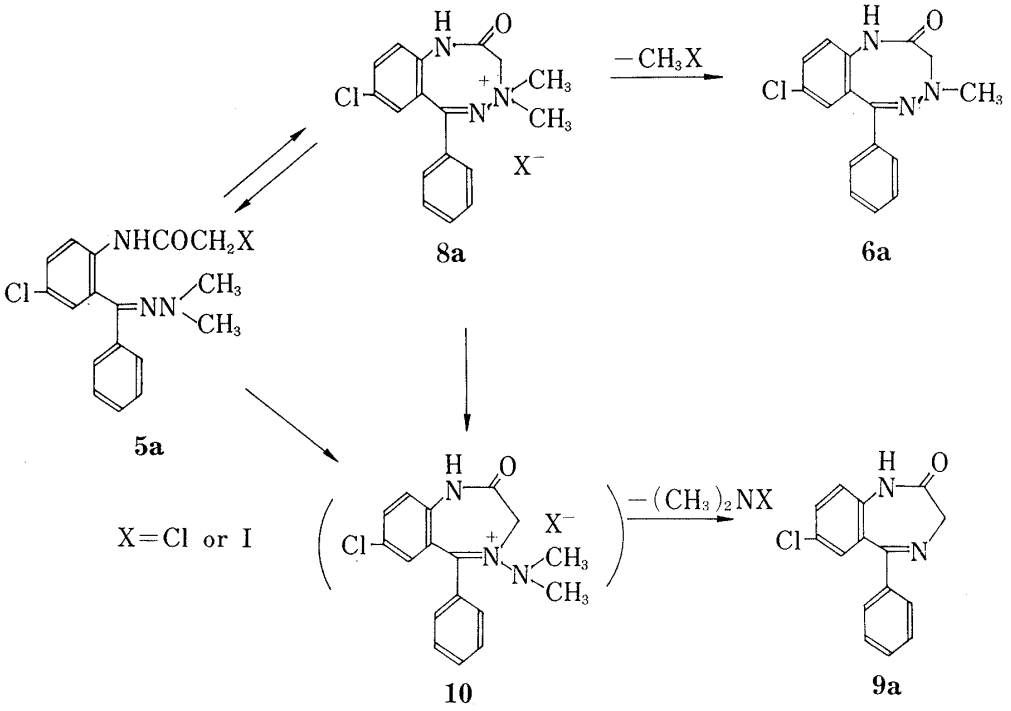
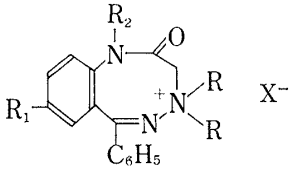


Chart 3

TABLE II. 1,4,5-Benzotriazocinium Salts (**8**)



Compound	R_1	R_2	NR_2	X	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd. (Found) C	H	N
a	Cl	H	$N(CH_3)_2$	I	154—155[a]	66	$C_{17}H_{17}ClIN_3O$ 1/2CH_3OH	45.92 (45.91)	4.18 (4.24)	9.18 (8.92)
b	Cl	CH_3	$N(CH_3)_2$	Cl	132—133[b]	50	$C_{18}H_{19}Cl_2N_3O$	59.35 (59.31)	5.26 (5.08)	11.54 (11.56)
c	CH_3	H	$N(CH_3)_2$	I	170—171[a]	68	$C_{18}H_{20}IN_3O$	51.32 (51.37)	4.79 (4.69)	9.97 (10.12)
e	H	H	$N(CH_3)_2$	I	170—171[a]	53	$C_{17}H_{18}IN_3O$	50.13 (50.00)	4.45 (4.35)	10.32 (10.39)
f	Cl	H		I	177—179[a]	61	$C_{20}H_{21}ClIN_3O$	49.86 (50.08)	4.39 (4.13)	8.72 (8.55)
g	Cl	H		I	185—187[a]	9	$C_{19}H_{19}ClIN_3O_2$	47.17 (47.28)	3.96 (3.78)	8.69 (8.60)

Recrystallized from *a*) methanol; *b*) dichloromethane–*n*-hexane.

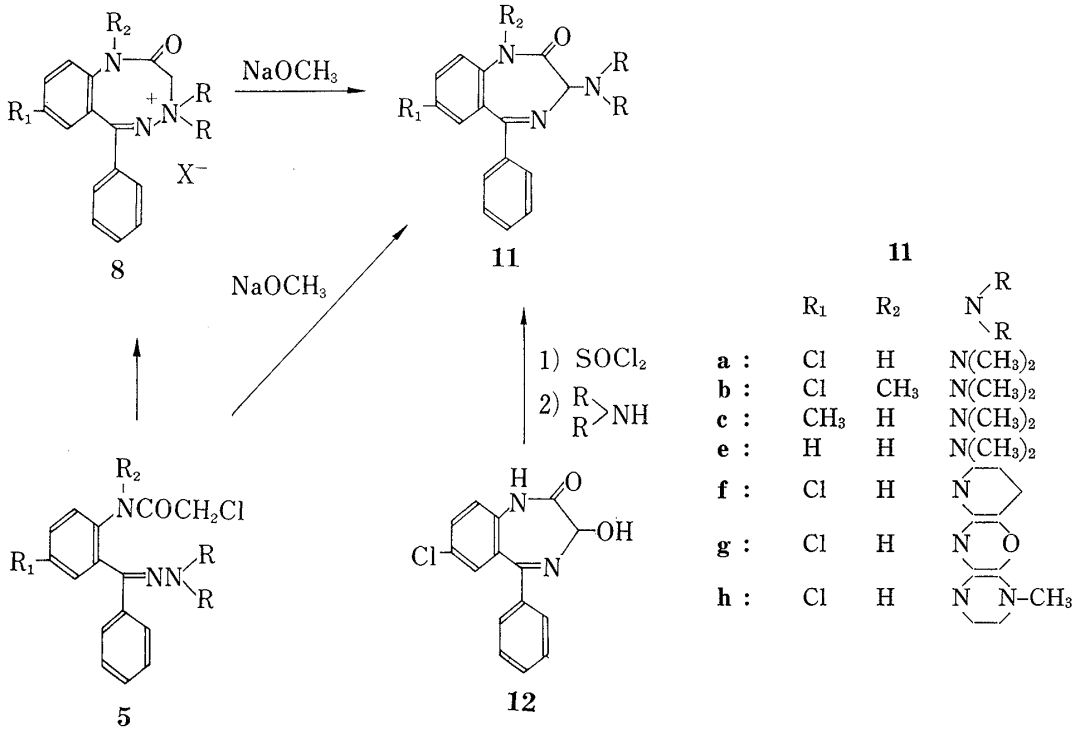
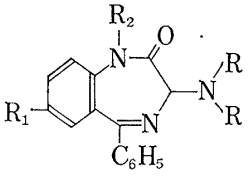


Chart 4

TABLE III. 3-(Substituted)amino-1,4-benzodiazepin-2-ones (**11**)



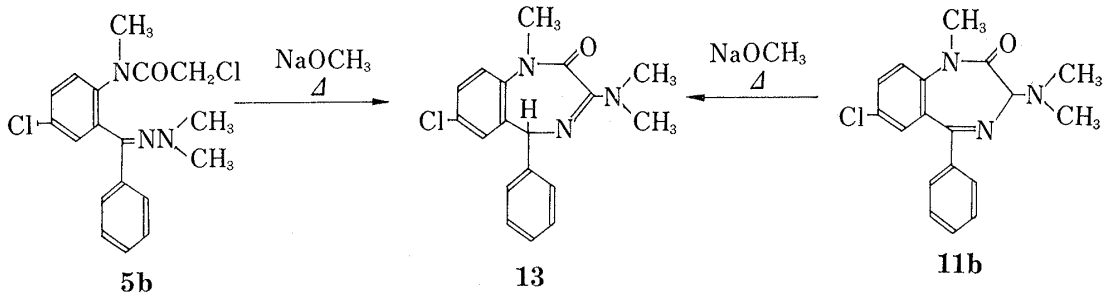
Compound	R_1	R_2	NR_2	mp (°C)	Yield (%) Method[a] A	B	Formula	Analysis (%) Calcd. (Found) C	H	N
a	Cl	H	$N(CH_3)_2$	217—218	79	74	$C_{17}H_{16}ClN_3O$	65.07 (65.34	5.14 5.09	13.39 13.32)
b	Cl	CH_3	$N(CH_3)_2$	144—145	78[b]	—[c]	$C_{18}H_{18}ClN_3O$	65.95 (66.16	5.53 5.44	12.82 12.72)
c	CH_3	H	$N(CH_3)_2$	220—222	88	84	$C_{18}H_{19}N_3O$	73.69 (73.93	6.53 6.53	14.33 14.28)
e	H	H	$N(CH_3)_2$	236—238	84	70	$C_{17}H_{17}N_3O$	73.13 (73.13	6.14 6.08	15.04 15.25)
f	Cl	H	N	229—230	72	35	$C_{20}H_{20}ClN_3O$	67.88 (67.78	5.70 5.54	11.88 11.67)
g	Cl	H	N O	225—227[d]	60	6	$C_{19}H_{18}ClN_3O_2$	64.13 (64.11	5.10 4.86	11.81 11.73)
h	Cl	H	N N-CH_3	223—225	—	13	$C_{20}H_{21}ClN_4O$	65.12 (65.23	5.74 5.62	15.19 14.92)

a) A: from **8**, B: from **5**.
b) Carried out under ice-cooling (see "Experimental").
c) Isolated as the isomer (**13**) (see "Experimental").
d) Lit.[14] mp 211—213°.

The Stevens rearrangement of quaternary ammonium salts on treatment with a base has been well documented.[13] Since 1,4,5-benzotriazocinium salts (**8**) are a kind of hydrazonium salt possessing an active methylene at C-3, they were expected to undetgo a Stevens-type rearrangement.

When **8a** was heated with sodium methoxide in methanol, the 3-dimethylamino-1,4-benzodiazepin-2-one (**11a**) was obtained in 79% yield. Compound **11a** was also obtained from **6a** by reaction with dimethyl sulfate followed by treatment with sodium methoxide. The structure of **11a** was confirmed by the identity of its melting point and IR and NMR spectra with those of the authentic compound synthesized unambiguously[14] from **12**[15] by chlorination followed by treatment with dimethylamine. Direct treatment of **5a** with sodium methoxide also afforded the same compound (**11a**) in good yield (74%). This rearrangement (**5a**→**11a**) is presumed to proceed *via* **8a**. Similarly **11c**, **e**, **f** and **g** were obtained from the corresponding **5** and **8** by treatment with sodium methoxide in methanol. Although the triazocinium salt (**8h**) from **5h** was not isolated, as mentioned above, treatment of **5h** with sodium methoxide afforded the rearranged product (**11h**) in 13% yield (Chart 4). These results are summarized in Table III.

In the case of **5b** and **8b**, the rearrangement was rather complicated because the initial product, 1,3-dihydro-3-dimethylamino-1-methyl-2*H*-1,4-benzodiazepin-2-one (**11b**), readily isomerizes[16] to 1,5-dihydro-3-dimethylamino-1-methyl-2*H*-1,4-benzodiazepin-2-one (**13**) on heating with sodium methoxide in methanol. Although rearrangement of the triazocinium salt (**8b**) was successfully conducted under ice-cooling to give **11b** in good yield (78%), direct rearrangement of **5b** did not proceed at low temperatures. At high temperature, **5b** underwent the rearrangement; however, the product isolated was not **11b** but the isomer (**13**) (Chart 5).



5b **13** **11b**

Chart 5

This base-catalyzed rearrangement of **5** and **8** provides a facile and convenient method for the synthesis of 3-(N,N-disubstituted)amino-1,4-benzodiazepines, some of which have interesting biological activities on the CNS.[14]

Experimental

All melting points were determined with a Yanagimoto micro melting point apparatus (a hot-stage type) and are uncorrected. IR spectra were measured on a Hitachi 215 spectrophotometer and NMR spectra on a Varian T-60 (60 MHz) or a Varian HA-100 (100 MHz) spectrometer using tetramethylsilane as an internal standard. The following abbreviations are used; s=singlet, d=doublet, q=quartet, m=multiplet and b=broad. Removal of solvents was performed on a rotary evaporator under water aspirator pressure. Extracted solutions were dried over sodium sulfate.

2-Amino-5-nitrobenzophenone N,N-Dimethylhydrazone (**4d**)——a) A solution of 4.8 g of 2-(2-amino-5-nitro-α-phenylbenzylideneamino)ethanol (**2d**),[9a] 3.0 g of AcOH and 4.0 g of N,N-dimethylhydrazine (**3a**)

13) S.H. Pine, *Organic Reactions*, **18**, 403 (1970).
14) S.C. Bell, R.J. McCaully, C. Gochman, S.J. Childress, and M.J. Gluckman, *J. Med. Chem.*, **11**, 457 (1968).
15) S.C. Bell and S.J. Childress, *J. Org. Chem.*, **27**, 1691 (1962).
16) An analogous isomerization was reported with 7-chloro-1,3-dihydro-3-ethylamino-1-methyl-6-phenyl-2*H*-1,4-benzodiazepin-2-one; R.Y. Ning, W.Y. Cheu, and L.H. Sternbach, *J. Org. Chem.*, **36**, 1064 (1971).

in 60 ml of MeOH was refluxed for 5 hr. After removal of the solvent, the crystalline residue was collected by filtration and washed with H_2O to give 4.5 g (93%) of **4d**. Recrystallization from AcOEt gave orange flakes, mp 199—200°. *Anal.* Calcd. for $C_{15}H_{16}N_4O_2$: C, 63.46; H, 5.67; N, 19.71. Found: C, 63.37; H, 5.58; N, 19.84. NMR (DMSO-d_6) δ: 2.43 (6H, s, $-N(CH_3)_2$), 6.87 (1H, d, $J=9$ Hz, arom. H), 7.2—7.6 (6H, m, arom. H), 7.90 (1H, q, $J=9$ Hz, 2.5 Hz, arom. H), 8.4 (2H, b, $-NH_2$).

Other 2-aminobenzophenone hydrazones (**4a**—**h**) were similarly prepared from the corresponding compounds **2** by reaction with **3**:

4b; yield 85%, pale yellow prisms (*n*-hexane), mp 95—97°, *Anal.* Calcd. for $C_{16}H_{18}ClN_3$: C, 66.77; H, 6.30; N, 14.60. Found: C, 66.67; H, 6.41; N, 14.68.

4h; yield 86%, pale yellow prisms (MeOH), mp 179—180°, *Anal.* Calcd. for $C_{18}H_{21}ClN_4$: C, 65.74; H, 6.44; N, 17.04. Found: C, 65.72; H, 6.32; N, 16.82.

Compounds **4a**, **4c**, **4e**, **4f** and **4g** were obtained as oily materials, and were used in subsequent reactions without further purification.

b) A mixture of 600 mg of 2-amino-5-nitrobenzophenone (**1d**), 500 mg of 2-methylimidazole·$1/2H_2SO_4$ and 1.5 ml of N,N-dimethylhydrazine (**3a**) was heated at 150° in a sealed tube for 5 hr. After cooling, the mixture was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was separated, washed with H_2O, dried and evaporated down. Treatment of the residue with AcOEt gave 45 mg (6%) of **4d** as orange flakes, mp 195—197°. The IR spectrum was identical with that of **4d** obtained by method a).

5-Chloro-2-chloroacetamidobenzophenone N,N-Dimethylhydrazone (**5a**)——Chloroacetyl chloride (2.0 ml) was added to an ice-cooled solution of 5.44 g of **4a** in 200 ml of ether with stirring. After stirring for 30 min, the mixture was poured into saturated aq. $NaHCO_3$ solution. The ether layer was separated, washed with H_2O, dried and evaporated to dryness to give 5.32 g (75%) of pale yellow prisms, mp 115—116°. Recrystallization from *n*-hexane gave pale yellow prisms, mp 115—116°. NMR ($CDCl_3$) δ: 2.67 (6H, s, $-N(CH_3)_2$), 4.12 (2H, s, $-CH_2-$), 7.1—7.6 (7H, m, arom. H), 8.01 (1H, d, $J=8$ Hz, arom. H), 9.90 (1H, b, -NH-).

Other hydrazones (**5b**—**h**) listed in Table I were prepared in a similar manner.

8-Chloro-3,4-dihydro-4-methyl-6-phenyl-1,4,5-benzotriazocin-2-one (**6a**)——A solution of 360 mg of **5a** and 180 mg of NaI in 7 ml of DMF was heated at 140° for 8 min. After cooling, the mixture was diluted with H_2O, and extracted with AcOEt. The extract was dried and evaporated down to give 145 mg (49%) of **6a** as pale yellow crystals. Recrystallization from CH_2Cl_2–*n*-hexane gave colorless needles, mp 134—136°. *Anal.* Calcd. for $C_{16}H_{14}ClN_3O$: C, 64.11; H, 4.71; N, 14.02. Found: C, 64.11; H, 4.69; N, 13.94. NMR ($CDCl_3$) δ: 2.90 (3H, s, $-NCH_3$), 3.80 (2H, b, $-CH_2-$), 7.0—7.6 (8H, m, arom. H), 9.30 (1H, s, -NH-). IR ν_{max}^{KBr} cm^{-1}: 1685 (CO).

Compounds **6b** and **6c** were obtained in a similar manner from **5b** and **5c**, respectively: **6b**; yield 51%, oil. The IR spectrum was identical with that of the compound obtained by methylation of **6a** (*vide infra*). **6c**; yield 52%, colorless fine needles (ether–*n*-hexane), mp 157—158°, *Anal.* Calcd. for $C_{17}H_{17}N_3O$: C, 73.09; H, 6.13; N, 15.04. Found: C, 72.83; H, 6.29; N, 14.84.

8-Chloro-3,4-dihydro-1,4-dimethyl-6-phenyl-1,4,5-benzotriazocin-2-one (**6b**)——A mixture of 0.5 ml of 2 N NaOMe/MeOH and 0.1 ml of CH_3I was added to a solution of 150 mg of **6a** in 5 ml of MeOH. After stirring for 5 hr at room temperature, the mixture was diluted with H_2O then extracted with $CHCl_3$. The extract was washed with H_2O, dried and concentrated to give 150 mg of **6b** as a colorless oil. NMR ($CDCl_3$) δ: 3.23, 3.29 (each 3H, s, $2\times-NCH_3$), 3.17, 4.29 (each 1H, d, $J=14$ Hz, $-CH_2-$), 7.0—7.4 (8H, m, arom. H). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1678 (CO).

7-Chloro-1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one (**9a**)——Compound **5a** (600 mg) was heated at 185—190° in an oil bath for 5 min. The dark brown tar formed was dissolved in 1 ml of acetone and treated with 10% ethanolic hydrogen chloride to give 130 mg (25%) of the hydrochloride of **9a**. Recrystallization from MeOH–acetone gave colorless crystals, mp 245—246°. Treatment of the hydrochloride with 10% NH_4-OH gave 80 mg (18%) of **9a**. Recrystallization from acetone afforded colorless prisms, mp 211—213° (lit.[11] mp 216—217°). The IR spectrum was identical with that of an authentic sample.[11]

Compounds **9b** and **9d** were similarly obtained from **5b** and **5d**, respectively: **9b**; yield 9%, mp 122—124° (lit.[11] mp 125—126°). **9d**; yield 18%, mp 220—222° (lit.[12] 224—226°). The IR spectra of **9b** and **9d** were identical with those of authentic samples.

8-Chloro-4-methyl-6-phenyl-1,2,3,4-tetrahydro-1,4,5-benzotriazocine (**7**)——Compound **6a** (1.90 g) was added portionwise to a suspension of 600 mg of $LiAlH_4$ in 35 ml of dry tetrahydrofuran. After stirring for 30 min at room temperature, the mixture was refluxed for 5 min, then treated with H_2O. The inorganic salt precipitate was removed by filtration and washed with ether. The organic phase was separated, washed with H_2O, dried and evaporated down to give 1.44 g (77%) of **7** as yellow crystals. Recrystallization from iso-Pr_2O gave pale yellow prisms, mp 156—157°. *Anal.* Calcd. for $C_{16}H_{16}ClN_3$: C, 67.24; H, 5.64; N, 14.70. Found: C, 67.13; H, 5.61; N, 14.49. NMR ($CDCl_3$) δ: 2.69 (3H, s, $-NCH_3$), 2.3—3.6 (4H, m, $-N(CH_2)_2N-$), 4.0 (1H, b, -NH-), 6.47—7.7 (8H, m, arom. H). IR ν_{max}^{KBr} cm^{-1}: 3420 (NH).

8-Chloro-3,4-dihydro-4,4-dimethyl-2(1*H*)-oxo-1,4,5-benzotriazocinium Iodide (**8a**)——NaI (9.0 g) was added to a stirred solution of 17.25 g of **5a** in 150 ml of acetone. After stirring the mixture at room temperature for 24 hr, the white precipitate was collected, and washed with H_2O and acetone to give 14.7 g (66.0%) of **8a**, mp 156—157° (dec.). Recrystallization from MeOH afforded colorless needles, mp 154—155° (dec.).

NMR (DMSO-d_6) δ: 3.47, 3.81 (each 3H, s, $\overset{+}{>}N(CH_3)_2$), 4 28, 4.58 (each 1H, d, $J=13$ Hz, $-CH_2-$), 7.2—7.8 (8H, m, arom. H), 10.98 (1H, s, –NH–). IR ν_{max}^{KBr} cm^{-1}: 1695 (CO).

The other N^1-unsubstituted-1,4,5-benzotriazocinium salts (**8c**, **8e**, **8f** and **8g**) listed in Table II were similarly prepared.

8-Chloro-3,4-dihydro-2(1*H*)-oxo-1,4,4-trimethyl-1,4,5-benzotriazocinium Chloride (8b)——A solution of 3.0 g of **5b** in 70 ml of acetone was stirred at room temperature for 4 hr. The white precipitate formed was collected by filtration and washed with ether to give 1.5 g (50%) of **8b**, mp 133—135° (dec.). Recrystallization from CH_2Cl_2–*n*-hexane gave colorless needles, mp 132—133° (dec.). NMR ($CDCl_3$) δ: 3.35 (3H, s, $-NCH_3$), 3.90, 4.15 (each 3H, s, $-N(CH_3)_2$), 4.52, 5.39 (each 1H, d, $J=13$ Hz, $-CH_2-$). IR ν_{max}^{KBr} cm^{-1}: 1678 (CO).

Thermolysis of 8a——a) A solution of 4.40 g of **8a** in 50 ml of DMF was heated at 140° for 10 min. After removal of the solvent, the residue was partitioned between AcOEt and H_2O. The AcOEt layer was separated, washed with H_2O, dried and concentrated to give 2.54 g (85%) of **6a**. Recrystallization from CH_2Cl_2-*n*-hexane gave colorless needles, mp 134—135°. The IR spectrum was identical with that of **6a** obtained from **5a**.

Compounds **8b** and **8c** similarly afforded **6b** (80%) and **6c** (63%), respectively.

b) Compound **8a** (440 mg) was heated at 170° for 3 min. The resulting tar was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was separated, washed with H_2O, dried and evaporated to dryness. The residue was chromatographed on silica gel using *n*-hexane–acetone (7: 3) as an eluent to give 185 mg of **6a** contaminated with a trace of **9a** as colorless crystals, mp 127°. Recrystallization from CH_2Cl_2–*n*-hexane gave 145 mg (49%) of **6a**, as colorless needles, mp 135—136°.

7-Chloro-1,3-dihydro-3-dimethylamino-6-phenyl-2*H*-1,4-benzodiazepin-2-one (11a)——a) A stirred suspension of 5.50 g of **8a** was treated with 20 ml of 2 N NaOMe/MeOH. The mixture was refluxed for 30 min. After removal of the solvent, the residue was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was separated, washed with H_2O, dried and evaporated down to give 3.39 g (79%) of **11a** as colorless crystals. Recrystallization from CH_2Cl_2–*n*-hexane gave colorless needles, mp 217—218° (dec.). *Anal.* Calcd. for $C_{17}H_{16}ClN_3O$: C, 65.07; H, 5.14; N, 13.39. Found: C, 65.34; H, 5.09; N, 13.32. The IR and NMR spectra were identical with those of the compound obtained by the following methods b), c) and d).

Compounds **11b**, **11c**, **11e**, **11f** and **11g** were similarly prepared by method a) (Table III).

b) A stirred suspension of 350 mg of **5a** in 6 ml of MeOH was treated with 4 ml of 2 N NaOMe/MeOH. The mixture was refluxed for 15 min, then the solvent was evaporared off. The residue was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was separated, washed with H_2O, dried and evaporated down to give 230 mg (74%) of **11a**. Recrystallization from CH_2Cl_2–benzene gave colorless needles, mp 217—218° (dec.).

Compounds **11c**, **11e**, **11f**, **11g** and **11h** were also prepared by method b) (Table III).

c) A mixture of 200 mg of **6a** and 1.5 ml of Me_2SO_4 was heated at 90° for 15 min, then 10 ml of ether was added. The precipitate was collected by decantation, and dissolved in a mixture of 4 ml of MeOH and 2 ml of 2 N NaOMe/MeOH. The solution was refluxed for 30 min. After removal of the solvent, the residue was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was separated, washed with H_2O, dried and concentrated to give 150 mg (72%) of **11a** as colorless crystals, mp 216—217° (dec.).

d) A mixture of 100 mg of 7-chloro-1,3-dihydro-3-hydroxy-2*H*-1,4-benzodiazepin-2-one (**12**)[15] and 0.2 ml of $SOCl_2$ was allowed to stand at room temperature for 5 min. The yellow precipitate was collected by filtration, washed with ether and added to 4 ml of *ca.* 10% $(CH_3)_2NH$–ether (w/v). After stirring for 20 min at room temperature, the mixture was poured into H_2O and extracted with AcOEt. The extract was washed with H_2O, dried and evaporated down to give 45 mg (41%) of **11a**. Recrystallization from CH_2Cl_2–benzene gave colorless needles, mp 217—218° (dec.). The IR and NMR spectra were identical with those of **11a** obtained by method a), b) or c).

Compounds **11f** (69%), **11g** (81%) and **11h** (41%) were also prepared from **12**. Their mp and IR spectra were identical with those of the same compounds prepared by method a) or b).

7-Chloro-1,3-dihydro-3-dimethylamino-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one (11b)——An ice cooled solution of 1.45 g of **8b** in 20 ml of MeOH was treated with 15 ml of 2 N NaOMe/MeOH. After stirring for 15 min, the mixture was diluted with H_2O and extracted with $CHCl_3$. The extract was washed with H_2O, dried and evaporated down to give 1.02 g (78%) of **11b** as colorless crystals. Recrystallization from CH_2Cl_2–*n*-hexane gave colorless prisms, mp 144—145°. NMR ($CDCl_3$) δ: 2.68 (6H, s, $-N(CH_3)_2$), 3.38 (3H, s, $-NCH_3$), 4.13 (1H, s, >CH–), 7.2—7.8 (8H, m, arom. H). IR ν_{max}^{KBr} cm^{-1}: 1678 (CO).

7-Chloro-1,5-dihydro-3-dimethylamino-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one (13)——a) A mixture of 600 mg of **5b**, 10 ml of MeOH and 5 ml of 2 N NaOMe/MeOH was refluxed for 40 min. After removal of the solvent, the residue was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was separated, washed with H_2O, dried and concentrated. The residue was chromatographed on silica gel using *n*-hexane–acetone (7: 3) as an eluent to give 170 mg (32%) of **13** as colorless crystals, mp 190—193°. The IR spectrum was identical with that of **13** obtained by method b).

b) A mixture of 330 mg of **11b** and 5 ml of 2 N NaOMe/MeOH was refluxed for 30 min. After cooling, the mixture was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was separated, washed with H_2O,

dried and evaporated down to give 290 mg (88%) of **13** as colorless crystals. Recrystallization from CH_2Cl_2–*n*-hexane gave colorless prisms, mp 193—194°. *Anal.* Calcd. for $C_{18}H_{18}ClN_3O$: C, 65.95; H, 5.53; N, 12.82. Found: C, 66.21; H, 5.52; N, 12.43. NMR ($CDCl_3$) δ: 2.90 (6H, s, $-N(CH_3)_2$), 3.63 (3H, s, $-NCH_3$), 5.46 (1H, s, $>CH-$), 6.49 (1H, b, arom. H), 7.2—7.7 (7H, m, arom. H). IR ν_{max}^{KBr} cm^{-1}: 1655 (CO).

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