against IBR virus and ICH virus was determined using secondary BFK cells and a dog kidney (DK) cell line (38th passage) obtained from Connaught Laboratories, Toronto, Canada. The cells were grown in CulturStat (minimal essential medium MEM, Earle Base) containing 10% inactivated fetal calf serum. Maintenance medium contained the following components by volume: 10% MEM, 10% $NaHCO_3$ (4.4% stock solution), 4% inactivated fetal calf serum, 1% nonessential amino acids, 1% penicillin (100 U/ml), 1% streptomycin (100 μg/ml), and 73% double-distilled deionized water. The cells were treated with trypsin or EDTA.[18] Confluent monolayers of BFK or DK cells were grown in plastic disposable microplates having flat-bottomed cups (Micro-Test II) and were used for all antiviral chemotherapy experiments.[9] The cytotoxicity of each compound was determined microscopically.[9]

Stability of IV in the Presence of Reducing Agents. IV is readily oxidized to the corresponding bis compound V, which is essentially devoid of antiviral activity. Therefore, it was necessary to incorporate a reducing agent into the assay medium in cell culture studies. In order to find a reducing agent devoid of cytotoxicity and that would also prevent the oxidation of IV, the effects of four reducing agents on cell cultures were studied microscopically.[9] The stability of IV was followed by TLC chromatography. Dithiothreitol (DTT) and GSH prevented oxidation of IV at concentrations of 50 μg/ml or higher, whereas mercaptoethanol was only partially effective up to a concentration of 78 mg/ml and ascorbic acid was ineffective. However, DTT was toxic to cells above 50 μg/ml, whereas GSH showed no cytotoxicity up to 250 μg/ml. Therefore, on the basis of the above results, GSH was incorporated at 100 μg/ml into the medium for all cell culture studies.

Toxicity Studies. IV (10 mg/ml) was dissolved in phosphate buffer (0.15 *M*, pH 7.2) containing GSH (3 mg/ml) and administered intraperitoneally to 20–25-g Swiss mice. Controls were injected with an equal volume of the above buffer.

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Synthesis and Central Nervous System Effects of 8,9-Dihydro[1]benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2*H*)-ones and [1]Benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2*H*)-ones

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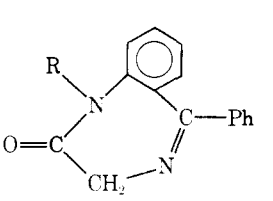
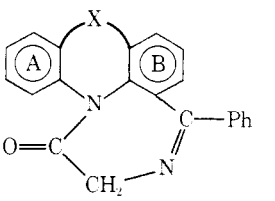
A series of 4-alkyl-8,9-dihydro[1]benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2*H*)-ones and brominated derivatives was synthesized. Two approaches for the synthesis of 4-alkyl[1]benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2*H*)-ones and brominated derivatives are described. All compounds were evaluated for CNS activity. None showed significant activity. The results obtained indicate that in the case of the 1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one a phenyl group at the 1 position causes a fall in CNS activity not only when it is *free* but also when *fused* to the benzodiazepine system.

A large number of 1,4-benzodiazepines have been synthesized by a variety of methods,[1] and extensive data on their pharmacological activity[2] have been accumulated over the past 15 years. Interesting observations[3] were also made by investigating the 1,4-benzodiazepinones of type 1.

Although it was recognized that a substituent larger than methyl at the 1 position had a negative effect on central nervous system (CNS) activity, our work has been centered on the fusion of tricyclic rings to the seven-membered diazepine ring system thus resulting in novel 1,4-benzodiazepinones of type **2**. These may be viewed as conformationally rigid analogs of CNS inactive compound **3** in which the precise spatial relationship between rings A and B can be varied by appropriate modification of the central ring. Of the several variants examined by Dreiding model studies, the most promising group for CNS biological activity appeared to be X = CH_2—CH_2, X = CH=CH, and X = S. In fact, these molecules could exhibit interesting CNS properties as they have stereochemistry and/or delocalization of electrons[4] different from the inactive compound **3**. Furthermore, they contain a condensed three-ring system similar to several CNS active compounds (10,11-dihydrodibenz[*b*,*f*]azepine, dibenz[*b*,*f*]azepine, and phenothiazine).



1



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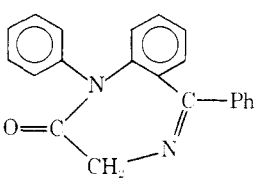
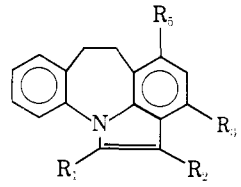


3

Table I. 6,7-Dihydroindolo[1,7-*ab*][1]benzazepines



No.	R_1	R_2	R_3	R_5	Mp, °C	Yield, %[a]	Crystn solvent[b]	Formula[c]
5	Me	Ph	H	H	131–133	32	A	$C_{23}H_{19}N$
6	Ph	Me	H	H	174–175	13	A	$C_{23}H_{19}N$
7	Ph	Me	Br	H	*d*			
8	Ph	Me	H	Br	144–145	40	E	$C_{23}H_{18}BrN$
9	Ph	Me	Br	Br	202–204[e]	25	B–P	$C_{23}H_{17}Br_2N$

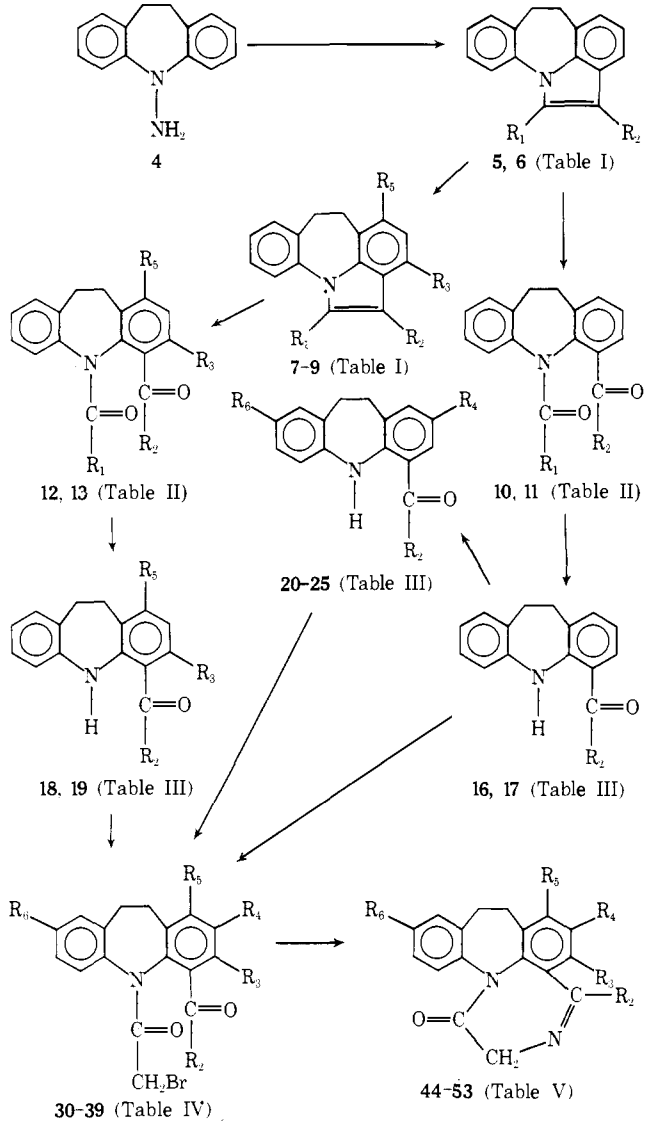
[a]No attempts were made to optimize yields. [b]A, Me_2CO; E, EtOH; B, C_6H_6; P, petroleum ether. [c]Analyses for C, H, N, and halogen were within ±0.4% of the theoretical value. [d]Not isolated; used crude in the next step. [e]NMR δ 7.55 (s, 1, H-4).

At the outset of our investigations, 4-phenyldiazepino-[6,7,1-*kl*]phenothiazin-1(2*H*)-one (**2**, X = S) was described by Hromatka et al.[5] Consequently, we now present only the synthesis and pharmacological results of 8,9-dihydro-4-phenyl[1]benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2*H*)-one (**2**, X = CH_2—CH_2) and 4-phenyl[1]benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2*H*)-one (**2**, X = CH=CH) in which a bromo substituent is or is not present at C-5, C-6, C-7, and C-11. The synthesis and pharmacological evaluation of 4-methyl analogs are presented too. Electron-withdrawing substituents could have a positive effect on the CNS activity.[3]

Chemistry. 8,9-Dihydro[1]benzazepino[3,2,1-*jk*][1,4]-benzodiazepin-1(2*H*)-ones (Table V, **44–53**) were prepared according to the general methods shown in Scheme I. It has been reported[6] that 5-amino-10,11-dihydro-5*H*-dibenz-[*b*,*f*]azepine (Scheme I, **4**) condenses with aldehydes and ketones to give suitable hydrazones which without isolation cyclize (Fischer cyclization) to 6,7-dihydroindolo[1,7-*ab*][1]benzazepines in ethanolic hydrogen chloride. Propiophenone condensed with **4** hydrochloride to give a hydrazone which cyclized to **6** (Table I) with ethanolic hydrogen chloride at reflux. Repetition of this reaction with 1-phenyl-2-propanone in ethanol at room temperature gave only **5** (Table I) whereas the use of ethanolic hydrogen chloride at reflux gave a mixture of **5** and **6** (Table I) which was readily separated by column chromatography on alumina. No reaction was observed between 6,7-dihydro-1-methyl-2-phenylindolo[1,7-*ab*][1]benzazepine (Table I, **5**) and *N*-bromosuccinimide, even after long reflux in carbon tetrachloride. In contrast, bromination of 6,7-dihydro-2-methyl-1-phenylindolo[1,7-*ab*][1]benzazepine (Table I, **6**) with 1.5 equiv of *N*-bromosuccinimide[7] was complete within 15 hr. Electrophilic attack on **6** (Table I) gave substitution of a bromine atom at C-3 (Table I, **7**) and C-5 (Table I, **8**). Examination of the resonance structures of the carbonium ions shows that hyperconjugation and two unshared electrons of the nitrogen atom are responsible for the substitution of these positions. The C-2 phenyl in compound **5** (Table I) is a deactivating group as it removes the unshared pairs of electrons from the nitrogen atom decreasing the transition state for substitution of a bromine atom at C-3 and C-5. The 5-bromo derivative **8** (Table I) was separated from **7** (Table I) by column chromatography on alumina. Repetition of this reaction with 3 equiv of *N*-bromosuccinimide gave only **9** (Table I).

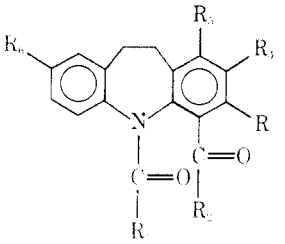
Oxidation of **5–8** (Table I) with chromic anhydride[8] in acetic acid gave 5-acyl-10,11-dihydro-5*H*-[*b*,*f*]azepines

Scheme I



(Table II, **10–13**). Facile conversion of **10–13** to 10,11-dihydro-5*H*-dibenz[*b*,*f*]azepines (Table III, **16–19**) was accomplished with aqueous sulfuric acid. Bromination of **16** and **17** (Table III) with 1.4 equiv of *N*-bromosuccinimide in refluxing carbon tetrachloride[9] gave a mixture of bromo de-

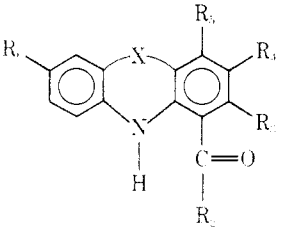
Table II. 5-Acyl-10,11-dihydro-5*H*-dibenz[*b*,*f*]azepines



No.	R_1	R_2	R_3	R_4	R_5	R_6	Mp, °C	Yield, %[a]	Crystn solvent[b]	Formula[c]
10	Me	Ph	H	H	H	H	*d*			
11	Ph	Me	H	H	H	H	146–148	21	EA	$C_{23}H_{19}NO_2$
12	Ph	Me	Br	H	H	H	191–192	19	EA	$C_{23}H_{18}BrNO_2$
13	Ph	Me	H	H	Br	H	163–165[e]	28	EA	$C_{23}H_{18}BrNO_2$
14	Me	Ph	H	Br	H	Br	205–207	75	B–P	$C_{23}H_{17}Br_2NO_2$
15	Ph	Me	H	Br	H	Br	179–181	44	EA	$C_{23}H_{17}Br_2NO_2$

[a]No attempts were made to optimize yields. [b]EA, EtOAc; B, C_6H_6; P, petroleum ether. [c]Analyses for C, H, N, and halogen were within ±0.4% of the theoretical value. [d]Not crystallized; purified by column chromatography on Florisil (ratio 1:50) with $CHCl_3$ as eluent. [e]NMR δ 7.49 (d, 1, J = 8 Hz, H-3).

Table III. 10,11-Dihydro-5*H*-dibenz[*b*,*f*]azepines and 5*H*-Dibenz[*b*,*f*]azepines



No.	R_2	R_3	R_4	R_5	R_6	X	Mp, °C	Yield, %[a]	Crystn solvent[b]	Formula[c]
16	Me	H	H	H	H	CH_2—CH_2	108–110[d]	72	P	$C_{16}H_{15}NO$
17	Ph	H	H	H	H	CH_2—CH_2	*e*			
18	Me	Br	H	H	H	CH_2—CH_2	*e*			
19	Me	H	H	Br	H	CH_2—CH_2	79–81	67	P	$C_{16}H_{14}BrNO$
20	Me	H	Br	H	H	CH_2—CH_2	102–104[f]	16	M	$C_{16}H_{14}BrNO$
21	Me	H	Br	H	Br	CH_2—CH_2	143–145[f]	30	M	$C_{16}H_{13}Br_2NO$
22	Me	H	H	H	Br	CH_2—CH_2	114–115[g]	35	P	$C_{16}H_{14}BrNO$[h]
23	Ph	H	Br	H	H	CH_2—CH_2	146–148	22	P	$C_{21}H_{16}BrNO$
24	Ph	H	Br	H	Br	CH_2—CH_2	106–108	28	P	$C_{21}H_{15}Br_2NO$
25	Ph	H	H	H	Br	CH_2—CH_2	117–119	42	M	$C_{21}H_{16}BrNO$
26	Me	H	H	H	H	CH=CH	98–99	19	P	$C_{16}H_{13}NO$
27	Ph	H	H	H	H	CH=CH	157–158	24	ET	$C_{21}H_{15}NO$
28	Me	H	Br	H	Br	CH=CH	165–167[i]	32	EA	$C_{16}H_{11}Br_2NO$
29	Ph	H	Br	H	Br	CH=CH	*e*			

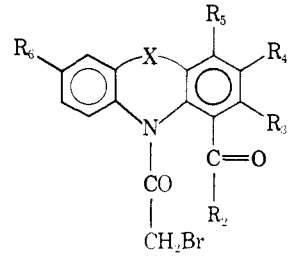
[a]No attempts were made to optimize yields. [b]P, petroleum ether; M, MeOH; ET, Et_2O; EA, EtOAc. [c]Compounds were analyzed for C, H, N, and halogen. Unless otherwise stated analyses are within ±0.4% of the theoretical value. [d]NMR δ 7.70 (dd, 1, J = 8 and 2 Hz, H-3). [e]Not crystallized; purified by column chromatography on Florisil with C_6H_6 as eluent. [f]NMR δ 7.76 (d, 1, J = 2 Hz, H-3). [g]NMR δ 7.70 (dd, 1, J = 8 and 2 Hz, H-7). [h]C: calcd, 60.77; found, 59.68. [i]NMR δ 5.85 (s, 2, H-10 and H-11).

rivatives (Table III, **20–25**) which was separated by column chromatography on Florisil.

Condensation of **16–25** (Table III) with bromoacetyl bromide followed by cyclization of the resulting bromoacetyl derivatives (Table IV, **30–39**) with methanolic ammonia[10] gave 8,9-dihydro[1]benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2*H*)-ones (Table V, **44–53**).

Two possible methods (A and B) for the conversion of **10** and **11** (Table II) and **21** and **24** (Table III) to [1]benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2*H*)-ones (Table V, **54–57**) are outlined in Scheme II. Method A involved monobromination[11] of **10, 11, 14,** and **15** (Table II) at C-10 or C-11 with subsequent simultaneous hydrolysis and dehydrobromination to give 5*H*-dibenz[*b*,*f*]azepines (Table III, **26–29**). Condensation of **26–29** with bromoacetyl bromide followed by cyclization of the resulting bromoacetyl derivatives (Table IV, **40–43**) with methanolic ammonia afforded in good yield the benzodiazepinones **54–57** (Table V). Method B involved monobromination of **30, 31, 35,** and **38** (Table IV) at C-10 or C-11 followed by simultaneous cyclization and dehydrobromination with methanolic ammonia to give **54–57** (Table V).

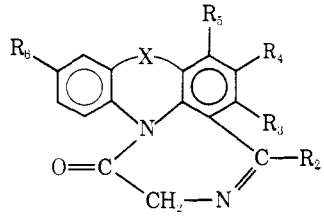
Table IV. 5-Bromoacetyl-10,11-dihydro-5*H*-dibenz[*b,f*]azepines and 5-Bromoacetyl-5*H*-dibenz[*b,f*]azepines



No.	R_2	R_3	R_4	R_5	R_6	X	Mp, °C	Yield, %[a]	Crystn solvent[b]	Formula[c]
30	Me	H	H	H	H	CH_2—CH_2	143–144	59	EA	$C_{18}H_{16}BrNO_2$
31	Ph	H	H	H	H	CH_2—CH_2	154–156	60	B–P	$C_{23}H_{18}BrNO_2$
32	Me	Br	H	H	H	CH_2—CH_2	*d*			
33	Me	H	H	Br	H	CH_2—CH_2	141–142	40	B	$C_{18}H_{15}Br_2NO_2$
34	Me	H	Br	H	H	CH_2—CH_2	161–163	75	ET	$C_{18}H_{15}Br_2NO_2$
35	Me	H	Br	H	Br	CH_2—CH_2	156–158	76	ET	$C_{18}H_{14}Br_3NO_2$
36	Me	H	H	H	Br	CH_2—CH_2	*d*			
37	Ph	H	Br	H	H	CH_2—CH_2	*d*			
38	Ph	H	Br	H	Br	CH_2—CH_2	175–177	65	EA	$C_{23}H_{16}Br_3NO_2$
39	Ph	H	H	H	Br	CH_2—CH_2	203–205	77	B–P	$C_{23}H_{17}Br_2NO_2$
40	Me	H	H	H	H	CH=CH	144–146	69	EA	$C_{18}H_{14}BrNO_2$
41	Ph	H	H	H	H	CH=CH	172–174	85	EA	$C_{23}H_{16}BrNO_2$
42	Me	H	Br	H	Br	CH=CH	*d*			
43	Ph	H	Br	H	Br	CH=CH	224–225	72	EA	$C_{23}H_{14}Br_3NO_2$

[a]No attempts were made to optimize yields. [b]EA, EtOAc; B, C_6H_6; P, petroleum ether; ET, Et_2O. [c]Analyses for C, H, N, and halogen were within ±0.4% of the theoretical value. [d]Not isolated; used crude in the next step.

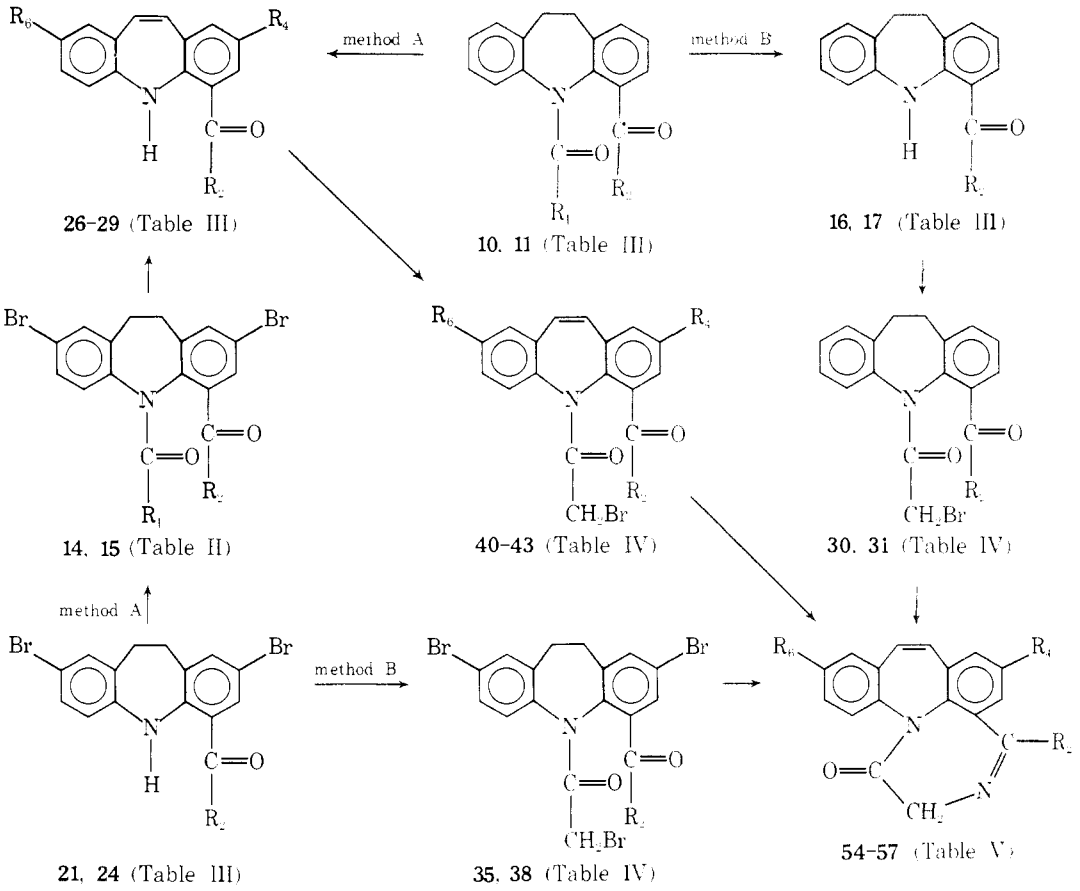
Table V. 8,9-Dihydro[1]benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2*H*)-ones and [1]Benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2*H*)-ones



No.	R_2[a]	R_3	R_4	R_5	R_6	X	Mp, °C	Yield, %[b]	Method	Crystn solvent[c]	Formula[d]
44	Me	H	H	H	H	CH_2—CH_2	174–175[e]	54		EA	$C_{18}H_{16}N_2O$
45	Ph	H	H	H	H	CH_2—CH_2	181–183[f]	45		I	$C_{23}H_{18}N_2O$
46	Me	Br	H	H	H	CH_2—CH_2	207–209[e]	61		EA	$C_{18}H_{15}BrN_2O$
47	Me	H	H	Br	H	CH_2—CH_2	201–203[e]	76		EA	$C_{18}H_{15}BrN_2O$
48	Me	H	Br	H	H	CH_2—CH_2	191–192[f]	60		EA	$C_{18}H_{15}BrN_2O$
49	Me	H	Br	H	Br	CH_2—CH_2	219–221[g]	75		EA	$C_{18}H_{14}Br_2N_2O$
50	Me	H	H	H	Br	CH_2—CH_2	237–238[f]	58		EA	$C_{18}H_{15}BrN_2O$
51	Ph	H	Br	H	H	CH_2—CH_2	194–196[h]	60		I	$C_{23}H_{17}BrN_2O$
52	Ph	H	Br	H	Br	CH_2—CH_2	229–231[h]	80		M	$C_{23}H_{16}Br_2N_2O$
53	Ph	H	H	H	Br	CH_2—CH_2	214–215[f]	76		EA	$C_{23}H_{17}BrN_2O$
54	Me	H	H	H	H	CH=CH	228–230[f]	66 (54)	A (B)	EA	$C_{18}H_{14}N_2O$
55	Ph	H	H	H	H	CH=CH	206–207[h]	36 (42)	A (B)	EA	$C_{23}H_{16}N_2O$[i]
56	Me	H	Br	H	Br	CH=CH	212–214[h]	55 (46)	A (B)	EA	$C_{18}H_{12}Br_2N_2O$
57	Ph	H	Br	H	Br	CH=CH	219–220[g]	70 (51)	A (B)	EA	$C_{23}H_{14}Br_2N_2O$

[a]All NMR spectra of the 4-phenyl derivatives showed a characteristic AB pattern for the two protons on C-2, namely two doublets centered at δ 4.90 (J = 11 Hz) and 4.10 (J = 11 Hz) when X = CH_2—CH_2 and two doublets centered at δ 4.80 (J = 11 Hz) and 3.95 (J = 11 Hz) when X = CH=CH. NMR spectra of the 4-methyl derivatives with X = CH_2—CH_2 showed a doublet centered at δ 4.60 (J = 11 Hz) and a doublet of quartets centered at δ 3.85 (J = 11 and 2 Hz) for the two protons on C-2 and a doublet centered at δ 2.55 (J = 2 Hz) for the methyl protons. NMR spectra of the 4-methyl derivatives with X = CH=CH showed a similar characteristic pattern for the two protons on C-2 and the methyl protons, namely two doublets centered at δ 4.60 (J = 11 Hz) and 2.60 (J = 2 Hz) and a doublet of quartets centered at δ 3.80 (J = 11 and 2 Hz). [b]No attempts were made to optimize yields. [c]EA, EtOAc; I, isopropyl ether; M, MeOH. [d]Compounds were analyzed for C, H, N, and halogen. Unless otherwise stated analyses are within ±0.4% of the theoretical value. [e]Ir 1685 cm^{-1} (amide C=O). [f]Ir 1680 cm^{-1} (amide C=O). [g]Ir 1690 cm^{-1} (amide C=O). [h]Ir 1695 cm^{-1} (amide C=O). [i]C: calcd, 82.12; found, 81.46.

Scheme II



Results and Discussion

All compounds **44–57** (Table V) were ineffective in protecting mice against seizures induced by strychnine[12] or pentylenetetrazole[13] up to a dose of 50 mg/kg po. The compounds, at the same dose, did not antagonize reserpine-induced ptosis[14] and hypothermia[15] or foot-shock induced aggressiveness in mice.[16] Behavioral and neurological changes induced in Swiss male mice by compounds **44–57** (Table V), giving doses up to 1000 mg/kg po, were examined by the Irwin test[17] and "rotarod" performance test according to Dunham and Miya.[18]

A slight sedation and a modest interference with coordination of motor activity were seen with the brominated compounds having X = CH_2—CH_2 (Table V, **46–53**) at the dose of 500 and 1000 mg/kg po, while convulsive symptoms occurred at the dose of 250 mg/kg po in the brominated compounds having X = CH=CH (Table V, **56** and **57**).

These results indicate that in the case of the 1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one a phenyl group at the 1 position causes a fall in CNS activity not only when it is *free* but also when *fused* to the benzodiazepine system. The CH_2—CH_2 and CH=CH bridges modify the geometry and the electronic density distribution of compound **3** without inducing any depressing or stimulating activity on the CNS.

Experimental Section

The melting points were taken in open capillary tubes using a Tottoli apparatus (N. Büchi, Flawil, Switzerland) and are uncorrected. All intermediates and final products were checked by ir and NMR spectroscopy (Perkin-Elmer 257 and Varian T-60A, respectively) and their spectra were found to be in agreement with the assigned structures. Ir and NMR spectra were obtained for KBr disks and for solutions in $CDCl_3$ (Me_4Si), respectively. "Alumina" refers to neutral Al_2O_3 B. III from E. Merck, Germany. "Florisil" refers to magnesium silicates (100–200 mesh) from Floridin Co., Pa.

6,7-Dihydro-1-methyl-2-phenyl- (5) and 6,7-Dihydro-2-methyl-1-phenylindolo[1,7-*ab*][1]benzazepine (6) (Table I). A mixture of 24.7 g (0.1 mol) of 5-amino-10,11-dihydro-5*H*-dibenz[*b*,*f*]azepine (Scheme I, 4) hydrochloride and 13.4 g (0.1 mol) of 1-phenyl-2-propanone in 100 ml of EtOH was refluxed for 1 hr with stirring. To the hot solution 50 ml (0.15 mol) of 3 *N* ethanolic HCl was added and the whole mixture was then heated under reflux for 1 hr. The mixture was cooled, NH_4Cl was filtered off, the solution was evaporated to dryness, and the crude material was extracted with $CHCl_3$. After washing with water, the dried solution was evaporated under reduced pressure to give 30 g of crude oil. NMR and GC indicated a 70:30 mixture of isomers **5** and **6**. After column chromatography of the mixture on alumina (ratio 1:200) using cyclohexane–$CHCl_3$ (9:1) as eluent and recrystallization from Me_2CO, 10 g of **5** (mp 131–133°) and 4 g of **6** (mp 174–175°) were obtained. This product **6** did not depress the melting point of the only compound obtained by Fischer cyclization of **4**·HCl with propiophenone in 3 *N* ethanolic HCl refluxing. Fischer cyclization of **4**·HCl with 1-phenyl-2-propanone in pure EtOH for 15 hr at room temperature gave only **5**.

3-Bromo- (7), 5-Bromo- (8), and 3,5-Dibromo-6,7-dihydro-2-methyl-1-phenylindolo[1,7-*ab*]benzazepine (9) (Table I). To a solution of 5.57 g (0.018 mol) of **6** in 25 ml of CCl_4 4.8 g (0.027 mol) of NBS was added and the suspension was heated at 85° for 15 hr. The mixture was cooled, the succinimide was filtered off, and the solution was evaporated under pressure to yield 7 g of red oil. NMR and GC of this material indicated that it was a 25:70:5 mixture of **7**, **8**, and **9**. Column chromatography of the mixture on alumina (ratio 1:50) using cyclohexane–$CHCl_3$ (9:1) as eluent and recrystallization from EtOH yielded 2.8 g of **8**, mp 144–145°. The bromo derivatives **7** and **9** were not isolated from the mixture. The 85:15 mixture of **7** and **8** obtained by column chromatography was used in the next oxidation step without further purification. Repetition of this reaction with 3 equiv of NBS and recrystallization from C_6H_6–petroleum ether gave 2.1 g of **9**, mp 202–204°.

4-Acetyl-5-benzoyl-10,11-dihydro-5*H*-dibenz[*b*,*f*]azepine (11) (Table II). A stirred solution of 7.73 g (0.025 mol) of **6** in 200 ml of AcOH was treated at 20° during 0.5 hr with a solution of 4.4

g (0.044 mol) of CrO_3 in 15 ml of water. The resulting mixture was stirred at room temperature for 1.5 hr, poured into water, and extracted with $CHCl_3$. The $CHCl_3$ solution was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure to yield 8.5 g of crude oil which was chromatographed on Florisil (ratio 1:50) using $CHCl_3$ as eluent. The first component (3 g) eluted was recrystallized from EtOAc to give 1.8 g of 11, mp 146–148°.

4-Acetyl-5-benzoyl-2,8-dibromo-10,11-dihydro-5*H*-dibenz[*b,f*]azepine (15) (Table II). To a solution of 17.8 g (0.045 mol) of 21 in 40 ml of C_6H_6 63.3 g (0.45 mol) of benzoyl chloride was added. The solution was refluxed for 5 hr, cooled, washed with 10% aqueous NaOH, dried (Na_2SO_4), and evaporated under reduced pressure to give 10 g of 15 which after recrystallization from EtOAc had mp 179–181°.

4-Acetyl-10,11-dihydro-5*H*-dibenz[*b,f*]azepine (16) (Table III). A stirred mixture of 17.07 g (0.05 mol) of 11 and 170 ml (0.204 mol) of 24 *N* aqueous H_2SO_4 was heated at 80° for 2 hr, cooled, and poured into ice–water. The resulting mixture was made alkaline with 10% NaOH and extracted several times with $CHCl_3$. The $CHCl_3$ solution was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure to yield 8.5 g of 16 (yellow) after crystallization from petroleum ether: mp 108–110°.

4-Acetyl-2-bromo- (20), 4-Acetyl-2,8-dibromo- (21), and 6-Acetyl-2-bromo-10,11-dihydro-5*H*-dibenz[*b,f*]azepine (22) (Table III). To a solution of 2.37 g (0.01 mol) of 16 in 20 ml of CCl_4 2.49 g (0.014 mol) of NBS was added and the resulting suspension was heated at 85° for 18 hr. The mixture was cooled and succinimide was filtered off. The solution was evaporated under reduced pressure to yield 3.6 g of orange oil. NMR and GC of this oil indicated that it was a 20:40:40 mixture of **20, 21,** and **22** which was separated by column chromatography on Florisil (ratio 1:200) using cyclohexane–C_6H_6 (1:1) as eluent. The first component eluted from the column was crystallized from MeOH to give 1.2 g of 21 (yellow), mp 143–145°. The second component eluted was crystallized from MeOH to give 0.5 g of **20** (yellow), mp 102–104°. The third bromo derivative was obtained by further elution of the column and was crystallized from petroleum ether to give 1.1 g of **22** (yellow), mp 114–115°. Repetition of this reaction with 2.2 equiv of NBS yielded only 21.

4-Benzoyl-5*H*-dibenz[*b,f*]azepine (27) (Table III). A mixture of 4.1 g (0.012 mol) of 10 in 120 ml of CCl_4 and 2.35 g (0.0132 mol) of NBS was photolized (two 200-W lamps) at 60° for 1.5 hr. The succinimide was filtered off and CCl_4 solution evaporated under reduced pressure to give a residue which was suspended in 50 ml (0.60 mol) of 24 *N* aqueous H_2SO_4. The mixture was stirred at 85° for 15 hr, cooled, and then poured into ice–water. The resulting mixture was made alkaline with 10% aqueous NaOH, stirred 1 hr at room temperature, and then extracted with $CHCl_3$. The $CHCl_3$ solution was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure to give a red oil which was purified by column chromatography on Florisil (ratio 1:100) with C_6H_6 as eluent. Crystallization from Et_2O gave 0.85 g of **27,** mp 157–158°.

4-Acetyl-5-bromoacetyl-10,11-dihydro-5*H*-dibenz[*b,f*]azepine (30) (Table IV). A solution of 3.56 g (0.015 mol) of 16 in 150 ml of C_6H_6 and 6 g (0.030 mol) of bromoacetyl bromide was refluxed for 3 hr, cooled, washed with 10% aqueous NaOH, dried (Na_2SO_4), and evaporated under reduced pressure to yield, after crystallization from EtOAc, 3.2 g of **30,** mp 143–144°.

8,9-Dihydro-4-methyl[1]benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2*H*)-one (44) (Table V). A solution of 6.9 g of NH_3 in 60 ml of MeOH was added to a suspension of 1.79 g (0.005 mol) of **30** in 100 ml of Et_2O. The resulting solution was stirred at room temperature overnight, the solvent was removed by distillation under reduced pressure, and the residue was partitioned between water and $CHCl_3$. The organic phase was washed with water, dried (Na_2SO_4), and evaporated to dryness under reduced pressure. The residue was crystallized from EtOAc to give 0.75 g of **44,** mp 174–175°.

6,11-Dibromo-4-phenyl[1]benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2*H*)-one (57) (Table V). Method A. This method is similar to that described previously for the compounds **44–53** (Table V).

Method B. A mixture of 8.09 g (0.014 mol) of **38** in 200 ml of CCl_4 and 2.74 g (0.0154 mol) of NBS was photolized (two 200-W lamps) at 60° for 1.5 hr. Succinimide was filtered off and CCl_4 solution was evaporated under reduced pressure to give a residue which was suspended in 500 ml of Et_2O. To this suspension a solution of 65 g of NH_3 in 500 ml of MeOH was added and the resulting solution was stirred at room temperature overnight. The solvent was evaporated to dryness under reduced pressure and the residue was partitioned between $CHCl_3$ and water. The $CHCl_3$ layer was dried over Na_2SO_4 and concentrated to dryness under reduced pressure. Crystallization of the residue from EtOAc gave 3.5 g of **57,** mp 219–220°.

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