

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%  $\text{NaHCO}_3$  (4.4% stock solution), 4% inactivated fetal calf serum, 1% nonessential amino acids, 1% penicillin (100 U/ml), 1% streptomycin (100  $\mu\text{g}/\text{ml}$ ), and 73% double-distilled deionized water. The cells were treated with trypsin or EDTA.<sup>18</sup> 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.<sup>9</sup> The cytotoxicity of each compound was determined microscopically.<sup>9</sup>

**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.<sup>9</sup> The stability of IV was followed by TLC chromatography. Dithiothreitol (DTT) and GSH prevented oxidation of IV at concentrations of 50  $\mu\text{g}/\text{ml}$  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  $\mu\text{g}/\text{ml}$ , whereas GSH showed no cytotoxicity up to 250  $\mu\text{g}/\text{ml}$ . Therefore, on the basis of the above results, GSH was incorporated at 100  $\mu\text{g}/\text{ml}$  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,<sup>1</sup> and extensive data on their pharmacological activity<sup>2</sup> have been accumulated over the past 15 years. Interesting observations<sup>3</sup> 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 =  $\text{CH}_2\text{—CH}_2$ , X =  $\text{CH=CH}$ , and X = S. In fact, these molecules could exhibit interesting CNS properties as they have stereochemistry and/or delocalization of electrons<sup>4</sup> 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).

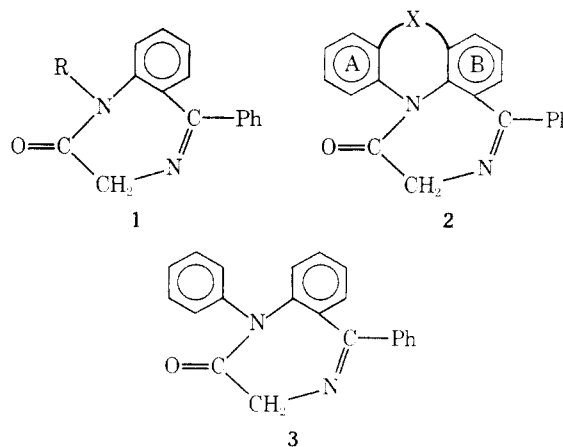
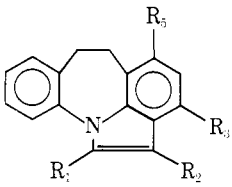


Table I. 6,7-Dihydroindolo[1,7-ab][1]benzazepines

No.					Mp, °C	Yield, % <sup>a</sup>	Crystn solvent <sup>b</sup>	Formula <sup>c</sup>
	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>5</sub>				
5	Me	Ph	H	H	131–133	32	A	C <sub>23</sub> H <sub>19</sub> N
6	Ph	Me	H	H	174–175	13	A	C <sub>23</sub> H <sub>19</sub> N
7	Ph	Me	Br	H	<i>d</i>			
8	Ph	Me	H	Br	144–145	40	E	C <sub>23</sub> H <sub>18</sub> BrN
9	Ph	Me	Br	Br	202–204 <sup>e</sup>	25	B–P	C <sub>23</sub> H <sub>17</sub> Br <sub>2</sub> N

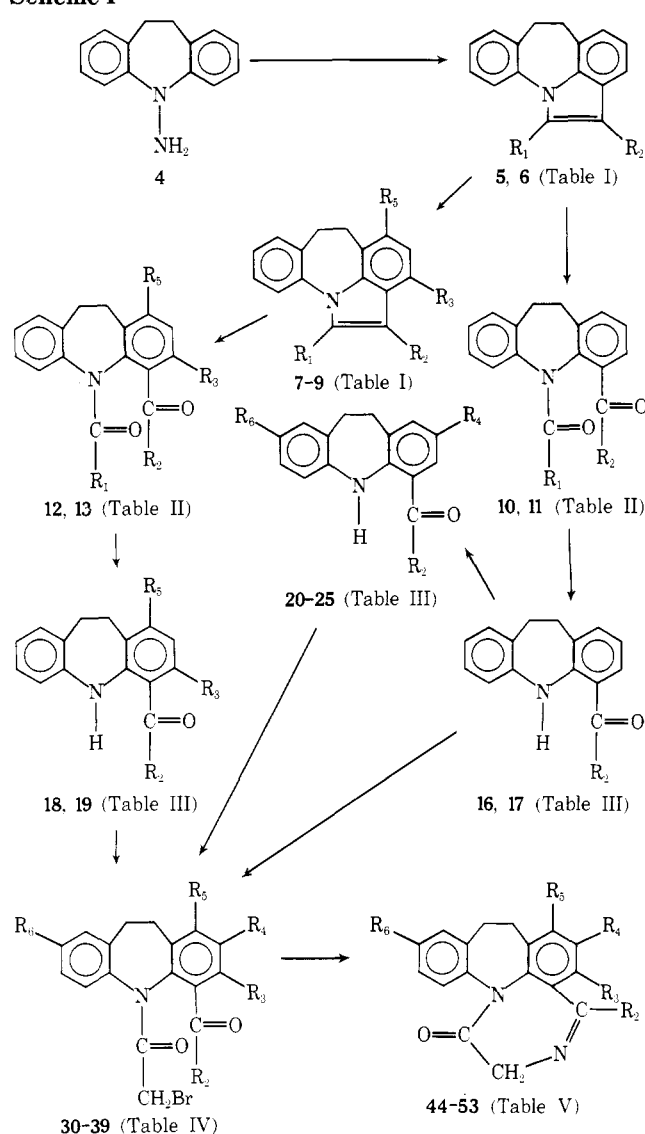
<sup>a</sup>No attempts were made to optimize yields. <sup>b</sup>A, Me<sub>2</sub>CO; E, EtOH; B, C<sub>6</sub>H<sub>6</sub>; P, petroleum ether. <sup>c</sup>Analyses for C, H, N, and halogen were within ±0.4% of the theoretical value. <sup>d</sup>Not isolated; used crude in the next step. <sup>e</sup>NMR δ 7.55 (s, 1, H-4).

At the outset of our investigations, 4-phenyldiazepino-[6,7,1-*kl*]phenothiazin-1(2H)-one (2, X = S) was described by Hromatka et al.<sup>5</sup> 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(2H)-one (2, X = CH<sub>2</sub>—CH<sub>2</sub>) and 4-phenyl[1]benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2H)-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.<sup>3</sup>

**Chemistry.** 8,9-Dihydro[1]benzazepino[3,2,1-*jk*][1,4]benzodiazepin-1(2H)-ones (Table V, 44–53) were prepared according to the general methods shown in Scheme I. It has been reported<sup>6</sup> that 5-amino-10,11-dihydro-5H-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<sup>7</sup> 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).

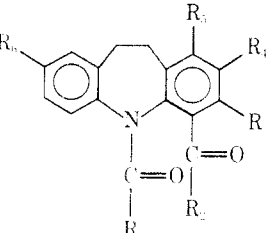
Oxidation of 5–8 (Table I) with chromic anhydride<sup>8</sup> in acetic acid gave 5-acyl-10,11-dihydro-5H-[*b,f*]azepines

Scheme I



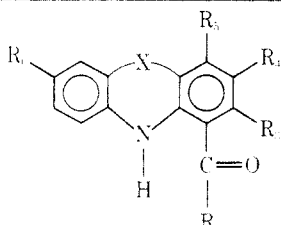
(Table II, 10–13). Facile conversion of 10–13 to 10,11-dihydro-5H-dibenz[*b,f*]azepines (Table III, 16–19) was accomplished with aqueous sulfuric acid. Bromination of 16 and 17 (Table III) with 1.4 equiv of *N*-bromosuccinimide in refluxing carbon tetrachloride<sup>9</sup> gave a mixture of bromo de-

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

								Yield, % <sup>a</sup>	Crystn solvent <sup>b</sup>	Formula <sup>c</sup>
No.	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>	R <sub>6</sub>	Mp, °C			
10	Me	Ph	H	H	H	H	<i>d</i>			
11	Ph	Me	H	H	H	H	146–148	21	EA	C <sub>23</sub> H <sub>13</sub> NO <sub>2</sub>
12	Ph	Me	Br	H	H	H	191–192	19	EA	C <sub>23</sub> H <sub>18</sub> BrNO <sub>2</sub>
13	Ph	Me	H	H	Br	H	163–165 <sup>e</sup>	28	EA	C <sub>23</sub> H <sub>18</sub> BrNO <sub>2</sub>
14	Me	Ph	H	Br	H	Br	205–207	75	B–P	C <sub>23</sub> H <sub>17</sub> Br <sub>2</sub> NO <sub>2</sub>
15	Ph	Me	H	Br	H	Br	179–181	44	EA	C <sub>23</sub> H <sub>17</sub> Br <sub>2</sub> NO <sub>2</sub>

<sup>a</sup>No attempts were made to optimize yields. <sup>b</sup>EA, EtOAc; B, C<sub>6</sub>H<sub>6</sub>; P, petroleum ether. <sup>c</sup>Analyses for C, H, N, and halogen were within  $\pm 0.4\%$  of the theoretical value. <sup>d</sup>Not crystallized; purified by column chromatography on Florisil (ratio 1:50) with CHCl<sub>3</sub> as eluent. <sup>e</sup>NMR  $\delta$  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 <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>	R <sub>6</sub>	X	Mp, °C	Yield, % <sup>a</sup>	Crystn solvent <sup>b</sup>	Formula <sup>c</sup>
16	Me	H	H	H	H	CH <sub>2</sub> —CH <sub>2</sub>	108–110 <sup>d</sup>	72	P	C <sub>16</sub> H <sub>15</sub> NO
17	Ph	H	H	H	H	CH <sub>2</sub> —CH <sub>2</sub>	<i>e</i>			
18	Me	Br	H	H	H	CH <sub>2</sub> —CH <sub>2</sub>	<i>e</i>			
19	Me	H	H	Br	H	CH <sub>2</sub> —CH <sub>2</sub>	79–81	67	P	C <sub>16</sub> H <sub>14</sub> BrNO
20	Me	H	Br	H	H	CH <sub>2</sub> —CH <sub>2</sub>	102–104 <sup>f</sup>	16	M	C <sub>16</sub> H <sub>14</sub> BrNO
21	Me	H	Br	H	Br	CH <sub>2</sub> —CH <sub>2</sub>	143–145 <sup>f</sup>	30	M	C <sub>16</sub> H <sub>13</sub> Br <sub>2</sub> NO
22	Me	H	H	H	Br	CH <sub>2</sub> —CH <sub>2</sub>	114–115 <sup>g</sup>	35	P	C <sub>16</sub> H <sub>14</sub> BrNO <sup>h</sup>
23	Ph	H	Br	H	H	CH <sub>2</sub> —CH <sub>2</sub>	146–148	22	P	C <sub>21</sub> H <sub>16</sub> BrNO
24	Ph	H	Br	H	Br	CH <sub>2</sub> —CH <sub>2</sub>	106–108	28	P	C <sub>21</sub> H <sub>15</sub> Br <sub>2</sub> NO
25	Ph	H	H	H	Br	CH <sub>2</sub> —CH <sub>2</sub>	117–119	42	M	C <sub>21</sub> H <sub>16</sub> BrNO
26	Me	H	H	H	H	CH=CH	98–99	19	P	C <sub>16</sub> H <sub>13</sub> NO
27	Ph	H	H	H	H	CH=CH	157–158	24	ET	C <sub>21</sub> H <sub>15</sub> NO
28	Me	H	Br	H	Br	CH=CH	165–167 <sup>i</sup>	32	EA	C <sub>16</sub> H <sub>11</sub> Br <sub>2</sub> NO
29	Ph	H	Br	H	Br	CH=CH	<i>e</i>			

<sup>a</sup>No attempts were made to optimize yields. <sup>b</sup>P, petroleum ether; M, MeOH; ET, Et<sub>2</sub>O; EA, EtOAc. <sup>c</sup>Compounds were analyzed for C, H, N, and halogen. Unless otherwise stated analyses are within  $\pm 0.4\%$  of the theoretical value. <sup>d</sup>NMR  $\delta$  7.70 (dd, 1, *J* = 8 and 2 Hz, H-3). <sup>e</sup>Not crystallized; purified by column chromatography on Florisil with C<sub>6</sub>H<sub>6</sub> as eluent. <sup>f</sup>NMR  $\delta$  7.76 (d, 1, *J* = 2 Hz, H-3). <sup>g</sup>NMR  $\delta$  7.70 (dd, 1, *J* = 8 and 2 Hz, H-7). <sup>h</sup>C: calcd, 60.77; found, 59.68. <sup>i</sup>NMR  $\delta$  5.85 (s, 2, H-10 and H-11).

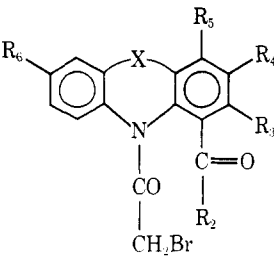
derivatives (Table III, 20–25) which was separated by column chromatography on Florisil.

Condensation of 16–25 (Table III) with bromoacetyl bromide followed by cyclization of the resulting bromoacetyl derivatives (Table IV, 30–39) with methanolic ammonia<sup>10</sup> 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 mono-

bromination<sup>11</sup> 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-5H-dibenz[b,f]azepines and 5-Bromoacetyl-5H-dibenz[b,f]azepines

										
No.	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>	R <sub>6</sub>	X	Mp, °C	Yield, % <sup>a</sup>	Crystn solvent <sup>b</sup>	Formula <sup>c</sup>
30	Me	H	H	H	H	CH <sub>2</sub> —CH <sub>2</sub>	143–144	59	EA	C <sub>18</sub> H <sub>16</sub> BrNO <sub>2</sub>
31	Ph	H	H	H	H	CH <sub>2</sub> —CH <sub>2</sub>	154–156	60	B–P	C <sub>23</sub> H <sub>18</sub> BrNO <sub>2</sub>
32	Me	Br	H	H	H	CH <sub>2</sub> —CH <sub>2</sub>	<i>d</i>			
33	Me	H	H	Br	H	CH <sub>2</sub> —CH <sub>2</sub>	141–142	40	B	C <sub>18</sub> H <sub>15</sub> Br <sub>2</sub> NO <sub>2</sub>
34	Me	H	Br	H	H	CH <sub>2</sub> —CH <sub>2</sub>	161–163	75	ET	C <sub>18</sub> H <sub>15</sub> Br <sub>2</sub> NO <sub>2</sub>
35	Me	H	Br	H	Br	CH <sub>2</sub> —CH <sub>2</sub>	156–158	76	ET	C <sub>18</sub> H <sub>14</sub> Br <sub>3</sub> NO <sub>2</sub>
36	Me	H	H	H	Br	CH <sub>2</sub> —CH <sub>2</sub>	<i>d</i>			
37	Ph	H	Br	H	H	CH <sub>2</sub> —CH <sub>2</sub>	<i>d</i>			
38	Ph	H	Br	H	Br	CH <sub>2</sub> —CH <sub>2</sub>	175–177	65	EA	C <sub>23</sub> H <sub>16</sub> Br <sub>3</sub> NO <sub>2</sub>
39	Ph	H	H	H	Br	CH <sub>2</sub> —CH <sub>2</sub>	203–205	77	B–P	C <sub>23</sub> H <sub>17</sub> Br <sub>2</sub> NO <sub>2</sub>
40	Me	H	H	H	H	CH=CH	144–146	69	EA	C <sub>18</sub> H <sub>14</sub> BrNO <sub>2</sub>
41	Ph	H	H	H	H	CH=CH	172–174	85	EA	C <sub>23</sub> H <sub>16</sub> BrNO <sub>2</sub>
42	Me	H	Br	H	Br	CH=CH	<i>d</i>			
43	Ph	H	Br	H	Br	CH=CH	224–225	72	EA	C <sub>23</sub> H <sub>14</sub> Br <sub>3</sub> NO <sub>2</sub>

<sup>a</sup>No attempts were made to optimize yields. <sup>b</sup>EA, EtOAc; B, C<sub>6</sub>H<sub>6</sub>; P, petroleum ether; ET, Et<sub>2</sub>O. <sup>c</sup>Analyses for C, H, N, and halogen were within  $\pm 0.4\%$  of the theoretical value. <sup>d</sup>Not isolated; used crude in the next step.

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

<sup>a</sup>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  $\delta$  4.90 ( $J = 11$  Hz) and 4.10 ( $J = 11$  Hz) when X = CH<sub>2</sub>—CH<sub>2</sub> and two doublets centered at  $\delta$  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<sub>2</sub>—CH<sub>2</sub> showed a doublet centered at  $\delta$  4.60 ( $J = 11$  Hz) and a doublet of quartets centered at  $\delta$  3.85 ( $J = 11$  and 2 Hz) for the two protons on C-2 and a doublet centered at  $\delta$  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  $\delta$  4.60 ( $J = 11$  Hz) and 2.60 ( $J = 2$  Hz) and a doublet of quartets centered at  $\delta$  3.80 ( $J = 11$  and 2 Hz). <sup>b</sup>No attempts were made to optimize yields. <sup>c</sup>EA, EtOAc; I, isopropyl ether; M, MeOH. <sup>d</sup>Compounds were analyzed for C, H, N, and halogen. Unless otherwise stated analyses are within  $\pm 0.4\%$  of the theoretical value. <sup>e</sup>Ir 1685 cm<sup>-1</sup> (amide C=O). <sup>f</sup>Ir 1680 cm<sup>-1</sup> (amide C=O). <sup>g</sup>Ir 1690 cm<sup>-1</sup> (amide C=O). <sup>h</sup>Ir 1695 cm<sup>-1</sup> (amide C=O). <sup>i</sup>C: calcd, 82.12; found, 81.46.



g (0.044 mol) of  $\text{CrO}_3$  in 15 ml of water. The resulting mixture was stirred at room temperature for 1.5 hr, poured into water, and extracted with  $\text{CHCl}_3$ . The  $\text{CHCl}_3$  solution was washed with water, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated under reduced pressure to yield 8.5 g of crude oil which was chromatographed on Florisil (ratio 1:50) using  $\text{CHCl}_3$  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-5H-dibenz[b,f]azepine (15) (Table II).** To a solution of 17.8 g (0.045 mol) of 21 in 40 ml of  $\text{C}_6\text{H}_6$  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 ( $\text{Na}_2\text{SO}_4$ ), 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-5H-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  $\text{H}_2\text{SO}_4$  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  $\text{CHCl}_3$ . The  $\text{CHCl}_3$  solution was washed with water, dried ( $\text{Na}_2\text{SO}_4$ ), 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-5H-dibenz[b,f]azepine (22) (Table III).** To a solution of 2.37 g (0.01 mol) of 16 in 20 ml of  $\text{CCl}_4$  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- $\text{C}_6\text{H}_6$  (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-5H-dibenz[b,f]azepine (27) (Table III).** A mixture of 4.1 g (0.012 mol) of 10 in 120 ml of  $\text{CCl}_4$  and 2.35 g (0.0132 mol) of NBS was photolyzed (two 200-W lamps) at 60° for 1.5 hr. The succinimide was filtered off and  $\text{CCl}_4$  solution evaporated under reduced pressure to give a residue which was suspended in 50 ml (0.60 mol) of 24 N aqueous  $\text{H}_2\text{SO}_4$ . 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  $\text{CHCl}_3$ . The  $\text{CHCl}_3$  solution was washed with water, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated under reduced pressure to give a red oil which was purified by column chromatography on Florisil (ratio 1:100) with  $\text{C}_6\text{H}_6$  as eluent. Crystallization from Et<sub>2</sub>O gave 0.85 g of 27, mp 157–158°.

**4-Acetyl-5-bromoacetyl-10,11-dihydro-5H-dibenz[b,f]azepine (30) (Table IV).** A solution of 3.56 g (0.015 mol) of 16 in 150 ml of  $\text{C}_6\text{H}_6$  and 6 g (0.030 mol) of bromoacetyl bromide was refluxed for 3 hr, cooled, washed with 10% aqueous NaOH, dried ( $\text{Na}_2\text{SO}_4$ ), 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(2H)-one (44) (Table V).** A solution of 6.9 g of  $\text{NH}_3$  in 60 ml of MeOH was added to a suspension of 1.79 g (0.005 mol) of 30 in 100 ml of Et<sub>2</sub>O. 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  $\text{CHCl}_3$ . The organic phase was washed with water, dried ( $\text{Na}_2\text{SO}_4$ ), 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(2H)-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  $\text{CCl}_4$  and 2.74 g (0.0154 mol) of NBS was photolyzed (two 200-W lamps) at 60° for 1.5 hr. Succinimide was filtered off and  $\text{CCl}_4$  solution was evaporated under reduced pressure to give a residue which was suspended in 500 ml of Et<sub>2</sub>O. To this suspension a solution of 65 g of  $\text{NH}_3$  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  $\text{CHCl}_3$  and water. The  $\text{CHCl}_3$  layer was dried over  $\text{Na}_2\text{SO}_4$  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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## References and Notes

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